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Attorneys for Plaintiffs and the Certified Classes

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

NEETA THAKUR, et al.,

Plaintiffs,

v.

DONALD J. TRUMP, et al.,

Defendants.

Case No. 3:25-cv-4737

DECLARATION OF RHONDA VOSKUHL

DECLARATION OF RHONDA VOSKUHL

I, Rhonda Voskuhl, declare as follows:

1. I have personal knowledge of the facts contained in this declaration and, if called as a witness, could and would testify competently to those facts.

2. I am a Professor of Neurology at the University of California Los Angeles School of Medicine. I hold the Jack H. Skirball Chair and have served as the Director of the UCLA Multiple Sclerosis Program since 2000. I am also a Faculty Neurologist for the UCLA Comprehensive Menopause Program. In the neurology clinic at UCLA, I treat patients with multiple sclerosis ("MS") and menopausal women with cognitive issues.

3. I earned an M.D. from Vanderbilt Medical School and subsequently completed neurology residency at the University of Texas Southwestern and a fellowship in neuroimmunology at the National Institutes of Health ("NIH"). In 1995, I joined the faculty of UCLA as an Assistant Professor in the Department of Neurology. I was promoted to Associate Professor in 2000 and full Professor in 2004. From 1995 to 2000, I served as the Scientific Director of the UCLA Multiple Sclerosis Program.

4. I have won numerous national and international awards for my work in neuroprotective treatment drug discovery, most recently including the John Dystel Prize in Multiple Sclerosis, 2024, from the American Academy of Neurology and the National MS Society, the most prestigious award in the field of MS. I was also awarded the Rachel Horne Prize for Women's Research in Multiple Sclerosis, 2023, from the European and American Committees for Treatment and Research in MS.

5. My research at UCLA focuses on determining how sex hormones and sex chromosomes cause sex differences in the onset and severity of neurodegenerative diseases. I am an internationally recognized expert in sex differences research, demonstrating protective effects of estrogen and testosterone treatment in preclinical models, which I translated to five clinical trials in patients. My lab was the first to show that estrogen receptor (ER) alpha and ER beta ligands act through distinct mechanisms to induce neuroprotection. I also discovered that an X chromosome gene (the histone demyethylase *Kdm6a*) increases neuroinflammation. In addition,

my lab was the first to use brain cell-specific and region-specific transcriptomics to investigate the molecular basis for disability-specific disease progression in MS. My lab also investigates the role of brain aging on neurodegeneration, identifying a sex hormone by age interaction whereby being estrogen deficient and midlife combine to induce cognitive decline, dorsal hippocampal atrophy, glial activation, and synaptic loss. The goal of my research is to use a brain region-specific, cell-specific, and sex-specific approach to identify neuroprotective treatment targets, then design clinical trials to repair neurodegeneration which are optimally tailored for sex and age.

6. I have authored more than 200 publications, including in prestigious journals such as *Nature*, *Lancet Neurology*, and the *Proceedings of the National Academy of Sciences.* These include showing how estrogen protects the brain from cognitive decline and regional brain atrophy during health and disease. My career was profiled in the February 2024 issue of *Lancet Neurology*, the preeminent neurology journal in the world.

7. I have been the recipient of a total of 79 research grants for my work from governmental and private sources. I have received 40 research grants from the NIH, many of which have been multi-year awards providing funds for 2, 3 4 or 5 years. Grants have provided continuous funding from 1997 to present. Throughout the last 28 years, I have never before received a notice from NIH freezing or rescinding previously awarded funding, up until NIH suspended a previously awarded grant funding active research work, as detailed below.

8. A true and correct copy of my biographical sketch is attached as Exhibit A.

Application for Grant Funding from the NIH

9. On July 8, 2022, I submitted, in conjunction with the UCLA Office of Contract and Grant Administration, an Application for Federal Assistance to the NIH for a project titled "Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach" (the "R35 Application").

10. The Project Narrative for the R35 Application explained:

> This R35 proposal will: 1) Extend our cell-specific and region-specific transcriptomics in astrocytes and oligodendrocytes to microglia and neurons, with cell:cell interactions revealed in mice double-labelled to show gene expression changes in two distinct cell

types in the same region in the same mouse, and 2) Determine if there are effects of sex and/or age on the most differentially expressed cell-specific and region-specific pathways. In summary, this R35 proposal takes our research to the next level: Identifying sex by age interactions in cell-specific and region-specific transcriptomics, neuropathology, and substructure atrophy on MRI.

The greatest unmet need in multiple sclerosis (MS) is to develop novel treatments targeting cells and processes within the central nervous system (CNS) to confer neuroprotection and repair disabilities, in not only relapsing remitting MS, but also in secondary progressive MS. A "one size fits all" neuroprotective treatment approach in MS will not work, since 1) MS patients are heterogenous regarding which disabilities are predominant, 2) being female versus male impacts rates of disability progression, and 3) aging corresponds with disability progression. This R35 will use a cell-specific, region-specific, and sex-specific approach to discover neurodegenerative targets optimized for each disability in MS models in females and males during young adulthood and aging.

11. The proposed project (the "R35 Project") built on work that I and my team had done over years:

a. My lab discovered sex chromosome effects in the immune system in MS models: we identified a gene on the X chromosome (*Kdm6a*) that escapes X-inactivation in CD4+T lymphocytes as a mechanism for increased susceptibility of females to autoimmune disease. Focusing on the CNS, we showed that in contrast to XX conferring an increase in autoimmunity, XY confers an increase in the neurodegenerative response to the same autoimmune attack. Indeed, my lab was the first to show an effect of sex chromosome complement in the CNS in any neurodegenerative disease model.

b. My lab used a cell-specific and region-specific transcriptomics approach to identify novel mechanisms underlying regional neuropathology in MS models and MS autopsy tissues. While this approach had been used in astrocytes during health, my lab was the first to use a cell-specific and region-specific transcriptomics approach in any neurodegenerative disease model.

c. Estrogens were known to be neuroprotective through actions on estrogen receptors (ERs) for decades, however which cell in the CNS mediated this neuroprotection in vivo remained unknown. My lab created cell-specific knock outs of ER alpha and ER beta to determine which CNS cell mediated neuroprotection in vivo. My lab was the first to identify which cell is responsible for estrogen mediated neuroprotection in vivo in any neurological

disease model.

12. The R35 Application requested $7,307,976.00 for an eight-year period (4/1/2023 – 03/31/2031); I was identified as the Project Director and Principal Investigator on the Application. The proposal would fund salaries for myself, four co-investigators, one graduate student, one senior lab technician, and one MRI lab technician.

13. A true and correct copy of the R35 Application dated July 8, 2022, is attached as Exhibit B.

Award of Grant Funding for R35 Grant

14. On May 8, 2023, the Department of Health and Human Services ("DHHS"), NIH, National Institute of Neurological Disorders and Stroke issued a Notice of Award, Federal Award Identification Number R35NS132150 (the "R35 Grant Award"), approving the R35 Application. The R35 Grant Award was awarded for a total of eight years, as sought in the R35 Application, for an amount of $876,448 for the May 15, 2023-April 30, 2024, budget period, and additional awards of $913,497 for the next seven years. The statutory authority for the award was "42 USC 241, 42 CFR 52."

15. R35 Awards are only granted to approximately ten neuroscience researchers per year across the United States.

16. My team and I began work on the R35 Project in May 2023, executing the research studies outlined in the grant application. NIH approved continuing funding for the R35 Project in each of the subsequent years.

17. During the initial two years of the eight-year R35 Grant Award, insights have been discovered in my lab which are clinically significant for patients.

a. My lab discovered that the resident immune cell of the CNS, the microglia, overexpresses the X chromosome gene (*Kdm6a*) in females, and this causes more brain inflammation. Pharmacologic blocking of this using metformin, a widely used diabetic drug with anti-aging and neuroprotective properties, worked better in females than in males. This has implications for the efficacy of metformin treatment in women and men today.

b. The supportive cell of the CNS, the astrocyte, was discovered to confer

neuroprotection during estrogen treatment in otherwise healthy females during midlife aging. Treatment specifically targeting estrogen receptor beta in astrocytes prevented cognitive decline, regional atrophy on brain MRI, and neuropathology. Gene expression changes in energy metabolism within astrocytes in the menopause model aligned with gene expression changes in brains of humans (menopausal women). Estrogen receptor specific targeting identifies a window of opportunity to stimulate estrogen receptor beta for protection in brain, while minimizing stimulation of estrogen receptor alpha in breast to reduce breast cancer risk.

c. My lab's findings suggest a critical balance between sex chromosomes and sex hormones in health and disease. A female sex chromosome (XX) gene drives neuroinflammation and neurodegeneration during aging, MS, and Alzheimer's Disease (AD). This is why women are more likely to get MS and AD. Balancing this, a female sex hormone (estrogen) is anti-inflammatory and neuroprotective in women at ages before menopause. However, when estrogen mediated neuroprotection is lost abruptly and permanently at menopause in otherwise healthy women (mean age 51 years), 60-70% experience cognitive domain specific symptoms. Brain regional changes on MRI align with cognitive complaints. Further, women with MS and AD have disability worsening and/or disease onset, respectively, at menopause.

d. The research in my lab resulted in me being the lead inventor on several UCLA patents in the U.S. and Europe that identify a novel estrogen treatment approach to prevent cognitive decline in aging, MS, and AD. The U.S. patents were licensed from UCLA by CleopatraRX, and blisterpacks of this patented hormone treatment were designed for menopausal women (PearlPAK). This new treatment is now commercially available across the U.S.

e. The suspended R35 research plan also includes finding neuroprotective treatments for men. Work in my lab is determining the balance between the role of male sex chromosome genes (XY) and male sex hormones (testosterone) in neuroinflammation and neuroprotection. The goal is to prevent neurodegeneration during andropause, when testosterone levels decrease gradually in men from age 30 to 70 years.

18. Overall, my work in animal models has tangible relevance to human health and

disease. I have designed and carried out several clinical trials, with two more now in planning stages. I am known for, indeed I was profiled in, the February 2024 issue of *Lancet Neurology*, entitled "Bedside to Bench to Bedside" research. This means clinical observations in patients ("Bedside") lead to treatment target discovery in animal models ("Bench") which lead to testing new treatments in human clinical trials ("Bedside").

19. A true and correct copy of the May 2023 R35 Grant Award is attached as Exhibit C. True and correct copies of additional Notices of Award, authorizing continuing funding, pursuant to the R35 Application and R35 Grant Award, issued in April 2024 and June 2025, are attached as Exhibits D and E.

Suspension of Grant Funding

20. On July 31, 2025, the UCLA Chancellor, Dr. Julio Frenk, received a letter from Jon Lorsch, the Acting Deputy Director for Extramural Research at NIH (the "Notice of Award Suspensions"). The Notice of Award Suspensions indicated that NIH was "hereby suspending the attached list of grant awards" and that UCLA researchers "must cease all activities on the awards and immediately discontinue drawing down funds from the Payment Management System (PMS) for any expenses incurred after receipt of this letter." The letter further stated that "under 45 CFR § 75.372 and 45 CFR § 75. 373, NIH may move to terminate an award" for various reasons. A copy of Notice of Award Suspensions was later forwarded to my email, together with a spreadsheet of suspended NIH grants. My R35 Grant Award is listed on the spreadsheet. A true and correct copy of the Notice of Award Suspensions is attached as Exhibit F.

21. On August 1, 2025, Tracey Fraser from the UCLA Office of Contract & Grant Administration sent an email instructing me to "***immediately stop incurring costs/expenditures on the grant(s) referenced above*** effective July 31, 2025." This "Stop Work Notice" was initially mistakenly sent to an inactive email address, rvoskuhl@ucla.edu, and a copy was not forwarded to my correct email address, rvoskuhl@mednet.ucla.edu, until later. A true and correct copy of the Stop Work Notice is attached as Exhibit G.

22. I first learned of the suspension of my grant on August 4, 2025, when I received an email from S. Thomas Carmichael, the Chair of the Department of Neurology at UCLA, inviting

me and the 23 other faculty in our department affected by grant suspensions to discuss our "lost grants," the "loss of supplies and other support for research" and the "substantial negative effect for faculty and their research programs." A true and correct copy of Dr. Carmichael's email is attached as Exhibit H.

23. I was not offered any reason for the suspension of my grant; any means of appealing this suspension; or informed of any other action I could take to reinstate the grant.

Harm Suffered from Termination of Grant Funding

24. I and my project team have suffered immediate harms as a result of NIH's actions in suspending this grant. These harms are continuing. Specifically:

a. The R35 Grant Award funded research conducted by myself, as well as by four co-investigators: A Faculty Specialist in genetic analysis and bioinformatics, a Faculty Professor in statistical genomics and bioinformatics, a Faculty Professor in neuroimaging, and a Faculty Research statistician. The Award also funded my lab's senior technician, an MRI lab technician, and graduate student researchers. It also funded part time work for 3 to 4 UCLA undergraduates each year who spend 10-15 hours per week working in my lab, as well as 1 to 2 undergraduates who work full time during their summer breaks.

b. My lab's only NIH grant is the R35 that was suspended. Importantly, an R35 from NIH NINDS precludes a researcher from applying for funding to NINDS for any other basic research grants during the duration of the R35 eight-year funding period. The R35 is intended to allow Professors with a track record of extraordinary success to have substantial and stable funding for eight years in order to address large scope questions. This is more efficient than spending substantial time and resources applying for numerous smaller, shorter-term grants in a piecemeal fashion. As a result of loss of my one and only NIH funding source, my lab is no longer able to purchase supplies for our experiments. I have informative, genetically engineered mice that took over 3 years to generate, since they model a disease aspect and/or deletion of a critical gene in neuropathogenesis. These mice will soon be lost, as will my ability to determine reasons for neurodegeneration in females and males, at adulthood and midlife aging. Based on my track record, my lab's research using them would likely have identified a treatment target to

provide rationale for design of a clinical trial tailored for either women or men at young adulthood or midlife with MS, cognitive decline in otherwise healthy people, or Mild Cognitive Impairment, a prelude to Alzheimer's Disease. I will soon have to let my staff go due to lack of funding. This team of researchers has taken two decades for me to gradually build. They have complex synergistic skills in neuroimmunology, neurogenetics, neuroendocrinology, neuropathology, and neurobehavior. An intangible is that we are an efficient and effective team. Rebuilding such a team would take me at least ten years. Research in my lab will grind to a halt. Any temporary pause, even for a few months, has lasting consequences in terms of our research productivity, our laboratory's output, and the publications we produce.

c. My co-investigators, who have highly specialized training but are more junior in their careers, will be harmed by a gap in publications, which will negatively impact their career progression and ability to secure future funding for their research. Without funding, I will not be able to retain or recruit graduate student researchers, which will harm graduate student training and career prospects. On average, I take in two undergraduates per year when they are UCLA sophomores or juniors who stay until they graduate, resulting in 4-6 at any given time. They learn how to do research, give presentations, win student awards, and become a co-author on publications. My research lab is a launch point for their career as they plan and apply for either M.D., Ph.D., or combined M.D., Ph.D. programs across the country. Each year, one will stay in my lab and work for a gap year, as they apply and get accepted to graduate school. Shutting down research in my lab will shut down the hopes and dreams of countless undergraduates. My lab is unique since it is truly translational, basic science applied to discovery of new treatments. Students love this. They will be lost with this suspension.

d. A pause in our research negatively impacts my subfield of neurology. My team will be unable to share our research findings at conferences and in scientific publications. I also do many media interviews about our science to inform and educate the public on our latest findings in the context of current knowledge in the field. This will end, since no more funding means no more findings. Since I am training the next generation of neuroscience researchers, including young faculty, postdoctoral fellows, graduate students and undergraduates, the future of

this field of research will be harmed by an indefinite pause in training. This goes beyond neurology to include the gynecologists and internists that I am training about the neurology of menopausal women with cognitive issues.

e. The U.S. public, which ultimately funds NIH grants, will also lose much of the value of their investment if my NIH grant is indefinitely suspended. Our research has already generated new insights into the molecular basis of disability-specific disease progression in MS. Multiple sclerosis affects nearly one million people in the United States, and since it usually starts in their 30s, patients must manage an approximate 50-year burden of disease. Work supported by this grant is aimed at developing novel treatments targeting cells and processes within the central nervous system to confer neuroprotection and repair disabilities for MS patients. Also, our research has already generated new insights into the molecular basis for cognitive decline during aging in people otherwise healthy, namely menopausal women and andropausal men. These issues impact everyone who lives long enough to go through menopause and andropause (over age 50). We already have UCLA licensed patents, with a novel hormone replacement therapy (HRT) now commercialized and on the market for menopausal women across the country as well as in the UCLA Comprehensive Menopause Program. Its foundation is in my lab's past NIH funded basic research and repurposing our findings in MS showing improved cognition and reduced regional brain atrophy in women with MS. NIH's withheld funding threatens the loss of clinically relevant research discoveries as well as current and future treatments.

I declare under penalty of perjury under the laws of the State of California and the United States that the foregoing is true and correct.

Executed this 22nd day of August, 2025, in Los Angeles, California.

DocuSigned by:
8833E07DB6D646A...
Rhonda Voskuhl

EXHIBIT A

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Rhonda R. Voskuhl, M.D.**

eRA COMMONS USER NAME (credential, e.g., agency login): VOSKUHL2

POSITION TITLE: **Professor of Neurology, Jack H. Skirball Chair**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Phillips University, Enid, OK	BS	05/1982	Biology
Vanderbilt Medical School, Nashville, TN	MD	06/1986	Medicine
Univ. of Texas Southwestern, Dallas, TX	Resident	06/1990	Neurology
NIH, Neuroimmunology Branch, Bethesda, MD	Fellow	04/1995	Neuroimmunology

A. Personal Statement

I have devoted my career to translational research based on clinical observations in patients using a "Bedside to Bench to Bedside" approach: Initially focusing on key clinical observations, disentangling underlying mechanisms at the lab bench, then designing clinical trials of new treatments based on these mechanisms. A key foundational clinical observation is the effect of being female versus male on MS and other neurodegenerative conditions, including aging. I am an internationally recognized expert in sex differences research, demonstrating protective effects of estrogen and testosterone treatment in preclinical models, which I translated to four clinical trials in patients. My lab was the first to show that estrogen receptor (ER) alpha and ER beta ligands act through distinct mechanisms to induce neuroprotection. I showed that ER beta ligation induced remyelination through direct action on oligodendrocytes, while downregulating innate immunity via actions on microglia. I also discovered that an X chromosome gene (the histone demyethylase *Kdm6a*) increases neuroinflammation. In addition, my lab was the first to use brain cell-specific and region-specific transcriptomics to investigate the molecular basis for disability-specific disease progression in MS. We use MS postmortem tissues from human subjects as well as human gene databases to validate genes identified in preclinical models. We have shown disability-specific brain atrophy in MS patients. My lab also investigates the role of brain aging on neurodegeneration, identifying a sex hormone by age interaction whereby being estrogen deficient and midlife combine to induce cognitive decline, dorsal hippocampal atrophy, glial activation, and synaptic loss. This is mediated by loss of ER beta in astrocytes and suggests a target to prevent disability worsening in women during menopause. The goal of my research is to use a brain region-specific, cell-specific, and sex-specific approach to identify neuroprotective treatment targets, then design clinical trials to repair neurodegeneration which are optimally tailored for sex and age. In the clinic I see patients with MS, and I am the faculty neurologist for the UCLA Comprehensive Menopause Program where I see otherwise healthy women with cognitive deficits during menopause.

Active funding: (suspended as of July 31, 2025)

R35 Research Program Awardee for 2023 (To approximately 10-15 neuroscientists per year across the U.S.)
NIH NINDS 05/15/2023 – 04/30/2031 Total $7,270,927
#R35NS132150 (PI Voskuhl)
Title: Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach
Goal: Develop treatments tailored for women and men that target neurodegenerative processes within the brain to repair disabilities.

Recent Publications to Highlight:

Deletion of the X gene, *Kdm6a*, in microglia reverses the disease-associated microglia transcriptome. ***Science Translational Medicine****,* in press, 2025.

Estrogen receptor beta in astrocytes modulates cognitive function in mid-age female mice**.** ***Nature Communications*** https://doi.org/10.1038/s41467-023-41723-7, Sept 29, 2023.

Together these two papers show the clinically relevant balance between: 1) a female sex chromosome (XX) gene which drives neuroinflammation and neurodegeneration in MS as well as brain aging in healthy females (as compared to men who are XY), *versus* 2) a female sex hormone (estrogen) which is anti-inflammatory and neuroprotective (as compared to men who have testosterone). This estrogen mediated neuroprotection is lost abruptly at menopause in women age 50-53 years, while testosterone mediated neuroprotection is lost gradually during andropause in men from age 30 to 70 years.

Reviews & Commentaries:
Voskuhl, R. Itoh, Y. The X factor in neurodegeneration. **Journal of Experimental Medicine,** Nov. 5, 2022.
Voskuhl, R., A new cell subtype that confers neuroprotection. **Nature Immunology**, Nov. 3, 2020.
Voskuhl, R., Klein, S., Sex is a biological variable - in the brain too. **Nature**, 568 (7751):171, 2019.
Voskuhl, R., Wang, H., Elashoff, R. Why use sex hormones in relapsing-remitting multiple? **Lancet Neurology**, 15:790, 2016.
Voskuhl, R., Gold, S. Sex-related factors in multiple sclerosis susceptibility and progression. **Nature Reviews Neurology,** 8:255, 2012.

B. Positions and Honors

Positions and Employment

2004-present Professor, Dept. of Neurology, UCLA, Los Angeles, CA
2023-present Faculty Neurologist, UCLA Comprehensive Menopause Program, Los Angeles, CA
2000-present Director, UCLA Multiple Sclerosis Program, UCLA, Los Angeles, CA
2000-2004 Associate Professor, Dept. of Neurology, UCLA, Los Angeles, CA
1995-2000 Scientific Director, UCLA Multiple Sclerosis Program, UCLA, Los Angeles, CA
1995-2000 Assistant Professor, Dept. of Neurology, UCLA, Los Angeles, CA
1994-1995 Senior Investigator, Neuroimmunology Branch, NIH, Bethesda, MD
1993-1994 Research Associate, Lab of Viral and Molecular Pathogenesis, NIH, Bethesda, MD
1990-1993 Clinical Associate, Neuroimmunology Branch, NIH, Bethesda, MD

Honors

2024-John Dystel Prize in Multiple Sclerosis, the most prestigious award in the field of MS.
2024-Lancet Neurology: Career Profile (February issue).
2023-Rachel Horne Prize in Women's Health Research in MS, ECTRIMS/ACTRIMS meeting Milan, 2023
2019-Kenneth P. Johnson Memorial Lecture, ACTRIMS annual meeting 2019
2018-Berlin Institute of Health (BIH) Excellence Award for Sex and Gender Aspects in Health Research
2018-UCLA Innovation Award, UCLA Campus-wide Technology Development Group Competition for 2018
2006-Jack H. Skirball Chair in MS Research
2001-California Congressman Henry Waxman Honorary Grant
1997-Harry Weaver Neuroscience Scholar of the National Multiple Sclerosis Society (NMSS)
1995-Outstanding Young Alumna, Phillips University
1994-Public Health Service Citation for Excellence in Research, National Institutes of Health (NIH)
1991-Annual Noble Lectureship Award
1988 and 1990-Texas Neurologic Society Annual Research Award for a Neurology Resident (twice)
1982-Oklahoma College All Star Women's Basketball Team
1982-Representative Phillipian - Overall Most Outstanding Senior Award, Phillips University
1979-1982-Biology Award (1979), Chemistry Award (1980), Science Award (1982), Phillips University
1978-1982-Four year full basketball scholarship - Two year Team Captain, Phillips University

Other Experience and Professional Memberships

Department of Defense (DOD) Congressionally Directed Medical Research Program's (CDMRP) Multiple Sclerosis Research Program (MSRP), Programmatic Panel, member, 2020-2023.

Member, NIH Study Section BDCN, 2002-2006; NIH Special Emphasis Panel NSD-C, 2009-2012; NIH Study Section Ad hoc: NSD-C / NSD-A, 2013-2017; HAI, 2018-2019; CNBT, 2021; Special Emphasis Panel review of Program Project Grants, NIAID, 2022; BRAIN Initiative Cell Atlas Network (BICAN) grants, NIH /

NIMH ZMH1 ERB-L (06), 2023, NIH ZNS1-SRB-E NINDS R35 Review Panel B, 2024. NIH Special Emphasis Panel, Aging Systems and Geriatrics study section NIH/CSR, 2025.

Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Steering Committee, 2007-2012: ACTRIMS Advisory Committee, 2015-present; ACTRIMS Resident Summit, 2017-2023; ACTRIMS Young Scientist Summit, 2018-2023.

European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), Faculty, 2023-present.

Presidential Leadership 6 year commitment to the Organization for the Study of Sex Differences (OSSD), President-Elect, 2018-2020; President, 2020-2022; Past-President, 2022-2024; OSSD Annual Meeting Organizing Committee, 2016-2018; NIH Office of Research on Women's Health (ORWH) / FDA Office of Women's Health Sex and Gender online course, 2019-2022.

Deutsche Forschungsgemeinschaft (DFG), German Federal Government for Excellence Cluster Initiatives, Clusters of Excellence Advisory Board Member, 2021-present.

Lead Principle Investigator for UCLA, Nancy Davis Center Without Walls, Race to Erase MS, 2019-present.

UCLA Comprehensive Menopause Care Program, Faculty Neurologist, 2023-present.

UCLA inventor on over 15 issued patents in the U.S. and Europe for a new treatment for neuroprotection: estriol treatment of cognitive decline during aging in otherwise healthy women, estriol treatment to prevent disability worsening and brain atrophy in MS women (R. Voskuhl sole inventor); novel ER beta ligand treatments for neuroprotection (R. Voskuhl & M. Jung, Co-Inventors). Co-Founder and Science Director for start-up (CleopatraRX) that licensed U.S. patents for a treatment to prevent cognitive issues of menopause.

C. Contributions to Science: Selected publications.

1. Clinical trials. I have translated basic findings from my lab on the effect of sex hormones in MS models to clinical trials in women and men with MS. First, I translated my lab's preclinical finding that the estrogen of pregnancy (estriol) is anti-inflammatory and neuroprotective. This had implications for mechanisms underlying the protection of pregnancy in MS. Translation entailed three clinical trials (2 multisite and 1 single site). The first estriol trial showed a reduction in enhancing lesions (*Annals of Neurology).* The 16 site estriol trial showed a reduction in relapses as powered as the primary outcome for a Phase 2 trial and an improvement in cognition as an exploratory (*Lancet Neurology* and featured by a Commentary). We then mapped estriol treatment induced sparing atrophy in cerebral cortex (*Brain & Behavior,* 2018), and showed an estriol treatment mediated reduction in serum neurofilament light chain (sNfL) levels (*Ann. Clin. & Trans, Neurol***.**, 2022). My lab was also the *first to show that testosterone treatment is protective in EAE* (*J. Immunology*, 159:3-6, 1997). We translated this to a pilot clinical trial in MS men (*Archives of Neurology* 64:683-688, 2007, aka *JAMA Neurology*), then mapped regions of testosterone mediated sparing of gray matter atrophy in MS men (*Neuroimage Clinical,* 4:454-460, 2014*).*

a. Sicotte, N., Liva, S.M., Klutch, R., Pfieffer, P., Bouvier, S., Odesa, S., Wu, T.C.J., Voskuhl, R.R. (2002) Treatment of multiple sclerosis with the pregnancy hormone estriol. **Annals of Neurology,** 52:421-428.

b. Voskuhl, R.R., Wang, H., and the Estriol Trial Study Group (2016) Estriol combined with glatiramer acetate for women with relapsing-remitting MS: A Randomised, Placebo-Controlled, Phase 2 Trial. **Lancet Neurology**, 15: 35-46. PMID 26621682.

*(Commentary: Voskuhl, R., Wang, H., Elashoff, R. **Lancet Neurology,** 2016, 15:790-791)

c. MacKenzie-Graham, A., Brook, J., Kurth, F., Itoh, Y., Meyer, C., Montag, M., Wang, H., Elashoff, R., Voskuhl, R.R. (2018) Estriol-mediated neuroprotection in multiple sclerosis localized by voxel-based morphometry. 8(9):e01086. **Brain & Behavior,** PMCID: PMC6160650.

d. Voskuhl, R.R., Kuhle J., Siddarth , P., Itoh, N., Patel, K., MacKenzie-Graham, A. (2022) Decreased Neurofilament Light Chain Levels In Estriol-Treated Multiple Sclerosis. **Annals of Clinical & Translational Neurology,** 9(8):1316-1320. PMID: 35770318.

e. Voskuhl, R.R. (2024) All women with multiple sclerosis should start hormone replacement therapy at menopause unless contraindicated: Yes. **Multiple Sclerosis Journal (MSJ)** 30(9):1107-1109. PMC11363466.

2. Identified the cell that mediates estrogen's neuroprotective effect *in vivo*. Estrogens were known to be neuroprotective through actions on estrogen receptors (ERs) for decades, however which cell in the CNS mediated this neuroprotection *in vivo* remained unknown. My lab created cell-specific knock outs of ER alpha and ER beta to determine which CNS cell mediated neuroprotection *in vivo*. *My lab was the first to identify which cell is responsible for estrogen mediated neuroprotection in vivo in any neurological disease model.* Most recently, we showed that Estriol and ER beta ligand treatment can induce remyelination in cerebral cortex

in the MS preclinical model, and showed that decreased ligation of ER beta in astrocytes in dorsal hippocampus mediates cognitive decline, dorsal hippocampal atrophy, and glial activation and synaptic loss in mid-life females in a preclinical model of menopause in otherwise healthy women.
a. Tiwari-Woodruff, S., Morales, L., Lee, R., Voskuhl, R.R. (2007) Differential Neuroprotective and Anti-inflammatory Effects of Estrogen Receptor (ER) α and ER β Ligand Treatment. **Proceedings of the National Academy of Sciences (PNAS),** 104:14813-14818, PMCID: PMC1976208.
b. Spence, R., Hamby, M., Umeda, E., Itoh, N., Du, S., Bondar, G., Lam, J., Ao, Y., Wisdom, A., Cao, Y., Sandoval, F., Sofroniew, M.V., Voskuhl, R.R. (2011) Neuroprotection mediated through estrogen receptor alpha on astrocytes. **Proceedings of the National Academy of Sciences (PNAS),** 108:8867-8872. PMCID: PMC3102368.
c. Spence, R.D., Wisdom, A.J., Cao, Y., Hill, H.M., Mongerson, C., Stapornkul, B., Itoh, N., Sofroniew, M.V., Voskuhl, R.R. (2013) Estrogen signaling through ER-alpha but not ER-beta on astrocytes mediates neuroprotection during EAE and decreases astrocyte levels of proinflammatory chemokines. **Journal of Neuroscience,** 33:10924-109333. PMCID: PMC3693061.
d. Kim, R., Hoffmann, A., Mangu, D. Kavosh, R., Jung, E., Itoh, N., Voskuhl, R.R. (2018) Estrogen Receptor Beta Ligand Acts on CD11c$^+$ Cells to Mediate Protection in Experimental Autoimmune Encephalomyelitis. **Brain**, 141:132-147. PMCID: PMC5837360.
e. Meyer, C.E., Smith, A.W., Padilla-Requerey A.A., Farkhondeh, V., Itoh, N., Itoh, Y., Gao, J.L., Herbig, P.D., Nguyen, Q., Ngo, K.H., Oberoi, M.R., Siddarth, P., Voskuhl, R.R., MacKenzie-Graham, A. (2023) Neuroprotection in cerebral cortex induced by the pregnancy hormone estriol. **Laboratory Investigation**, 103: 8, 100189.
f. Itoh, N., Itoh, Y., Meyer, C.S., Suen, T., Cortez Delgado, D., Rivera Lomeli, M., Wendin, S., Somepall, S.S., Golden, L., MacKenzie-Graham, A., Voskuhl, R.R. (2023) Estrogen receptor beta in astrocytes modulates cognitive function in mid-age female mice**. Nature Communications***.* https://doi.org/10.1038/s41467-023-41723-7

3. Sex chromosome effects on autoimmunity and neurodegeneration. *My lab was the first to show sex differences in EAE using its relapsing-remitting model* (*Annals of Neurology,* 39:724-733, 1996). Over the last decade, my research has been discussed by others in *Nature* editorials three times regarding how sex differences can lead to insights into disease. I also am first author of an editorial on the subject (*Nature*, 568:171, 2019). My lab discovered sex chromosome effects in the immune system in both the MS and lupus models. We then identified a gene on the X chromosome (*Kdm6a*) that escapes X-inactivation in CD4+T lymphocytes as a mechanism for increased susceptibility of females to autoimmune disease. Also, we published that parental imprinting of the X chromosome can lead to sex differences in autoimmunity. Focusing on the CNS, we showed that in contrast to XX conferring an increase in autoimmunity, XY confers an increase in the neurodegenerative response to the same autoimmune attack. Indeed, *my lab was the first to show an effect of sex chromosome complement in the CNS in any neurodegenerative disease model* (in 2014). See below for special recognition, commentaries, and editorial highlights of publications in this field.
a. Smith-Bouvier, D.L., Divekar, A.A., Sasidhar, M., Du, S., Tiwari-Woodruff, S., King, J.K., Arnold, A.P., Voskuhl, R.R. **(**2008) A role for sex chromosome complement in the female bias in autoimmune disease. **Journal of Experimental Medicine,** 20205(5):1099-108, PMCID: PMC2373842.
b. Du, S., Itoh, I., Askarinam, S., Hill, H., Arnold, A., Voskuhl, R.R. (2014) XY Sex Chromosome Complement, Compared with XX, in the CNS Confers Greater Neurodegeneration During EAE. **Proceedings of the National Academy of Sciences (PNAS),** 111:2806-2811. PMCID: PMC3932937.
*(Recognized in ***Lancet Neurology*** as one of the top 5 in MS for 2014).
c. Itoh, Y., Golden, L., Itoh, N., Matsukawa, M., Ren, E., Tse, V., Arnold, A.P., Voskuhl, R.R. (2019) The X-linked histone demethylase *Kdm6a* in CD4+ T lymphocytes modulates autoimmunity. **Journal of Clinical Investigation (JCI),** https://doi.org/10.1172/JCI126250, 130:3852-3863, PMCID: PMC6715385.
*(Commentary on this article in **JCI** 130:3536-3538, 2019.)
d. Golden, L.C., Itoh, Y., Itoh, N, Iyengar, S., Coit, P., Salama, Y., Arnold, A.P., Sawalha AH, Voskuhl, R.R. (2019) Parent-of-origin differences in DNA methylation of X chromosome genes in T lymphocytes. **Proceedings of the National Academy of Sciences (PNAS),** PMCID: PMC6936674.
*(Editorial Highlight of this paper “In This Issue” section **PNAS**.)
e. Voskuhl, R.R., Itoh, Y. (2022) The X Factor in Neurodegeneration. **Journal of Experimental Medicine**, 10.1084/jem.20211488.
f. Itoh, Y., Itoh, N., Wendin, S., Higgins, N., Voskuhl, R.R., (2025) Deletion of the X gene, *Kdm6a*, in microglia

reverses the disease-associated microglia transcriptome. **Science Translational Medicine.** In press.

4. Basic insights into neurodegeneration. These studies used a cell-specific and region-specific transcriptomics approach to identify novel mechanisms underlying regional neuropathology in MS models and MS autopsy tissues. While this approach had been used in astrocytes during health, *my lab was the first to use a cell-specific and region-specific transcriptomics approach in any neurodegenerative disease model* (in 2018).
a. Itoh,Y. Voskuhl, R.R. (2017) Cell specificity dictates similarities in gene expression in multiple sclerosis, Parkinson's disease, and Alzheimer's disease. **PLoS One**, 12:e0181349, PMCID 5513529.
b. Itoh, N., Itoh, Tassoni, A., Ren, E., Kaito, M., Ohno, A., Y., Ao, Y., Farkhondeh, V., Johnsonbaugh, H., Burda, J. Sofroniew, M.V., Voskuhl, R.R. (2018) Cell-Specific and Region-Specific Transcriptomics in the multiple sclerosis model: Focus on astrocytes. **Proceedings of the National Academy of Sciences (PNAS)**, 115:E302-E309, PMCID: PMC5777065.
c. Voskuhl, R.R., Itoh, N., Tassoni, A., Matsukawa, M., Ren, E., Tse, V., Jang, E., Suen, T., Itoh, Y. (2019) Gene expression in oligodendrocytes during remyelination reveals cholesterol homeostasis as a therapeutic target in multiple sclerosis. **Proceedings of the National Academy of Sciences (PNAS)**, 116 (20):1-130-10139, PMCID: PMC6525478.
d. Tassoni, A., Farkhondeh, V., Itoh, Y., Itoh, N., Sofroniew, M.V., Voskuhl, R.R. (2019) The astrocyte transcriptome in EAE optic neuritis shows complement activation and reveals a sex difference in astrocytic C3 expression. **Scientific Reports**, 9:10010-22, PMCID: PMC6620300.
e. Voskuhl, R., MacKenzie-Graham, A., (2022) Chronic Experimental Autoimmune Encephalomyelitis is an Excellent Model to Study Neuroaxonal Degeneration in Multiple Sclerosis", **Frontiers in Molecular Neuroscience***. Vol. 15:* 10.3389/fnmol.2022.1024058.
f. Itoh, N., Itoh, Y., Stiles, L., Voskuhl, R.R. (2023) Sex differences in the neuronal transcriptome and synaptic mitochondrial function in cerebral cortex of a multiple sclerosis model. ***Frontiers in Neurology*** *Vol. 14*: doi: 10.3389/fneur.2023.1268411

5. Other Clinical Research. I initially studied immune responses in the peripheral blood of MS patients during the hormone treatment trials where I was the PI. Then I focused on the CNS. In collaboration with Dr. MacKenzie-Graham, *we mapped 3 different MS disabilities to distinct gray matter regions, which* was highlighted by an editorial in *JAMA Neurology. We also showed sex differences in regional gray matter atrophy in MS patients* by comparing gray matter atrophy in female MS vs female healthy controls and by comparing male MS vs male healthy controls (to remove the confound of sex differences in healthy brain).
a. Soldan, S.S., Alvarez-Retuerto, A.I., Sicotte, N.L., Voskuhl, R.R. (2003) Th1 to Th2 immune shift in female MS patients treated with the pregnancy hormone estriol, **Journal of Immunology,** 11:6267-6274.
b. Gold, S., Chalifoux, S., Giesser, B., Voskuhl, R.R. (2008) "Immune Modulation and Increased Neurotrophic Factor Production in Multiple Sclerosis Patients treated with Testosterone." **Journal of Neuroinflammation,** 5:32: 1-8. PMID: PMC2518142.
c. MacKenzie-Graham, A., Kurth, F., Itoh, Y., Wang, H., Montag, M., Elashoff, R., Voskuhl, R. (2016) Disability-Specific Atlases of Gray Matter Loss in Relapsing-Remitting Multiple Sclerosis. **JAMA Neurology**, 73:944-953, PMCID: 27294295
*(Editorial highlight in same issue of **JAMA Neurology, (**2016), 73(8):910-912.
d. Voskuhl, R.R., Patel, K., Paul, F., Gold, S.M., Scheel, M., Kuchling, J., Cooper, G., Asseyer, S., Chien, C., Brandt, A.U., Meyer, C.E., MacKenzie-Graham, A. (2020) Sex Differences in Brain Atrophy in Multiple Sclerosis. **Biology of Sex Differences**, 11(1):49. PMCID: PMC7456053.

Completed recent funding with R. Voskuhl as PI:

National Institutes of Health / NINDS / RO1	9/30/18 – 5/31/23	Total $2,194,376
#RO1NS109670	(PI Voskuhl)	

Title: Neuroprotection in MS: A Cell-specific and Region-specific Transcriptomics Approach
Goal: Understand neurodegenerative mechanisms in preclinical models of MS in females and males.

National Institutes of Health / NINDS / RO1	12/01/16 - 6/30/21	Total $2,138,929
#RO1NS096748	(PI Voskuhl)	

Parental imprinting of the X chromosome: Effects on neurodegeneration
Goal: Determine effects of X imprinting on gene expression in neuroimmunology

EXHIBIT B

PI: **VOSKUHL, RHONDA R**	Title: Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach	
Received: 07/08/2022	FOA: NS22-038	Council: 01/2023
Competition ID: FORMS-G	FOA Title: Research Program Award (R35 Clinical Trial Optional)	
1 R35 NS132150-01	Dual:	Accession Number: 4732963
IPF: 577505	Organization: UNIVERSITY OF CALIFORNIA LOS ANGELES	
Former Number:	Department: Neurology	
IRG/SRG: ZNS1 SRB-H (26)	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 591,985 Year 2: 591,985 Year 3: 591,985 Year 4: 591,985 Year 5: 591,985 Year 6: 591,985 Year 7: 591,985 Year 8: 591,985	Animals: Y Humans: N Clinical Trial: N Current HS Code: 10 HESC: N HFT: N	New Investigator: Early Stage Investigator:
Senior/Key Personnel:	*Organization:*	*Role Category:*
Rhonda Voskuhl MD	The Regents of the University of California, Los Angeles	PD/PI
Yuichiro Itoh PhD	The Regents of the University of California, Los Angeles	Co-Investigator
Jin Zhou PhD	The Regents of the University of California, Los Angeles	Co-Investigator
Allan MacKenzie-Graham PhD	The Regents of the University of California, Los Angeles	Co-Investigator
Prabha Siddarth PhD	The Regents of the University of California, Los Angeles	Co-Investigator

Additions for Review

Accepted Publication	Accepted Publication
Other	Accepted Publication and Late Breaking Data

OMB Number: 4040-0001
Expiration Date: 12/31/2022

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	State Application Identifier

1. TYPE OF SUBMISSION*

❍ Pre-application ● Application ❍ Changed/Corrected Application

4.a. Federal Identifier

b. Agency Routing Number

c. Previous Grants.gov Tracking Number

2. DATE SUBMITTED 2022-07-08

Application Identifier

5. APPLICANT INFORMATION **UEI*:** RN64EPNH8JC6

Legal Name*: The Regents of the University of California, Los Angeles
Department:
Division:
Street1*: Office of Contract and Grant Administration
Street2: 10889 Wilshire Boulevard, Suite 700
City*: Los Angeles
County: Los Angeles County
State*: CA: California
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 90095-1406

Person to be contacted on matters involving this application
Prefix: First Name*: Lydia Middle Name: Last Name*: McHam Suffix:
Position/Title: Contract and Grant Analyst
Street1*: 10889 Wilshire Boulevard, Suite 700
Street2:
City*: Los Angeles
County: Los Angeles County
State*: CA: California
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 90095-1406
Phone Number*: (310) 794-0167 Fax Number: Email: lydia.mcham@research.ucla.edu

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** 1-956006143-A1

7. TYPE OF APPLICANT* H: Public/State Controlled Institution of Higher Education

Other (Specify):
Small Business Organization Type ❍ Women Owned ❍ Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

● New ❍ Resubmission
❍ Renewal ❍ Continuation ❍ Revision

If Revision, mark appropriate box(es).
❍ A. Increase Award ❍ B. Decrease Award ❍ C. Increase Duration
❍ D. Decrease Duration ❍ E. Other *(specify)* :

Is this application being submitted to other agencies?* ❍Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach

12. PROPOSED PROJECT
Start Date* Ending Date*
04/01/2023 03/31/2031

13. CONGRESSIONAL DISTRICTS OF APPLICANT
CA-033

SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: Dr. First Name*: Rhonda Middle Name: R. Last Name*: Voskuhl Suffix: MD
Position/Title: Professor
Organization Name*: The Regents of the University of California, Los Angeles
Department: Neurology
Division: David Geffen School of Medicine
Street1*: 635 Charles E. Young Drive South
Street2: 475D Neuroscience Research Bldg 1
City*: Los Angeles
County: Los Angeles County
State*: CA: California
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 90095-7334
Phone Number*: (310) 206-4636 Fax Number: (310) 206-9801 Email*: rvoskuhl@ucla.edu

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested*	$7,307,976.00
b. Total Non-Federal Funds*	$0.00
c. Total Federal & Non-Federal Funds*	$7,307,976.00
d. Estimated Program Income*	$0.00

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:
DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR
○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: Ms. First Name*: Jessica Middle Name: Last Name*: Kim Suffix:
Position/Title*: Senior Contract and Grant Analyst
Organization Name*: The Regents of the University of California, Los Angeles
Department: Office of Contract & Grant Adm
Division:
Street1*: 10889 Wilshire Boulevard, Suite 700
Street2:
City*: Los Angeles
County: Los Angeles County
State*: CA: California
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*: 90095-1406
Phone Number*: 310-983-3673 Fax Number: Email*: jessica.kim@research.ucla.edu

Signature of Authorized Representative*
Jessica Kim

Date Signed*
07/08/2022

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:Cover_Letter1071187008.pdf

424 R&R and PHS-398 Specific
Table Of Contents

Project/Performance Site Location(s)

Project/Performance Site Primary Location

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	The Regents of the University of California, Los Angeles
UEI:	RN64EPNH8JC6
Street1*:	635 Charles E. Young Drive
Street2:	GNRB 479, 476, 480, 484; lab bays 21-24
City*:	Los Angeles
County:	Los Angeles
State*:	CA: California
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	90095-7334
Project/Performance Site Congressional District*:	CA-033

Project/Performance Site Location 1

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	The Regents of the University of California, Los Angeles
UEI:	RN64EPNH8JC6
Street1*:	1100 Glendon
Street2:	Suite 1820
City*:	Los Angeles
County:	Los Angeles
State*:	CA: California
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	90095-7394
Project/Performance Site Congressional District*:	CA-030

Project/Performance Site Location 2

❍ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name:	Regents of the University of California, Los Angeles
UEI:	RN64EPNH8JC6
Street1*:	635 Charles E. Young Drive
Street2:	GNRB 225Y, 225Z, 225Z1
City*:	Los Angeles
County:	Los Angeles
State*:	CA: California
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	90095-1769
Project/Performance Site Congressional District*:	CA-033

Additional Location(s) File Name:

OMB Number: 4040-0010
Expiration Date: 12/31/2022

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ❍ **Yes** ● **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ❍ Yes ❍ No

If YES, check appropriate exemption number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6 _ 7 _ 8

If NO, is the IRB review Pending? ❍ **Yes** ❍ **No**

IRB Approval Date:

Human Subject Assurance Number

2. Are Vertebrate Animals Used?* ● **Yes** ❍ **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ● Yes ❍ No

IACUC Approval Date:

Animal Welfare Assurance Number A3196-01

3. Is proprietary/privileged information included in the application?* ❍ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ❍ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ❍ Yes ❍ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ❍ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ● **Yes** ❍ **No**

6.a. If yes, identify countries: Germany

6.b. Optional Explanation: See attached other attachment on foreign justifications

	Filename
7. Project Summary/Abstract*	R35_Abstract1071243889.pdf
8. Project Narrative*	Project_Narrative1071122653.pdf
9. Bibliography & References Cited	Reference_Cited1071243920.pdf
10.Facilities & Other Resources	Facilities_Resources1071122655.pdf
11.Equipment	Equipment1071122656.pdf
12. Other Attachments	Bibliography_Voskuhl1071243921.pdf R35_Mentoring1071243922.pdf Foreign Justification.pdf

Multiple sclerosis (MS) is an autoimmune, neurodegenerative disease with inflammation, demyelination, axonal damage, glial activation and synaptic loss. There are relapses and permanent disabilities. Despite success of treatments targeting cells in the immune system, there is an unmet need for treatments targeting cells in central nervous system (CNS) to repair disabilities. Four observations provide rationale for a new approach to neurodegeneration in MS: 1) MS patients are heterogenous in their disabilities, and distinct disabilities (walking, vision, cognition, coordination) are served by different CNS regions, 2) Even in healthy brain, a given CNS cell type differs in gene expression from one brain region to another, 3) Being female versus male impacts disability worsening, and 4) Aging aligns with disability progression. Here, we will use a cell-specific, region-specific, and sex-specific approach to discover optimal treatment targets for distinct disabilities in MS women and men.

Bedside to Bench to Bedside in MS: Clinical observations of sex differences are investigated at the preclinical level then translated back to the clinic as trials designed for each sex. Preclinical use of female and male mice with experimental autoimmune encephalomyelitis (EAE) entails *in vivo* MRI for region-specific atrophy, neuropathology of each region, RNA-sequencing of distinct CNS cells in each region, immunohistochemistry validation of top genes in highly differentially expressed pathways, cell-specific conditional knockout (CKO) of target genes to reverse phenotype, and knockdown of target genes with pharmacologic treatment to reverse phenotype. The effect of genetic (CKO vs WT) and/or pharmacologic (treatment vs placebo) interventions on reversal of gene expression is determined in each sex. Human MS data guide preclinical research at three checkpoints: i) MRI in females and males with MS revealing sex differences in substructure atrophy prioritize regions in EAE with atrophy, ii) Single nuclei RNA-seq analyses in females and males with MS revealing gene pathways of interest prioritize gene pathways in EAE, iii) immunohistochemistry in females and males using MS postmortem tissues validate immunohistochemistry in EAE. Substitution of use of female versus male mice (as above) with use of gonadectomized versus gonadally intact mice will reveal activational effects of sex hormones. Use of Four Core Genotype mice will reveal sex chromosome effects versus developmental hormone effects. Use of young versus old mice will reveal the effect of aging.

This R35 proposal will: 1) Extend our **cell-specific and region-specific transcriptomics** in astrocytes and oligodendrocytes to microglia and neurons, with cell:cell interactions revealed in mice double-labelled to show gene expression changes in two distinct cell types in the same region in the same mouse, and 2) Determine if there are effects of **sex** and/or **age** on the most differentially expressed cell-specific and region-specific pathways. In summary, this R35 proposal takes our research to the next level: Identifying sex by age interactions in cell-specific and region-specific transcriptomics, neuropathology, and substructure atrophy on MRI.

The greatest unmet need in multiple sclerosis (MS) is to develop novel treatments targeting cells and processes within the central nervous system (CNS) to confer neuroprotection and repair disabilities, in not only relapsing remitting MS, but also in secondary progressive MS. A “one size fits all” neuroprotective treatment approach in MS will not work, since 1) MS patients are heterogenous regarding which disabilities are predominant, 2) being female versus male impacts rates of disability progression, and 3) aging corresponds with disability progression. This R35 will use a cell-specific, region-specific, and sex-specific approach to discover neurodegenerative targets optimized for each disability in MS models in females and males during young adulthood and aging.

FACILITIES AND OTHER RESOURCES

PROJECT SCIENTIFIC ENVIRONMENT

University of California, Los Angeles*. Home Institution of all investigators.*
UCLA has outstanding the expertise in all the areas required in this proposal, namely neuroimmunology, neuroscience, bioinformatics, neurogenomics, and neuroimaging. Together this creates an environment of highly complementary areas of expertise, thereby assuring success of this challenging project.

FACILITIES & RESOURCES

Laboratories / Office / Computing

Dr. Rhonda Voskuhl: Dr. Voskuhl's private office is in the Neuroscience Research Building, 4th floor, in the center of the UCLA Medical Campus. It is a southwest corner office 479C (30x20 feet) and houses 2 Mac computers. The Voskuhl labs and consists of four rooms (479, size 28x40 ft; 476, size 22x30 ft; 480, size 22x30 ft. and 484, size 28x30 ft) and dedicated mouse rooms with, while her dedicated mouse rooms include Rooms 420A and 420K. 479 is lab bench space for histology, FACS staining, PCR, preparation of total RNAs from tissues and cells, polyA+ RNA isolations, gel electrophoresis, etc. It contains 10 desktop computers and also has a chemical hood. Room 476 is used for murine cell culture and incubation and contains 2 sterile hoods. Room 480 is used for human PBMC preparation, generation of TCLs, and incubation, proliferative assays and ELISAs. It has one sterile hood and a Beta plate counter with cell harvester. Room 484 is dedicated to immunofluorescence and electrophysiological studies. Room 420A is Dr. Voskuhl's mouse procedure room. It is used for immunizations, behavioral testing, the dissection of mice, adoptive transfers, eye bleeds, etc. Room 420K is Dr. Voskuhl's mouse return room where mice with EAE are returned for housing to permit frequent behavioral testing. Mice are bred in a barrier facility on the basement floor of RB1. All mice being generated or received from a vender prior to experiments are housed in this common barrier facility. ***Animal Housing and Care.*** Animal care is provided by the Division of Laboratory Animal Medicine at UCLA, which is an approved AAALAC facility. In total Dr. Voskuhl's animal space can house approximately 1300 mice at any given time. Her lab has a special mouse procedure room (#420A) that is available for surgeries (immunizations, dissections), behavioral analyses, and adoptive transfers. Dr. Voskuhl's lab also includes a mouse return room (#420K) where mice are returned for housing following procedures. A common barrier facility on the basement floor of the same building for breeding, housing and routine care and disease surveillance.

Dr. Yuichiro Itoh: Dr. Itoh's private office is in the Neuroscience Research Building. Dr. Itoh's office is in 479B (20x20 feet). It houses 2 computers for bioinformatics analyses of transcriptomes. Dr. Itoh uses the Voskuhl lab for wet lab work to complement his computational analyses identifying novel targets. His office is adjacent to Dr. Voskuhl's office.

Dr. Jin Zhou: Dr. Zhou will provide gene expression and methylation statistical analyses, as well as providing access to the database for dissemination to the public. As an Associate Professor in the Department of Medicine Statistics (DOMStat) Core, UCLA Division of General Internal Medicine and Health Services Research, she has full access to all of the resources and staff in the DOMStat Core. Her office is in the DOMStat floor of 1100 Glendon Avenue, Suite 11820, a block away from the UCLA main campus.

Dr. Allan MacKenzie-Graham: Dr. MacKenzie-Graham's private office is adjacent to his laboratory. The MacKenzie-Graham laboratory comprises three rooms in the Neuroscience Research Building Facility 2nd floor (see below). The wet lab (225Z) is approximately 225 square feet with bench space for perfusion, sample preparation, optical clearing (CLARITY), histology, immunohistochemistry, gel electrophoresis, and hybridization of blots. Dr. MacKenzie-Graham's office space is 96 square feet (225Z-1), adjacent to the lab. A postdoctoral office space of 76 square feet (225Z-2) is also adjacent to the lab. Individual compute resources are described in the Equipment section. As a member of the Ahmanson-Lovelace Brain Mapping Center faculty, Dr. MacKenzie-Graham has unlimited access to the compute and storage resources described below.

Dr. Prabha Siddarth: Dr. Siddarth will provide high-level statistical analyses to the investigators and she has access to SIStat, the biostatistics core in UCLA's Semel Institute for Neuroscience and Human Behavior. SIStat provides affiliated projects with software tools and direct services such as database creation and management and quality assurance. Dr. Siddarth's office space is 125 square feet (Suite 37-444), and adjacent to her office is a large office space to house graduate students, postdoctoral fellows and interns. As a

member of the Semel Institute's research faculty, Dr. Siddarth has unlimited access to many high performance computer systems in the Semel Institute.

UCLA Core facilities, all of which are readily available for this proposal:

UCLA Informatics Center for Neurogenetics and Neurogenomics (ICNN)

UCLA Department of Medicine Statistics Core (DOMStat)

UCLA Semel Institute Biostatistics Core (SIStat)

Mitochondrial function / Synaptosome Core

UCLA Brain Mapping Core for Neuroimaging

The Neuroscience Research Building Facility houses the research MRI scanners (PRISMA for humans and the 7T for mice):

The faculty, staff and major physical resources to be used by this project are housed in the Neuroscience Research Building Facility. The NRB Facility resides within the Department of Neurology at the UCLA School of Medicine. The facility was designed and furnished for the acquisition, processing, and storage of brain image data from a variety of sources.

Physical Infrastructure: The facility is physically located in the Neuroscience Research Building (NRB), occupying approximately 8,425-ft² of the building's second floor. The space is comprised of a reception area, Director and faculty offices, a modern computer room, a user area, wet labs, a conference room, and the Data Immersive Visualization Environment (DIVE) discussed here within. The data center in this space includes a raised floor, a 130 KVa UPS/PDU capable of providing uninterruptible power to all equipment housed in the room, dual Leibert air conditioning units, humidity control, and a fire suppression mechanism. A sophisticated event notification system is integrated in this space to automatically notify personnel of any abnormal power, water, or HVAC issues that arise. Immediately adjacent to this machine room is a user space with eighteen individual stations separated by office partitions. Each station is equipped with a four copper Gigabit network ports and 802.11n wireless signals for networked image processing, visualization and statistical analysis. To provide telephony services, the facility relies on Voice over IP (VoIP) technology. VoIP units, including wireless handsets, are distributed throughout the laboratory. In addition, the conference room and the DIVE are equipped with supplementary H.232 videoconferencing systems.

Having reached the power, cooling, and physical capacity limits of the second-floor data center, the facility was augmented with an additional 2,127-ft² space on the building's first floor containing a state-of-the-art data center and additional offices. The office space can support up to twenty researchers and is outfitted with the same technological specifications as the existing facility. The 580-ft² data center is outfitted with an "in-row" cooling solution that regulates temperatures strictly within the server racks—as opposed to the traditional raised floor, hot-cold aisle technique that uses more energy to cool the entire room. Multiple chilled water lines are fed from the building to a Rittal TS 8 rack system, which houses the servers and provides in-row cooling. The racks are fully enclosed and deliver chilled air to the front of the machines while recycling warm air exhausted at the rear. During normal operation, keeping the air within the system provides maximum efficiency, but should a component fail, once temperatures reach 80°F the magnetic locks on the rack doors are programmed to release, forcing the doors open to provide ambient air to the machines. A 550KVa Eaton UPS provides uninterruptable power to the facility's current equipment and is sized to accommodate future large hardware expansions. In order to support the additional personnel and computational resources, the data center is equipped with multiple 10 Gigabit connections in a fault-tolerant, load-balanced configuration that interconnect with the primary data center.

Finally, a tertiary 800-ft² data center, located in UCLA's Reed Building, is shared with the Department of Neurology. This physically separated building primarily houses tape-based backup systems, to provide a failsafe data backup in case of a catastrophic event at NRB. This third data center is connected to our primary by dual, redundant Gigabit fiber connections as well as dual single-mode fibrechannel connections to extend the facility's storage area network (SAN).

Compute Resources: Rapid advancements in imaging technology have provided researchers with the ability to produce very high-resolution, time-varying, multidimensional data sets of the human brain. The complexity of the new data, however, requires immense computing and storage capabilities. To meet the computational requirement, the NRB Facility houses the following high-performance computing (HPC) clusters:

- a 306-node Oracle V20z cluster. Each compute node has dual 2.4GHz AMD Opteron processors with 8GB of memory (612 cores total)
- an 80-node Oracle X2200 M2 cluster. Each compute node has dual 2.2GHz quad-core AMD Opteron processors and 16GB of memory (640 cores total)
- a 416 node HP ProLiant SL2x170z G6 cluster. Each compute node contains dual quad-core 2.66GHz Xeon 5500 processors and 24 gigabytes of memory (3,328 cores total)

To augment the facility's cluster resources, a group of 8 HP DL580 G7 32-core 2.4GHz X7550 machines, each with 256GB RAM, provide the high-memory computing requirements needed for biomedical applications, particularly gene sequencing.

Storage Resources. The NRB facility is architected using a fault-tolerant, high-availability systems design to ensure 24/7 functionality. To complement its computational systems, the laboratory uses high performance network attached storage (NAS) and SAN technologies to accommodate current and projected storage requirements. The facility’s current capacity is approximately 4 petabytes of online and offline storage.

To meet the extensive I/O demands of the laboratory’s HPC clusters and address the bottlenecks inherent in traditional NAS technology, the facility has deployed three EMC-Isilon parallel storage clusters, with a combined capacity of 1.5 petabytes. These clusters accommodate a variety of network filesystem protocols including NFS, Samba and iSCSI. Each modular, self-contained Isilon storage node contains a standalone fileserver with both hard disk and solid-state drives, processors, memory, and network interfaces. As additional nodes are added, all aspects of the cluster scale symmetrically, including capacity, throughput, memory, and fault tolerance. Each storage node is wired using dual 10 Gigabit Ethernet connections in order to provide maximum throughput to the computational resources.

The SAN hardware infrastructure is comprised of an SGI TP9400 & TP9500 storage arrays, Oracle 3510 & 7410 storage arrays, dual robotic tape silos, and a full complement of Brocade fibrechannel switches, providing 200 terabytes of fault-tolerant disk storage. Alternate paths exist throughout the fabric so that no single point of failure exists, guaranteeing access to critical data and processing power. The NRB facility utilizes two tape silos, a Storagetek SL8500 and a Quantum i6000 with a combined capacity of approximately 2.5 petabytes, to store mirrored copies of the facility's online, spinning-disk data. The i6000 tape silo is housed in the Reed data center, providing a secondary backup source and, owing to physical separation, comprising an element of a disaster recovery plan.

Additional Resources: The NRB Facility houses over 100 additional servers that provide the basis of its Enterprise-grade infrastructure. Basic services including DNS, DHCP, and SMTP relays are all deployed in redundant pairs. Authentication is handled using Active Directory, with performance, security, and failsafe best-practice considerations in mind. The facility also contains a ten-node VMWare vSphere cluster, allowing for rapid deployment of non-critical services as well as dedicated development and Q&A environments. The facility employs two Juniper hardware load balancers that split TCP/IP traffic between multiple, identical servers. Aside from load balancing generic network traffic, the units accelerate SSL communication, which is particularly important in transferring bulk amounts of sensitive research.

Postproduction Suite: The NRB Facility has a format and resolution-independent postproduction suite with A/V capture equipment and multiple video decks, including a Sony DSR 80 and a UVW 1800, capable of playing and recording in digital, component, Y/C and composite video. For audio, the suite has a Sony V77 sound processor, a 16-channel Mackie mixer, a 120-watt Crown amplifier and a JBL surround speaker package. In addition, the suite utilizes a 16-channel A/D Sierra router, a Miranda A/D converter and a DPS transcoder to facilitate video and audio signal routing. This equipment is connected to the Reality Monster described above for video and audio capture of real-time 3-D content processed by the supercomputer. Uncompressed content creation is done with AJA’s HD-capable digital disk recorder. To complement this hardware, the laboratory utilizes a variety of professional 3D and motion graphics packages, including Maya, Lightwave, and the full Adobe suite. The NRB Facility is also capable of virtual reality content creation to complement the visualization and stereoscopic capabilities of the DIVE, discussed below.

Network Resources: The NRB Facility intranet consists of 100baseT, Gigabit and 10 Gigabit Ethernet as well as an IEEE 802.11n compliant wireless network. Two Cisco Catalyst 3560G units and three

Enterprise-grade Cisco Catalyst 6500 Layer 3 switches provide redundant routing and non-blocking switching from the outside world to and from public-facing services, end-user workstations, and the network's core. A Juniper MX960, which is capable of handling 5.12 Terabytes/sec of traffic, connects the compute clusters to the Isilon storage, separating them as much as possible the rest of the network in order to reduce latency and increase throughput. The facility's routers and twenty Juniper switches use the Open Short Path First protocol to provide fast and fault-tolerant routing. System configurations for networking devices, as well as kernel-level parameters for Linux clients, are highly tuned to provide near line-level rates.

The facility is connected to the Cenic backbone of Internet2 via dual fiber Gigabit lines and utilizes a Cisco Firewall Services Module for edge network security. Both software-based PPTP and hardware-based SSL Virtual Private Network communications are provided for remote productivity and collaboration via encrypted communication.

Data Immersive Visualization Environment (DIVE): The DIVE features a 12' 150-degree floor-to-ceiling curved screen, on which real-time computer graphics, high definition video, stereoscopic 3D visualizations, or even simple slideshows are projected. The space provides investigators with the unique ability to visually "step inside" their data and analyze it in new ways. The projection system of the DIVE is comprised of a spherical hard-shell screen and three ceiling-mounted 3-chip DLP active stereo capable projectors, each rated at 5000 ANSI Lumens with a native 1280X1024 SXGA resolution. The projectors support optical blending of 12.5%, digital image warping and CLO, or constant light option, to ensure that image quality is maintained throughout the array. Two visualization workstations, each with dual NVIDIA graphics cards, drive these projectors, producing a 3840X1024 immersive display. A sophisticated A/V matrix along with an AMX remote control system facilitate audio and video routing from the DIVE to the conference room or other displays throughout the facility.

Magnetic Resonance Imaging Core Laboratory:

The Bruker Biospin 7.0 Tesla 30 cm clear bore MRI/MRS system is located in a 535 square foot space in the UCLA Ahmanson-Lovelace Brain Mapping Center. Three gradient systems are available: 1) a 200 mm inner diameter with a maximum gradient strength of 200 mT/m; 2) a 116 mm inner diameter with a maximum gradient strength of 400 mT/m, and 3) a 60 mm inner diameter with a maximum gradient strength of 950 mT/m. A variety of radio frequency volume coils and surface coils are available for use with these gradient systems, including three birdcage transmit/receive coils with inner diameters of 18mm, 35mm and 72mm. The instrument is capable of the full spectrum of modern neuroimaging including structural MRI, functional MRI, perfusion MRI, diffusion tensor MRI, and multinuclear MR spectroscopy. While the instrument is optimized for neuroimaging studies of rodents, it is also capable of imaging other body areas in rodents, including the heart and visceral organs. Imaging of postmortem tissue samples is also feasible. Full physiological monitoring is available including core temperature control and monitoring of heart and ventilation rate, end-tidal PCO2 and (non-invasive) blood pressure. A surgical suite, which includes a surgical microscope and a downdraft air exhaust table, is located in the adjoining room. The surgery and magnet rooms are equipped with isoflurane gas anesthesia equipment. A dedicated Linux workstation operating the Bruker Paravision software is available for offline image and spectroscopy processing. The 7.0 T 30 cm MRI Laboratory is available for use by UCLA-affiliated investigators who have research studies that require imaging of small animals, various phantoms and postmortem tissues. Operation and maintenance costs are recovered through user fees. From 8 AM to 6 PM, user fees are $200/hour. From 6 PM to 8 AM, user fees are the lesser of $125/hour (for scans 4 hours or less) or a capped $500 total overnight charge for up to 14 hours.

Description of Institutional Environment

UCLA, which ranks among the nation's top research universities, provides an excellent environment for all aspects related of the proposed research. The university is organized into a hierarchy of centers, institutes, departments and laboratories, each of which offers unique facilities that together form a strong network of research, educational and collaborative opportunities to provide an outstanding environment for career development and advancement. State-of-the art image acquisition and analysis facilities render UCLA particularly suited for career enhancement in the field of neuroimaging.

The Center for the Health Sciences at UCLA provides the most advanced medical technologies and cutting-edge research programs available. The David Geffen School of Medicine at UCLA is ranked ninth in the

country in NIH research funding and third for research dollars from all sources. The Brain Research Institute (BRI) is another organization that spans 26 different academic departments at UCLA. This institute serves to unite the highly diverse UCLA neuroscience community by initiating and fostering interdepartmental cooperation in research and education. The BRI's mission is to increase understanding of how the brain works, how it develops and how it responds to experience, injury and disease using multidisciplinary efforts to understand the nervous system at multiple levels with diverse technologies. In addition to the many training and collaborative opportunities provided by the BRI, which will be available to me through my position at the Department of Neurology, the BRI and the Neuropsychiatric Institute (NPI) offer the NPI Grand Rounds and the Joint Seminars in Neuroscience weekly. Internationally renowned speakers in the field are invited to present at these events.

The Department of Neurology within the David Geffen School of Medicine at UCLA possesses its own well-established research programs. These programs cover brain mapping and neuroimaging, and many other research agendas pertaining to neurological, neurosurgical and psychiatric populations. This department has been ranked #1 or #2 in NIH funding since 2002 and is also richly endowed with philanthropic donations. The Department of Neurology maintains strong collaborative ties with the NPI and most neurology faculty are also members of the BRI. Importantly, the Department of Neurology houses the ALBMC, which will provide the important facilities for this proposal as described above. Intellectual interactions and technical expertise are widely available in this laboratory environment, which includes several other key faculty members and a large technical and administrative staff.

Research at the Ahmanson-Lovelace Brain Mapping Center is also particularly relevant to the research and career goals described in this proposal. Research programs include refining and validating tools to integrate neuroscientific information across methods, populations, laboratories and species to promote a unified and standardized model of the working brain. This center provides training to students and colleagues, as befits a program within the School of Medicine, to better understand human neurological, neurosurgical and/or psychiatric disorders. A weekly seminar is provided that presents research related to these topics in an informal setting. In the past, I have presented at this seminar and with the opportunity to do so in the future, will benefit from the valuable feedback provided by Brain Mapping faculty, students and collaborators. The Brain Mapping Center is an outstanding environment for promoting career development in the field of neuroimaging research. As described above, it is among the most sophisticated image acquisition and image analysis neuroimaging laboratories in the country. Scanner access, computer resources, network resources and expertise will be readily available to me in this environment.

Overall, UCLA offers a fertile and productive research environment for established as well as junior scientists. The facilities and resources at UCLA are world class with several libraries and extensive computing facilities. The training opportunities are vast, with many focused programs in different departments that are accessible to developing scientists such as myself. Few other locations in the world offer the exceptional computer science-based image analysis technologies and imaging facilities of the ALBMC. In short, there is no better place to complete this proposal.

MAJOR EQUIPMENT

University of California, Los Angeles
As a premiere research institution, UCLA has cutting-edge facilities and technologies available for use by faculty and staff named in this application. Access to these facilities is greatly facilitated by the highly interactive and collaborative culture at our institution.

UCLA Core facilities, all of which are readily available for this proposal:

UCLA Informatics Center for Neurogenetics and Neurogenomics (ICNN)

UCLA Department of Medicine Statistics Core (DOMStat)

UCLA Semel Institute Biostatistics Core (SIStat)

UCLA Brain Mapping Core for Neuroimaging

Mitochondrial function / Synaptosome Core

Other within UCLA:

Microscopy and morphometric equipment: One Zeiss Axioplan II photomicroscope equipped for brightfield, differential interference contrast (DIC), and fluorescence illumination, with digital photography and storage (Axiovision), and computer controlled stage (x and y axis) and computer controlled z axis. Morphometric image analysis systems, Stereo Investigator and Neurolucida by MicroBrightfield Inc.. Consortium member with unlimited access to a Zeiss Scanning Confocal Laser Microscope
Tissue culture and general lab equipment: 3 tissue culture hoods, 2 incubators, liquid nitrogen storage tanks, Betaplate, Leica vibroslicer, PCR machine, Sorval centrifuge, Beckman ultracentrifuge, spectrophotometer, Revco Ultralow freezer, incubators, Olympus spin disc confocal with motorized stage, and Olympus fluorescence microscopes, a cryostat for tissue sectioning. Core facilities include a dark room for film development. The Neurobiology Core facility has an electron microscope. The UCLA Flow Cytometry core Facility is located across the street from RB1. An irradiator on the B floor of CHS is also available with an annual charge. Core Real Time PCR facilities are located in the Gonda building, adjacent to NRB1.
Surgical equipment: Two Zeiss operating microscopes with floor boom stands, video cameras and monitors. Two Kopf small animal stereotaxic devices with adapters for mouse. Two gas (isoflurane) anesthesia devices of veterinary grade quality with adapters for mouse and use with stereotaxic equipment. A comprehensive supply of high quality microsurgical instruments. Small autoclave for instruments.
In the Life Science Building: slide scanner, high quality color printers, machine shop and technical support in electronics. Leica RMXA compound brightfield/darkfield fluorescence microscope and color video camera, Leica dissection microscope, cryostat and rotary and sledge microtomes; spectrophotometer; two Zeiss operation (dissecting) microscopes; laminar flow hood; regulated CO_2 and low-oxygen incubators for tissue culture; autoclave; inverted phase microscope, Beckmann CS15-R refrigerated centrifuge, four thermal cyclers, ABI7300 real time PCR machine, shaker baths, incubators, hybridization ovens, gel documentation system, Speedvac. Behavioral testing apparatus: Accuscan hotplate, open field apparatus, elevated plus maze, water baths.

UCLA Intellectual and Developmental Disabilities Research Center (IDDC) Core services in confocal microscopy, image analysis. Brain Research Institute (BRI) core services in histology, electron microscope access, confocal microscopy and imaging.

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Lastly, I have presented as an invited speaker at numerous scientific meetings about our research publications, since January 1, 2021 this includes (but is not limited to): Americas Committee for Treatments and Research in Multiple Sclerosis (ACTRIMS) 2/25/21; Organization for the Study of Sex Differences (OSSD) 5/3/21; ACTRIMS Young Investigator Annual Meeting 5/28/21; Federation of Clinical Immunology Societies (FOCIS) 6/8/21; MSXchange / Montreal 11/5/21; International Society of Neuroimmunology (ISNI) 11/10/21; Nancy Davis Race to Erase MS 11/12/21; Alberta MS Network Seminar Series 1/20/22; Neuroimmunology Conferences of Stanford University 4/18/22; ACTRIMS Young Scientist Annual Meeting 4/20/22; Organization for the Study of Sex Differences (OSSD) 5/3/22; Ohio State Univ. Grand Rounds 5/17/22; American Aging Association Annual Meeting 5/20/22; Precision Medicine World Conference (PMWC2022) 6/30/22; Americas School of Neuroimmunology (ASNI) 7/12/22.

Zero papers have been retracted. The only Erratum in my career was misspelling of a middle author’s name in our Brain paper in 2018.

Mentoring, Service, and Inclusion

1) A description of commitment and dedication to mentorship and training in neuroscience research.

My track record which shows longstanding and recent commitment and dedication to mentorship and training in neuroscience (neuroimmunology and neurodegeneration) research:

At UCLA, I have mentored 12 postdoctoral fellows in my lab, 10 Ph.D. graduate students in my lab, 8 Ph.D. graduate students in other labs where I was co-mentor or a member on their PhD committees, 11 graduate students in my lab in non-Ph.D. programs, 67 UCLA undergraduates in my lab (with an average of 3 years each, with several working full time in one gap year after graduation), 2 nonUCLA undergraduates in my lab in summers, and 8 high school students in my lab in summers (often for 2 summers each). There would have been even more, but in March 2020 undergraduates and high school students were not allowed in labs at UCLA due to COVID pandemic safety rules. That said, graduate students and postdocs were allowed to be in the lab at different locations and times, with other work done remotely. Fortunately, all levels of trainees have fully returned to the lab, with masks, vaccinations, and COVID testing. I have also served as a faculty mentor to 7 junior faculty. As the UCLA MS Program Director, I recently envisioned and captured donor funding, led a national recruitment search, and worked with the UCLA Dept of Neurology Chair and West Los Angeles Veteran's Administration Chair to hire three MS junior faculty since 2018. All three were recruited from elite institutions (Harvard, Stanford, Penn).

I have worked with my research trainees to develop their careers. My trainees have received 50 awards, including 4 NIH F31 NRSA awards for graduate students and 4 National MS Society Postdoctoral Fellowships, a National Science Foundation Fellowship to teach science classes in predominantly Latin American high school and elementary schools, 19 training awards on the UCLA Laboratory of Neuroendocrinology NIH training grants(T32 HD007228), and 7 training awards on the UCLA Brain Research Institute (BRI) training grant. Over 90% of my peer reviewed research articles have had at least one trainee as a co-author. My postdoctoral fellows and graduate students have received numerous travel awards to present at meetings and won best poster awards at international, national, and UCLA competitions. These awards, papers, and presentations have propelled their careers across the spectrum: high school students getting accepted to top ranked universities; undergraduates getting accepted to Ph.D. programs, medical schools, and M.D., Ph.D. programs; graduate students getting desired postdoctoral fellowships; postdoctoral fellows getting positions as academic faculty or in the pharmaceutical industry; and junior faculty getting independent funding and tenure (Associate Professor). Space limitations do not allow listing of each.

In addition, I have given lectures to UCLA Dept of Neurology residents each year for over two decades and have been a formal lecturer in two UCLA classes each year in "Controversies in Clinical Trials" 2011-2020 and in "Neuroendocrinology of Reproduction", 2015-2020. I have participated in numerous CME courses, one of which was the NIH/ORWH/FDA sponsored Sex and Gender Course in Immunology (in 2019). This is a guide to teach researchers how to study sex as a biologic variable (SABV).

2) A description of my ongoing and planned outreach and mentoring activities, to enhance workforce diversity in the applicant's laboratory NOT-OD-20-031.

Track record in promoting diversity:

My background complies with NOT-NS-21-049 "NIH Research Grant (RO1) Applications from Individuals from Diverse Backgrounds, Including Under-Represented Minorities." I meet criteria in three categories:

1. Being female.
2. Growing up in the small rural town of Hennessey, Oklahoma (around 2,000 people) with a zip code (73742) that is listed by NIH as a low socio-economic region.
3. My mother was from eastern Oklahoma (Okemah) and was part Native American.

Leadership in advancing diversity:

1. As President of the Organization for the Study of Sex Differences, I established a new committee "Equity, Diversity, and Inclusion (EDI)", 2020.
2. ACTRIMS Annual Young Scientist Forum, Panelist on Advancing Diversity, 2020-present.
3. Laboratory of Neuroendocrinology, Lecturer Summer Series for Minority Students, 2011-2013.

Publications in advancing diversity:

1. Klein, R. S., Voskuhl, R., Segal, B. M., et al. Speaking out about gender imbalance in invited speakers improves diversity. ***Nature Immunology***, 18:475-478, 2017.

2. Voskuhl, R., Klein, S. Sex is a biological variable - in the brain too, ***Nature***, 568:171, 2019

Mentoring Minorities: Women as minorities in science.

1. Over 70% of all postdoctoral fellows, graduate students, undergrads, and high school students mentored by me have been female. My current graduate student is female (Ashley Loureiro, 2022-present), with yet another prospective female graduate student doing a rotation in the fall 2022 quarter. My other current graduate student is a Latin American male (Diego Cortez-Delgado).
2. I was chosen by an All Girls high school (Marymount High School) in Los Angeles to serve as a mentor and role model for women in leadership roles in the STEM field. I worked with Marymount to pioneer their summer internship program for high school girls from 2012-2017. The “SAILL Internship Program” grew exponentially in the first 5 years after its conception, starting with 2 girls per summer and expanding over the years to approximately 50 per summer. This introduces high school girls to STEM fields through experience in research labs, clinics and other professional work settings. It is now Marymount High School’s flagship program.

Mentoring Minorities: Ethnic minorities in science:

1. Laurie Morales, undergraduate independent research project, plus worked as lab asst. for a gap year before medical school. She was coauthor on several papers, one as first author in the *Proceedings of the National Academy of Sciences* (2006), functioning at the level of a graduate student, (2002-2006), Latin American.
2. Francisco Sandoval, undergraduate independent research project and worked as lab asst. for a gap year before going to a Master’s Program, (2007-2011). He obtained a Minority Biomedical Research Fellowship – Research Initiative for Scientific Enhancement (2011), Latin American.
3. Marina Ollervides-Ziehn, graduate student in Voskuhl lab (2008-2012). She received an NIH training grant fellowship from LNE (2009-2010), and was funded by the National Science Foundation to teach science classes in predominantly Latin American high school and elementary schools (2011-2012). She received her Ph.D. in in 2012, Latin American.
4. Rory Spence, graduate student in Voskuhl lab (2009-2013). He received NIH training grant fellowships from MCIP (2008-2011) and LNE (2011-2013), received Ph.D in 2013, Latin American.
5. Darian Mangu, undergraduate independent research project, (2015-2018), African American.
6. Emma Difippo, undergraduate independent research project, (2013-2015), Latin American.
7. Kevin Herrera, undergraduate independent research project, (2016-2018), Latin American.
8. Michelle Rivera, undergraduate independent research project, (2020-present) Latin American.
9. Diego Cortez-Delgado, graduate student, (2021-present) Latin American.

Outreach and mentoring activities to enhance diversity:

I hold leadership positions in two international organizations which focus on advancing diversity.

First, as President of the Organization for the Study of Sex Differences (OSSD), I established a new committee in 2020, the Equity, Diversity, and Inclusion (EDI) Committee. I tasked this committee with insuring EDI in all OSSD activities. The EDI has input during monthly executive meetings regarding how to enhance diversity via 1) the Program Committee so that diversity characterizes our annual meeting, 2) the Awards Committee so that award recipients include those of diverse backgrounds. At OSSD’s annual meeting in May 2021, my first annual meeting as President, more awards were presented to under-represented minorities (URM) than ever before, 3) the Nominations Committee increased the number of URM that run for OSSD Officer positions, and 4) the Membership & Communications Committee increased diversity in OSSD membership through social media. Our 2022 annual meeting was the most diverse to date. Thus, I have raised awareness of EDI in all OSSD activities. Our Jobs Board is where OSSD members reach out to a diverse applicant pool to hire, and URM candidates can post their CVs to potential OSSD faculty. OSSD studies sex differences due to sex hormones and sex chromosomes, as well as social and environmental factors. OSSD welcomes the LGBTQ+ community to its activities as we pursue complex issues related to sex and gender.

The second leadership position is with Americas Committee for Research and Treatment in MS (ACTRIMS) Annual Young Scientist Summit, as a Panelist on Advancing Diversity. As a faculty member on this panel each year, I get to meet and listen to URM trainees as they navigate the challenges they encounter. Being together and sharing experiences and ideas provides connections and a support system. Possible management solutions to problems they encounter are discussed leveraging how other’s experiences. Working with this group will also hopefully attract more URM trainees to my lab.

3) A description of planned activities during the grant period.

Promoting equitable scientific environments: I have and will continue to serve on UCLA graduate school admissions interview panels, taking into account the desire for a diverse class. I will draw attention to

performance by some that is exceptional in light of their disadvantaged background. I will continue to Chair and be a Member of panels for faculty recruitment and retention, as well as for selection of endowed chairs at UCLA. I will continue to mentor junior faculty, postdoctoral fellows, graduate students, undergraduates, and high school students, often either females, other under-represented minorities, or economically disadvantaged backgrounds, so they can reach their full potential. This will include encouraging them to apply for awards and submit posters and standing presentations at national and international meetings. When they succeed, it is not only for them, but also for others who identify with them. I will continue to co-author publications to advance diversity in selection of speakers for scientific meetings, and I will continue to serve on panels that select who speaks at meetings, to insure balance and diversity. I will continue to take advantage of support programs and diversity training offered by UCLA's EDI Office. Training offers time to reflect on one's own unintentional bias and increases awareness of impacts of our actions on others. I have often looked around the room at our lab meetings and been truly surprised at how diverse we are. Backgrounds are so different, yet these cultural differences fade, becoming invisible in the shared enthusiasm for the scientific discussion. It seems like such a "small world after all", not only at Disneyland Los Angeles, but also in my lab.

4) A description of significant contributions of service to the research community (e.g. study section service).

My track record of service to the research community:
National MS Society (NMSS), ad hoc reviewer of pilot grants, 1996-2010.
National Institutes of Health (NIH) Task Force on Women's Health 1997.
National MS Society Task Force on Gender and Autoimmunity 1997.
National Institutes of Health Study Section, ad hoc reviewer (BDCN), 1999-2002.
National MS Society Advisory Committee on Fellowships 2000-2002.
International ad hoc reviewer for French MS Society, 2002-present; Australian MS Society, 2003-present. Dutch MS Society, 2013, Ireland MS Society Medical Research Council, UK, 2017.
National Institutes of Health Study Section, chartered member and ad hoc reviewer (BDCN-4), 2002-2006.
National Multiple Sclerosis Society Scientific Advisory Peer Reviewer, Study Section A, 2007-2011.
Federation of Clinical Immunology Societies (FOCIS) Steering Committee, 2007-2008.
American Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Steering Committee, 2007-2012.
Scientific Review Committee for the joint meeting of the American (ACTRIMS), European (ECTRIMS) and Latin American (LACTRIMS) Programs, 2008.
Immune Tolerance Network (ITN) Steering Committee, 2009-2011.
National Institutes of Health Study Section, ad hoc reviewer, (NSD-C), 2009-2012.
Congressionally Directed Medical Research Program, Integration Panel, Department of Defense, 2013-2014.
National Institutes of Health Study Section NSD-C / NSD-A, ad hoc, 2013-2017
Organizing Committee, Organization for the Study of Sex Differences (OSSD), 2016-2018.
National Institutes of Health Study Section Ad hoc: HAI, 2018-2019.
National Institutes of Health Study Section ZNS1 SRB-H 12: R35 NIH grant reviews, 2019.
National Institutes of Health grant review: Sex and gender RFA: Special Emphasis Panel ZRG-1 The Intersection of Sex and Gender Influences on Health and Disease. 2020.
National Institutes of Health Study Section, ad hoc reviewer, CNBT, 2021.
National Institutes of Health Special Emphasis Panel review of Program Project grants, NIAID, 2022.
ACTRIMS, Advisory Committee, 2015-present.
ACTRIMS Annual Resident Summit (abstract reviewer and panelist), 2017-present;
ACTRIMS Annual Young Scientist Forum (invited speaker future MS therapies), 2018-present.
Nancy Davis Center Without Walls: Vision Setting & Patient Forum Panels UCLA site PI, 2019-present.
Department of Defense (DOD) Congressionally Directed Medical Research Program's (CDMRP) Multiple Sclerosis Research Program (MSRP), Programmatic Panel, 2020-present.
Organization for the Study of Sex Differences (OSSD), 6 year commitment: President-Elect, 2018-2020; President, 2020-2022; Past-President, 2022-2024.
Deutsche Forschungsgemeinschaft (DFG), German Federal Government for Excellence Cluster Initiatives, Clusters of Excellence Advisory Board Member, 2021-present.
Americas School of Neuroimmunology (ASNI), Faculty, 2022; International Society of Neuroimmunology (ISNI) Invited Speaker 2021.

Foreign Justification

Our collaborator Dr. Friedemann Paul of Univ. of Berlin, Germany transferred an existing database of multiple sclerosis and match healthy controls' clinical and imaging data to UCLA over a year ago. We will use the database that we now have in place at UCLA to conduct the research as described in the proposal (see Dr. Paul Letter of Support). This represents a scientifically useful dataset that Dr. Paul was willing to share with the UCLA team at no cost given that our scientific interests align with finding region-specific and sex-specific effects in multiple sclerosis. Dr. Paul is fully funded by German government, and as such no salary is requested from this proposal.

The collaboration between UCLA and Univ of Berlin began in the form a joint grant from the National Multiple Sclerosis Society (U.S.A.). The grant was to Univ. of Berlin with UCLA a subcontract. While the pilot funding ended a few years ago, collaboration between the two academic teams continued as a publication (Voskuhl, R.R., Patel, K., Paul, F., Gold, S.M., Scheel, M., Kuchling, J., Cooper, G., Asseyer, S., Chien, C., Brandt, A.U., Meyer, C.E., MacKenzie-Graham, A. Sex Differences in Brain Atrophy in Multiple Sclerosis. *Biology of Sex Differences*, 11(1):49. PMID: PMC7456053, 2020).

Here we are continuing to leverage this valuable resource and scientific collaboration in light of mutual research goals through further use of the larger, longitudinal database as described herein.

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: Dr. First Name*: Rhonda Middle Name R. Last Name*: Voskuhl Suffix: MD

Position/Title*:	Professor
Organization Name*:	The Regents of the University of California, Los Angeles
Department:	Neurology
Division:	David Geffen School of Medicine
Street1*:	635 Charles E. Young Drive South
Street2:	475D Neuroscience Research Bldg 1
City*:	Los Angeles
County:	Los Angeles County
State*:	CA: California
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	90095-7334

Phone Number*: (310) 206-4636 Fax Number: (310) 206-9801

E-Mail*: rvoskuhl@ucla.edu

Credential, e.g., agency login: VOSKUHL2

Project Role*: PD/PI Other Project Role Category:

Degree Type: MD Degree Year: 1986

Attach Biographical Sketch*: File Name: R35_Biosketch_Voskuhl1071243835.pdf

Attach Current & Pending Support: File Name: NIH_OS_Voskuhl1071122820.pdf

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Yuichiro Middle Name Last Name*: Itoh Suffix: PhD

Position/Title*: Research Scientist
Organization Name*: The Regents of the University of California, Los Angeles
Department: Neurology
Division: David Geffen School of Med
Street1*: 710 Westwood Plaza
Street2:
City*: Los Angeles
County: Los Angeles County
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 90095-7334

Phone Number*: 310-825-9340 Fax Number:

E-Mail*: yito@mednet.ucla.edu

Credential, e.g., agency login: YUICHIROITO2

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: PhD Degree Year: 2001

Attach Biographical Sketch*: File Name: Bioketch_Itoh1071123011.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Jin Middle Name Last Name*: Zhou Suffix: PhD

Position/Title*: Associate Professor
Organization Name*: The Regents of the University of California, Los Angeles
Department: Medicine
Division: GIM & HSR
Street1*: 1100 Glendon Avenue
Street2: Suite 850
City*: Los Angeles
County: Los Angeles County
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 90024-3503

Phone Number*: 310-794-3111 Fax Number:

E-Mail*: JinZhou@mednet.ucla.edu

Credential, e.g., agency login: jinjinzhou

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: PhD Degree Year: 2011

Attach Biographical Sketch*: File Name: Biosketch_Zhou1071186260.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Allan Middle Name Last Name*: MacKenzie-Graham Suffix: PhD

Position/Title*: Associate Professor
Organization Name*: The Regents of the University of California, Los Angeles
Department: Neurology
Division: David Geffen School of Med
Street1*: 635 Charles E. Young Drive
Street2: NRB 225Z2
City*: Los Angeles
County: Los Angeles County
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 90095-1769

Phone Number*: 310-267-5153 Fax Number: 310-206-7282

E-Mail*: amg@ucla.edu

Credential, e.g., agency login: MACKENZIEG2

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: PhD Degree Year: 2006

Attach Biographical Sketch*: File Name: Biosketch_MacKenzie_Graham1071243205.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Prabha Middle Name Last Name*: Siddarth Suffix: PhD

Position/Title*:
Organization Name*: The Regents of the University of California, Los Angeles
Department: Semel Institute/Psychiatry
Division: Psychiatry
Street1*: 760 Westwood Plaza
Street2:
City*: Los Angeles
County: Los Angeles County
State*: CA: California
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 90095-1759

Phone Number*: 310-825-4295 Fax Number:

E-Mail*: psiddarth@mednet.ucla.edu

Credential, e.g., agency login: siddarth2

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: PhD Degree Year: 1988

Attach Biographical Sketch*: File Name: Biosketch_Siddarth1071186552.pdf

Attach Current & Pending Support: File Name:

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Rhonda R. Voskuhl, M.D.**

eRA COMMONS USER NAME (credential, e.g., agency login): VOSKUHL2

POSITION TITLE: **Professor of Neurology, Jack H. Skirball Chair in Multiple Sclerosis Research**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Phillips University, Enid, OK	BS	05/1982	Biology
Vanderbilt Medical School, Nashville, TN	MD	06/1986	Medicine
Univ. of Texas Southwestern, Dallas, TX	Resident	06/1990	Neurology
NIH, Neuroimmunology Branch, Bethesda, MD	Fellow	04/1995	Neuroimmunology

A. Personal Statement

I have devoted my career to translational research based on clinical observations in multiple sclerosis (MS) patients, from disentangling mechanisms in preclinical models to designing clinical trials of new treatments in a "Bedside to Bench to Bedside" approach. My lab was the first to use a cell-specific and region-specific transcriptomics approach to investigate the molecular basis for disability-specific disease progression in MS models. We also used MS postmortem tissues to validate genes identified in MS models. Collaboration with Dr. MacKenzie-Graham included neuroimaging of disability-specific regional gray matter atrophy in MS patients. I am an internationally recognized expert in sex differences research, demonstrating protective effects of estrogen and testosterone treatment in MS models, which I translated to 4 clinical trials in MS. At the lab bench, I was the first to show that estrogen receptor (ER) alpha and ER beta ligands were protective in EAE, acting through distinct mechanisms. I showed that ER beta ligation induced remyelination through direct action on oligodendrocytes, while downregulating innate immunity in central nervous system (CNS) by acting on microglia/macrophages, and that ER alpha ligation targeted astrocytes. I also discovered distinct roles for sex chromosomes in the immune system and the CNS in the MS model. Most recently, my lab began investigating the role of brain aging in worsening disability progression. My overarching mission is to use a region-specific, cell-specific, and sex-specific approach to identify novel treatment targets for females and males in MS preclinical models, then translate these findings to the clinic by designing trials to halt and repair of neurodegeneration, with enrollment optimally tailored for MS women and men.

My expertise in neuroimmunology, neuroscience, and sex differences is shown by comments/reviews:

Voskuhl, R. Itoh, Y. The X Factor in Neurodegeneration. **Journal of Experimental Medicine,** invited, minor revision, 2022.

Killestein, J., Schoonheim, M.M., Voskuhl, R., B-cell depletion and COVID-19 severity in MS. **Neurology,** 97:885, 2021.

Voskuhl, R. The effect of sex on MS risk and disease progression. **Multiple Sclerosis.** 26(554), 2020.

Voskuhl, R., A new cell subtype that confers neuroprotection. **Nature Immunology**, Nov. 3, 2020.

Voskuhl, R., Klein, S., Sex is a biological variable - in the brain too. **Nature**, 568 (7751):171, 2019.

Voskuhl, R., Wang, H., Elashoff, R. Why use sex hormones in relapsing-remitting multiple? **Lancet Neurology**, 15:790, 2016.

Voskuhl, R., Gold, S. Sex-related factors in multiple sclerosis susceptibility and progression. **Nature Reviews Neurology,** 8:255, 2012.

Ongoing projects and recently completed projects I would like to highlight:

NIH RO1NS109670 **Voskuhl (PI)** 12/01/18-11/30/23

Neuroprotection in MS: A Cell-specific and Region-specific Transcriptomics Approach

Goal: Understand neurodegenerative mechanisms in preclinical models of MS.

NIH RO1NS096748 **Voskuhl (PI)** 9/01/16-8/31/21

Parental Imprinting of the X Chromosome: Effects on Neurodegeneration

Goal: Determine effects of X imprinting on gene expression in the CNS during EAE.

The Conrad Hilton Foundation #18394 **Voskuhl (PI)** 7/1/19-6/30/22
Disability-specific disease modifying treatments (DMTs) in multiple sclerosis (MS)
Goal: Investigation of disability-specific treatments in EAE, MS, and brain aging.
NIH R21NS121806 **MacKenzie-Graham (PI)** 04/01/21-03/31/23
The Mechanism of Gray Matter Atrophy in Experimental Autoimmune Encephalomyelitis
Goal: To determine the role of oxidative stress in gray matter atrophy in EAE.
Role: Co-Investigator
NIH RO1NS112287 **Peter Clark (PI)** 7/1/19-6/30/24
Non-invasive Imaging of Brain Infiltrating T lymphocytes in a Mouse Model of EAE with PET
Goal: To image inflammation in vivo in EAE.
Role: Co-Investigator

My background complies with the NIH definition of an under-represented minority (NOT-NS-21-049). I meet criteria in three categories: 1) Being female, 2) Growing up in the small rural town of Hennessey, Oklahoma (around 2,000 people) with a zip code (73742) that is listed by NIH as a low socio-economic region, and 3) My mother was from eastern Oklahoma (Okemah) and was part Native American. Being a women from a rural, low income location has always been very challenging. I feel strongly that people in challenging circumstances should be supported. That is why I now serve on committees to enhance diversity, and I have a strong track record of recruiting women and URM in my lab as trainees. I worked with an All Girls High School (Marymount High School) for 5 years to start and nurture their mentorship program for “Girls in STEM”. It is very successful, and it is now their flagship program. Advancing the study of inclusion of women in science and research was one of the reasons why I become the President of the Organization for the Study of Sex Differences (OSSD). OSSD supports the development of women and URMs in career development as they aim to study the effect of sex on health and disease. Within months of becoming OSSD President in 2020, I started its Equality, Diversity, and Inclusion (EDI) committee. This committee is empowered to impact all aspects of OSSD activities: social media, officer nominations, annual meeting program, travel and poster awards, to name a few. In my recent tenure as OSSD President, I strengthened relationships with the Society for Women’s Health Research (SWHR) and the NIH Office of Research on Women’s Health (ORWH) so that our three organizations work closer together to advance our common goal of advancing inclusion of females in the study of sex as a biologic variable (SABV) in preclinical research and clinical research to promote precision therapeutic discoveries optimal for both women and men.

B. Positions and Honors

Positions and Employment

2004-present Professor, Dept. of Neurology, UCLA, Los Angeles, CA
2000-present Director, UCLA Multiple Sclerosis Program, UCLA, Los Angeles, CA
2000-2004 Associate Professor, Dept. of Neurology, UCLA, Los Angeles, CA
1995-2000 Scientific Director, UCLA Multiple Sclerosis Program, UCLA, Los Angeles, CA
1995-2000 Assistant Professor, Dept. of Neurology, UCLA, Los Angeles, CA
1994-1995 Senior Investigator, Neuroimmunology Branch, NIH, Bethesda, MD
1993-1994 Research Associate, Lab of Viral and Molecular Pathogenesis, NIH, Bethesda, MD
1990-1993 Clinical Associate, Neuroimmunology Branch, NIH, Bethesda, MD

Honors

2019-Kenneth P. Johnson Memorial Lecture, ACTRIMS annual meeting 2019
2018-Berlin Institute of Health (BIH) Excellence Award for Sex and Gender Aspects in Health Research
2018-UCLA Innovation Award, UCLA Campus-wide Technology Development Group Competition for 2018
2006-Jack H. Skirball Endowed Chair in MS Research
2001-California Congressman Henry Waxman Honorary Grant
1997-Harry Weaver Neuroscience Scholar of the National Multiple Sclerosis Society (NMSS)
1995-Outstanding Young Alumna, Phillips University
1994-Public Health Service Citation for Excellence in Research, National Institutes of Health (NIH)
1991-Annual Noble Lectureship Award
1988 and 1990-Texas Neurologic Society Annual Research Award for a Neurology Resident (twice)
1982-Oklahoma College All Star Women’s Basketball Team

1982-Overall Most Outstanding Senior Award, Phillips University
1979-1982-Biology Award (1979), Chemistry Award (1980), Science Award (1982), Phillips University
1978-1982-Four year full basketball scholarship - Two year Team Captain, Phillips University

Other Experience and Professional Memberships

Department of Defense (DOD) Congressionally Directed Medical Research Program's (CDMRP) Multiple Sclerosis Research Program (MSRP), Programmatic Panel, member, 2/6/2020-present.

Member, NIH Study Section BDCN, 2002-2006; NIH Special Emphasis Panel NSD-C, 2009-2012; NIH Study Section Ad hoc: NSD-C / NSD-A, 2013-2017; HAI, 2018-2019; CNBT, 2021; Special Emphasis Panel review of Program Project grants, NIAID, 2022.

Americas Committee for Treatments and Research in Multiple Sclerosis (ACTRIMS) Steering Committee, 2007-2012: ACTRIMS Advisory Committee, 2015-present; ACTRIMS Resident Summit, 2017-present; ACTRIMS Young Scientist Summit, 2018-present.

Presidential Leadership 6 year commitment to the Organization for the Study of Sex Differences (OSSD), President-Elect, 2018-2020; President, 2020-2022; Past-President, 2022-2024; OSSD Annual Meeting Organizing Committee, 2016-2018; NIH Office of Research on Women's Health (ORWH) / FDA Office of Women's Health Sex and Gender online course, 2020.

Deutsche Forschungsgemeinschaft (DFG), German Federal Government for Excellence Cluster Initiatives, Clusters of Excellence Advisory Board Member, 2021-present.

Americas School of Neuroimmunology (ASNI), Faculty, 2022; International Society of Neuroimmunology (ISNI) Invited Speaker 2021.

Lead Principle Investigator for UCLA, Nancy Davis Center Without Walls, Race to Erase MS, 2019-present.

C. Contributions to Science: Selected peer-reviewed publications.

1. Sex chromosome effects on autoimmunity and neurodegeneration. *I was the first to show sex differences in EAE using its relapsing-remitting model* (*Annals of Neurology,* 39:724-733, 1996). Over the last decade, my research has been discussed by others in *Nature* editorials three times regarding how sex differences can lead to insights into disease. I also am first author of an editorial on the subject (*Nature*, 568:171, 2019). My lab discovered sex chromosome effects in the immune system in both the MS and lupus models. We then identified a gene on the X chromosome (*Kdm6a*) that escapes X-inactivation in CD4+T lymphocytes as a mechanism for increased susceptibility of females to autoimmune disease. Also, we published that parental imprinting of the X chromosome can lead to sex differences in autoimmunity. Focusing on the CNS, we showed that in contrast to XX conferring an increase in autoimmunity, XY confers an increase in the neurodegenerative response to the same autoimmune attack. Indeed, *my lab was the first to show an effect of sex chromosome complement in the CNS in any neurodegenerative disease model* (in 2014). See below for special recognition, commentaries, and editorial highlights of publications in this field.

a. Smith-Bouvier, D.L., Divekar, A.A., Sasidhar, M., Du, S., Tiwari-Woodruff, S., King, J.K., Arnold, A.P., Voskuhl, R.R. **(**2008) A role for sex chromosome complement in the female bias in autoimmune disease. **Journal of Experimental Medicine,** 20205(5):1099-108, PMCID: PMC2373842.

b. Du, S., Itoh, I., Askarinam, S., Hill, H., Arnold, A., Voskuhl, R.R. (2014) XY Sex Chromosome Complement, Compared with XX, in the CNS Confers Greater Neurodegeneration During EAE. **Proceedings of the National Academy of Sciences (PNAS),** 111:2806-2811. PMCID: PMC3932937.
*(Recognized in ***Lancet Neurology*** as one of the top 5 in MS for 2014).

c. Itoh, Y., Golden, L., Itoh, N., Matsukawa, M., Ren, E., Tse, V., Arnold, A.P., Voskuhl, R.R. (2019) The X-linked histone demethylase *Kdm6a* in CD4+ T lymphocytes modulates autoimmunity. **Journal of Clinical Investigation (JCI),** https://doi.org/10.1172/JCI126250, 130:3852-3863, PMCID: PMC6715385.
*(Commentary on this article in **JCI** 130:3536-3538, 2019.)

d. Golden, L.C., Itoh, Y., Itoh, N, Iyengar, S., Coit, P., Salama, Y., Arnold, A.P., Sawalha AH, Voskuhl, R.R. (2019) Parent-of-origin differences in DNA methylation of X chromosome genes in T lymphocytes. **Proceedings of the National Academy of Sciences (PNAS),** PMCID: PMC6936674.
*(Editorial Highlight of this paper "In This Issue" section **PNAS**.)

2. Basic insights into neurodegeneration. These studies used a cell-specific and region-specific transcriptomics approach to identify novel mechanisms underlying regional neuropathology in MS models and MS autopsy tissues. While this approach had been used in astrocytes during health, *my lab was the first to use a cell-specific and region-specific transcriptomics approach in any neurodegenerative disease model* (in 2018).

a. Itoh,Y. Voskuhl, R.R. (2017) Cell specificity dictates similarities in gene expression in multiple sclerosis, Parkinson's disease, and Alzheimer's disease. **PLoS One**, 12:e0181349, PMCID 5513529.
b. Itoh, N., Itoh, Tassoni, A., Ren, E., Kaito, M., Ohno, A., Y., Ao, Y., Farkhondeh, V., Johnsonbaugh, H., Burda, J. Sofroniew, M.V., Voskuhl, R.R. (2018) Cell-Specific and Region-Specific Transcriptomics in the multiple sclerosis model: Focus on astrocytes. **Proceedings of the National Academy of Sciences (PNAS)**, 115:E302-E309, PMCID: PMC5777065.
c. Voskuhl, R.R., Itoh, N., Tassoni, A., Matsukawa, M., Ren, E., Tse, V., Jang, E., Suen, T., Itoh, Y. (2019) Gene expression in oligodendrocytes during remyelination reveals cholesterol homeostasis as a therapeutic target in multiple sclerosis. **Proceedings of the National Academy of Sciences (PNAS)**, 116 (20):1-130-10139, PMCID: PMC6525478.
d. Tassoni, A., Farkhondeh, V., Itoh, Y., Itoh, N., Sofroniew, M.V., Voskuhl, R.R. (2019) The astrocyte transcriptome in EAE optic neuritis shows complement activation and reveals a sex difference in astrocytic C3 expression. **Scientific Reports**, 9:10010-22, PMCID: PMC6620300.

3. Identified the cell that mediates estrogen's neuroprotective effect *in vivo* in the MS model. Estrogens were known to be neuroprotective through actions on estrogen receptors (ERs) for decades, however which cell in the CNS mediated this neuroprotection *in vivo* remained unknown. My lab created cell-specific knock outs of ER alpha and ER beta to determine which CNS cell mediated neuroprotection *in vivo*. *My lab was the first to identify which cell is responsible for estrogen mediated neuroprotection in vivo in any neurological disease model.*
a. Tiwari-Woodruff, S., Morales, L., Lee, R., Voskuhl, R.R. (2007) Differential Neuroprotective and Anti-inflammatory Effects of Estrogen Receptor (ER) α and ER β Ligand Treatment. **Proceedings of the National Academy of Sciences (PNAS),** 104:14813-14818, PMCID: PMC1976208.
b. Spence, R., Hamby, M., Umeda, E., Itoh, N., Du, S., Bondar, G., Lam, J., Ao, Y., Wisdom, A., Cao, Y., Sandoval, F., Sofroniew, M.V., Voskuhl, R.R. (2011) Neuroprotection mediated through estrogen receptor alpha on astrocytes. **Proceedings of the National Academy of Sciences (PNAS),** 108:8867-8872. PMCID: PMC3102368.
c. Spence, R.D., Wisdom, A.J., Cao, Y., Hill, H.M., Mongerson, C., Stapornkul, B., Itoh, N., Sofroniew, M.V., Voskuhl, R.R. (2013) Estrogen signaling through ER-alpha but not ER-beta on astrocytes mediates neuroprotection during EAE and decreases astrocyte levels of proinflammatory chemokines. **Journal of Neuroscience,** 33:10924-109333. PMCID: PMC3693061.
d. Kim, R., Hoffmann, A., Mangu, D. Kavosh, R., Jung, E., Itoh, N., Voskuhl, R.R. (2018) Estrogen Receptor Beta Ligand Acts on $CD11c^+$ Cells to Mediate Protection in Experimental Autoimmune Encephalomyelitis. **Brain**, 141:132-147. PMCID: PMC5837360.

4. Clinical trials. I have translated basic findings in my lab to four Phase 2 clinical trials in MS. First, I translated my lab's preclinical finding that the estrogen of pregnancy (estriol) is anti-inflammatory and neuroprotective. *This has implications for the mechanism underlying the protection of pregnancy in MS.* Translation entailed three clinical trials (2 multisite and 1 single site). The first estriol trial showed a reduction in enhancing lesions (*Annals of Neurology).* The 16 site estriol trial showed a reduction in relapses as powered as the primary outcome for a Phase 2 trial and an improvement in cognition as an exploratory (*Lancet Neurology* and featured by a Commentary). We then mapped estriol treatment induced sparing atrophy in cerebral cortex (*Brain & Behavior,* 2018), and showed an estriol treatment mediated reduction in serum neurofilament light chain (sNfL) levels (*Ann. Clin. & Trans, Neurol*., 2022). My lab was also the *first to show that testosterone treatment is protective in EAE* (*J. Immunology*, 159:3-6, 1997). We translated this to a pilot clinical trial in MS men (*Archives of Neurology* 64:683-688, 2007, aka *JAMA Neurology*), then mapped regions of testosterone mediated sparing of gray matter atrophy in MS men (*Neuroimage Clinical,* 4:454-460, 2014*).*
a. Sicotte, N., Liva, S.M., Klutch, R., Pfieffer, P., Bouvier, S., Odesa, S., Wu, T.C.J., Voskuhl, R.R. (2002) Treatment of multiple sclerosis with the pregnancy hormone estriol. **Annals of Neurology,** 52:421-428.
b. Voskuhl, R.R., Wang, H., and the Estriol Trial Study Group (2016) Estriol combined with glatiramer acetate for women with relapsing-remitting MS: A Randomised, Placebo-Controlled, Phase 2 Trial. **Lancet Neurology**, 15: 35-46. PMID 26621682.
*(Commentary: Voskuhl, R., Wang, H., Elashoff, R. **Lancet Neurology,** 2016, 15:790-791)
c. MacKenzie-Graham, A., Brook, J., Kurth, F., Itoh, Y., Meyer, C., Montag, M., Wang, H., Elashoff, R., Voskuhl, R.R. (2018) Estriol-mediated neuroprotection in multiple sclerosis localized by voxel-based morphometry. 8(9):e01086. **Brain & Behavior,** PMCID: PMC6160650.

d. Voskuhl, R., Kuhle J., Siddarth , P., Itoh, N., Patel, K., **MacKenzie-Graham, A**. (2022) Decreased Neurofilament Light Chain Levels In Estriol-Treated Multiple Sclerosis. **Annals of Clinical & Translational Neurology,** doi:10.1002/acn3.51622. PMID: 35770318.

5. Clinical Research. I initially studied immune responses in the peripheral blood of MS patients during the hormone treatment trials where I was the PI. Then I focused on the CNS. In collaboration with Dr. MacKenzie-Graham, *we mapped 3 different MS disabilities to distinct gray matter regions, which* was highlighted by an editorial in *JAMA Neurology*. *We also showed sex differences in regional gray matter atrophy in MS patients* by comparing gray matter atrophy in female MS vs female healthy controls and by comparing male MS vs male healthy controls (to remove the confound of sex differences in healthy brain).
a. Soldan, S.S., Alvarez-Retuerto, A.I., Sicotte, N.L., Voskuhl, R.R. (2003) Th1 to Th2 immune shift in female multiple sclerosis patients treated with the pregnancy hormone estriol, **Journal of Immunology,** 11:6267-6274.
b. Gold, S., Chalifoux, S., Giesser, B., Voskuhl, R.R. (2008) "Immune Modulation and Increased Neurotrophic Factor Production in Multiple Sclerosis Patients treated with Testosterone." **Journal of Neuroinflammation,** 5:32: 1-8. PMID: PMC2518142.
c. MacKenzie-Graham, A., Kurth, F., Itoh, Y., Wang, H., Montag, M., Elashoff, R., Voskuhl, R. (2016) Disability-Specific Atlases of Gray Matter Loss in Relapsing-Remitting Multiple Sclerosis. **JAMA Neurology**, 73:944-953, PMCID: 27294295
*(Editorial highlight in same issue of **JAMA Neurology, (**2016), 73(8):910-912.
d. Voskuhl, R.R., Patel, K., Paul, F., Gold, S.M., Scheel, M., Kuchling, J., Cooper, G., Asseyer, S., Chien, C., Brandt, A.U., Meyer, C.E., MacKenzie-Graham, A. (2020) Sex Differences in Brain Atrophy in Multiple Sclerosis. **Biology of Sex Differences**, 11(1):49. PMCID: PMC7456053.

See URL for list of publications:

https://pubmed.ncbi.nlm.nih.gov/?term=%28%28rhonda+voskuhl%5BAuthor%5D%29+OR+Voskuhl+RR%5BAuthor%5D%29+OR+voskuhl+r%5BAuthor%5D&sort=date

OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 09/30/2024)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Itoh, Yuichiro

eRA COMMONS USER NAME (credential, e.g., agency login): YUICHIROITO2

POSITION TITLE: Project Scientist

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Tohoku University, Sendai, Miyagi	BS	03/1996	Molecular Biology
Tohoku University, Sendai, Miyagi	PHD	03/2001	Molecular and Cell Biology
UCLA, Los Angeles, California	Postdoctoral Fellow	11/2007	

A. Personal Statement

I have over 24 years' experience in molecular biology and genetics. In the beginning, as a graduate student, I cloned novel sex chromosome linked genes in chicken, and contributed to development of concepts regarding avian sex chromosomes, which were relatively unstudied at that time. I used methods of cytology including karyotyping of metaphases, mapping of DNA and RNA probes to chromosomes, immunohistochemistry, gene cloning and manipulation. In Dr. Art Arnold's lab at UCLA, I discovered that in birds, sex chromosome dosage compensation is ineffective, an unexpected result based on previous work where dosage compensation of the X chromosome in mammals is quite effective. The major focus of the lab was to understand the role of sex chromosomes in brain development. In these studies and others, I have utilized bioinformatics and global analysis of the transcriptome. Over last several years, working with the Voskuhl team, I have led the RNA sequencing and bioinformatics analysis using a cell-specific and region-specific approach to discover disability specific neuroprotective treatments for multiple sclerosis (MS). To this end, we have several papers published using RiboTag technology showing gene expression changes in various parts of the CNS during health and disease, with my contribution of applying bioinformatics to study cell type specific transcriptomes. Also, we published a paper reporting the deleterious effect of *Kdm6a* gene in CD4+ T-cells in MS mouse model, which could explain the sex bias of autoimmune diseases. Thus, I am ideally suited for work in this proposal that utilizes RiboTag technology and bioinformatics, to determine cell-specific, region-specific, sex-specific, and age-specific molecular mechanisms in disease, to develop the tailored treatments in women and men with MS.

1. Itoh Y, Golden LC, Itoh N, Matsukawa MA, Ren E, Tse V, Arnold AP, Voskuhl RR. The X-linked histonedemethylase Kdm6a in CD4+ T lymphocytes modulates autoimmunity. J Clin Invest. 2019 Aug12;129(9):3852-3863. PubMed Central PMCID: PMC6715385.
2. Voskuhl RR, Itoh N, Tassoni A, Matsukawa MA, Ren E, Tse V, Jang E, Suen TT, Itoh Y. Geneexpression in oligodendrocytes during remyelination reveals cholesterol homeostasis as a therapeutictarget in multiple sclerosis. Proc Natl Acad Sci U S A. 2019 May 14;116(20):10130-10139. PubMedCentral PMCID: PMC6525478.
3. Itoh N, Itoh Y, Tassoni A, Ren E, Kaito M, Ohno A, Ao Y, Farkhondeh V, Johnsonbaugh H, Burda J,Sofroniew MV, Voskuhl RR. Cell-specific and region-specific transcriptomics in the multiple sclerosismodel: Focus on astrocytes. Proc Natl Acad Sci U S A. 2018 Jan 9;115(2):E302-E309. PubMed CentralPMCID: PMC5777065.

4. Itoh Y, Voskuhl RR. Cell specificity dictates similarities in gene expression in multiple sclerosis,Parkinson's disease, and Alzheimer's disease. PLoS One. 2017;12(7):e0181349. PubMed CentralPMCID: PMC5513529.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2019 – Project Scientist, UCLA, Los Angeles, CA
2010 – 2019 Assistant Researcher, UCLA, Los Angeles, CA
2007 – 2010 Staff Research Associate III, UCLA, Los Angeles, CA
2002 – 2007 Postdoctoral Fellow, UCLA, Los Angeles, CA
2001 – 2002 Postdoctoral Research Associate, Tohoku University

Honors

2002 – 2002 Yamada Life Science Foundation Award, Yamada Life Science Foundation
1998 – 2001 3 year stipend and partial research support, Japan Society for the Promotion of Science
1999 – 2000 Inui Memorial Foundation Award, Inui Memorial Foundation

C. Contributions to Science

1. <Sex difference of neurodegenerative disease> Using the cell specific conditional knock out mice, I showed the deleterious role of X-linked histone demethylase Kdm6a in CD4+ T-cells in MS mouse model, indicating the importance of this X escapee gene in the sexually dimorphism of autoimmune disease. In addition, transcriptome and methylome analysis showed the parental epigenetic difference in X chromosome.

a. Golden LC, Itoh Y, Itoh N, Iyengar S, Coit P, Salama Y, Arnold AP, Sawalha AH, Voskuhl RR. Parent-of-origin differences in DNA methylation of X chromosome genes in T lymphocytes. Proc Natl Acad Sci U S A. 2019 Dec 10; PubMed Central PMCID: PMC6936674.
b. Itoh Y, Golden LC, Itoh N, Matsukawa MA, Ren E, Tse V, Arnold AP, Voskuhl RR. The X-linked histone demethylase Kdm6a in CD4+ T lymphocytes modulates autoimmunity. J Clin Invest. 2019 Aug 12;129(9):3852-3863. PubMed Central PMCID: PMC6715385.
c. Voskuhl RR, Sawalha AH, Itoh Y. Sex chromosome contributions to sex differences in multiple sclerosis susceptibility and progression. Mult Scler. 2018 Jan;24(1):22-31. PubMed Central PMCID: PMC5823689.

2. <Neurodegenerative disease in mouse models> I carried out genetic studies to reveal mechanisms underlying neurodegeneration in the mouse model of multiple sclerosis, experimental autoimmune encephalomyelitis. This entailed defining the transcriptome of astrocytes and doing bioinformatics pathway analyses in a cell-specific and region-specific manner.

a. Tassoni A, Farkhondeh V, Itoh Y, Itoh N, Sofroniew MV, Voskuhl RR. The astrocyte transcriptome in EAE optic neuritis shows complement activation and reveals a sex difference in astrocytic C3 expression. Sci Rep. 2019 Jul 10;9(1):10010. PubMed Central PMCID: PMC6620300.
b. Voskuhl RR, Itoh N, Tassoni A, Matsukawa MA, Ren E, Tse V, Jang E, Suen TT, Itoh Y. Gene expression in oligodendrocytes during remyelination reveals cholesterol homeostasis as a therapeutic target in multiple sclerosis. Proc Natl Acad Sci U S A. 2019 May 14;116(20):10130-10139. PubMed Central PMCID: PMC6525478.
c. Itoh N, Itoh Y, Tassoni A, Ren E, Kaito M, Ohno A, Ao Y, Farkhondeh V, Johnsonbaugh H, Burda J, Sofroniew MV, Voskuhl RR. Cell-specific and region-specific transcriptomics in the multiple sclerosis model: Focus on astrocytes. Proc Natl Acad Sci U S A. 2018 Jan 9;115(2):E302-E309. PubMed Central PMCID: PMC5777065.

3. <Neurodegenerative disease in humans> As a translational application of our basic discoveries, I applied a data mining approach to determine cell specific transcriptome features in human neurodegenerative diseases (multiple sclerosis, Alzheimer's Disease and Parkinson's Disease). I was also involved data analyses, including heatmap representations of clinical and MRI data in studies in multiple sclerosis patients.

a. MacKenzie-Graham A, Brook J, Kurth F, Itoh Y, Meyer C, Montag MJ, Wang HJ, Elashoff R, Voskuhl RR. Estriol-mediated neuroprotection in multiple sclerosis localized by voxel-based morphometry. Brain Behav. 2018 Sep;8(9):e01086. PubMed Central PMCID: PMC6160650.

b. Itoh Y, Voskuhl RR. Cell specificity dictates similarities in gene expression in multiple sclerosis, Parkinson's disease, and Alzheimer's disease. PLoS One. 2017;12(7):e0181349. PubMed Central PMCID: PMC5513529.

c. MacKenzie-Graham A, Kurth F, Itoh Y, Wang HJ, Montag MJ, Elashoff R, Voskuhl RR. Disability-Specific Atlases of Gray Matter Loss in Relapsing-Remitting Multiple Sclerosis. JAMA Neurol. 2016 Aug 1;73(8):944-53. PubMed Central PMCID: PMC6415681.

4. <Sex chromosome mouse models> To study sex difference, we have been using several different mouse models to separately analyze the sex chromosome, organizational, and activational factors. One of the major mouse model, four core genotypes, has Sry deletion from Y chromosome and Sry-transgene insertion on autosome. Although this model has been used in many different studies, its transgenic character had not been carefully investigated. We characterized this mouse model at the sequence level and reported. I also contributed in several studies utilizing sex chromosome mouse models, as a biostatistician and a cytogeneticist.

a. Ghosh MK, Chen KE, Dill-Garlow R, Ma LJ, Yonezawa T, Itoh Y, Rivera L, Radecki KC, Wu QP, Arnold AP, Muller HK, Walker AM. Sex Differences in the Immune System Become Evident in the Perinatal Period in the Four Core Genotypes Mouse. Front Endocrinol (Lausanne). 2021;12:582614. PubMed Central PMCID: PMC8191418.

b. Umar S, Cunningham CM, Itoh Y, Moazeni S, Vaillancourt M, Sarji S, Centala A, Arnold AP, Eghbali M. The Y Chromosome Plays a Protective Role in Experimental Hypoxic Pulmonary Hypertension. Am J Respir Crit Care Med. 2018 Apr 1;197(7):952-955. PubMed Central PMCID: PMC6020406.

c. Itoh Y, Arnold AP. Are females more variable than males in gene expression? Meta-analysis of microarray datasets. Biol Sex Differ. 2015;6:18. PubMed Central PMCID: PMC4640155.

d. Itoh Y, Mackie R, Kampf K, Domadia S, Brown JD, O'Neill R, Arnold AP. Four core genotypes mouse model: localization of the Sry transgene and bioassay for testicular hormone levels. BMC Res Notes. 2015 Mar 7;8:69. PubMed Central PMCID: PMC4354741.

5. <Sex chromosome studies in birds and mammals> In animals with heteromorphic sex chromosomes, dosage compensation of sex-chromosome genes is thought to be critical for species survival. Despite the molecular mechanism of X chromosome dosage compensation in mammals was well studied, the one in birds has not been understood. In birds, females (ZW) and males (ZZ) differ in the number of Z chromosomes. We published the first global analysis of chicken and zebra finch genes, and showed that Z chromosome dosage compensation is inefficient. On the other hand, in bovine blastocysts, X chromosome inactivation is not complete. We reported the global analysis of bovine blastocysts genes, showing that X genes regulate A (autosomal) genes. The zebra finch is often studied because of its interesting behavior and neurobiology. Unfortunately, genetic information on this species has been lacking. Using molecular and cytogenetic techniques, I characterized zebra finch chromosomes and found chromosomal polymorphisms and evolutionary arrangement. I also reported novel chicken and zebra finch W chromosome repetitive sequence which is the major component of W sequence. The information which I reported contributed to the zebra finch genome project. I also established two zebra finch cell lines to provide materials to the community.

a. Itoh Y, Arnold AP. X chromosome regulation of autosomal gene expression in bovine blastocysts. Chromosoma. 2014 Oct;123(5):481-9. PubMed Central PMCID: PMC4170013.

b. Itoh Y, Replogle K, Kim YH, Wade J, Clayton DF, Arnold AP. Sex bias and dosage compensation in the zebra finch versus chicken genomes: general and specialized patterns among birds. Genome Res. 2010 Apr;20(4):512-8. PubMed Central PMCID: PMC2847754.

c. Itoh Y, Melamed E, Yang X, Kampf K, Wang S, Yehya N, Van Nas A, Replogle K, Band MR, Clayton DF, Schadt EE, Lusis AJ, Arnold AP. Dosage compensation is less effective in birds than in mammals. J Biol. 2007;6(1):2. PubMed Central PMCID: PMC2373894.

d. Itoh Y, Mizuno S. Molecular and cytological characterization of SspI-family repetitive sequence on the chicken W chromosome. Chromosome Res. 2002;10(6):499-511. PubMed PMID: 12489831.

See URL at
https://www.ncbi.nlm.nih.gov/myncbi/yuichiro.itoh.1/bibliography/public

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BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Zhou, Jin

eRA COMMONS USER NAME (credential, e.g., agency login): JINJINZHOU

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Nanjing Normal University, Nanjing, China	BA	06/2002	Mathematics
Nankai University, Tianjin, China	MS	06/2005	Applied Mathematics
University of California, Los Angeles, CA	PhD	03/2011	Biomathematics
Harvard University, Boston, MA	Postdoctoral Fellowship	08/2013	Biostatistics

A. Personal Statement

I am an Associate Professor at the Department of Medicine Statistics Core, UCLA Division of General Internal Medicine and Health Services Research. I was trained in mathematics, statistics, and genetics. My work on statistical genomics and biomedical informatics focuses on developing statistically powerful and computationally efficient tools for biobank scale genetic association studies, metagenomics data analysis, and personalized treatment prediction using electronic medical records (EHRs) data. My career goal is to be at the interface of statistics, genetics, and biomedical informatics and better utilize “big” health-related data for personalized healthcare. I have extensive expertise in dissecting the genetic components of complex diseases. Besides methodological development, I have broad collaboration experiences. I have collaborated with clinicians and epidemiologists at the University of Arizona and Channing's Laboratory at Brigham and Women's Hospital (BWH) for their bulk and single cell transcriptomics studies. I am also an active contributor of Million Veteran Program (MVP). My roles range from study design to developing the detailed analysis plan. My experience is ideally suited to my role in the proposed research in this R35 which will involve creation of a transcriptomics database from central nervous system tissues of RiboTag mice from 4 specific cell types, multiple brain regions, two sexes, and three ages to do metagenomics data analyses to identify cell-specific gene expression targets tailored by disability, sex, and age.

Ongoing and recently completed projects that I would like to highlight include:

VA-Department of Energy Joint Research Concept
Role: Co-PI | PI: Reaven
07/01/2022 – 06/30/2024
Dynamic Prediction of Short-Term and Long-Term Diabetes Complications Leveraging Massive Electronic Health Records, Million Veteran Project, Machine Learning/Artificial Intelligence, and High-Performance Computing

NSF DMS-2054253
Role: MPI | Contact PI: H. Zhou
07/01/2021 - 06/30/2025
Statistical methods and computational algorithms for biobank data

NIH/NHLBI, R21 HL150374
Role: Zhou (Contact PI) | MPI: Reaven
08/01/2020-07/31/2023
A Role for Glycemic Variation in Optimizing Management of Diabetes and Vascular Complications

NIH/NHGRI, R01 HG006139
Role: Co-I | Subaward PI: Sobel
07/01/2020–06/30/2024
Genomics, EHRs, GPUs, and Next Generation Computational Statistics

ABRC, ADHS16-162409
Role: PI
03/01/2017-02/28/2021
Develop Data-Driven Precision T2D Treatment Regime using Veteran Healthcare Database

NIH/NIDDK, K01 DK106116
Role: PI
08/11/2016-08/31/2020 (NCE)
Develop T2D Patient-Centered Treatment Suggestion Rule Using EMR Data

Phoenix VA Health Care System, 015969-0001
10/15/2019-09/30/2020
PVAHCS IPA Agreement for Jin Zhou

NIH/NIDDK/NIEHS, R01 DK123113
Role: Co-I | PI: Zhao
09/01/2020-06/30/2025
Molecular Mechanism Underlying the Regulation of Manganese Homeostasis

NIH/NHLBI, R01 HL149744
09/01/2020-08/31/2025
Role: Co-I | Polverino
B Cell-Adaptive Immune Profile in Emphysema-Predominant COPD

Citations:

1. C. A. German, J. S. Sinsheimer, Y. C. Klimentidis, H. Zhou, and **J. J. Zhou**. (2020) Ordered multinomial regression for genetic association analysis of ordinal phenotypes at biobank scale. Genetic Epidemiology. 44(3): 248-260. PMID: 31879980
2.
3. Doubleday K, Zhou H, Fu H, **Zhou JJ**. An Algorithm for Generating Individualized Treatment Decision Trees and Random Forests. J Comput Graph Stat. 2018;27(4):849-860. 2018 Jun 14. PMID: 32523325; PMCID: PMC7286561.
4. M. Vujkovic, J. M. Keaton, J. A. Lynch, D. R. Miller, **J. J. Zhou**, et al. (2020) Discovery of 318 new risk loci for type 2 diabetes and related vascular outcomes among 1.4 million participants in a multi-ethnic meta-analysis, Nature Genetics, 52:680-691. PMID: 32541925 PMCID: PMC7343592

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2021-Present	Associate Professor, UCLA Department of Medicine Statistics Core, Los Angeles, CA
2019-2021	Associate Professor, University of Arizona, College of Public Health, Tucson, AZ
2013-2019	Assistant Professor, University of Arizona, College of Public Health, Tucson, AZ
2015-Present	Membership Committee Member, Caucus Women in Statistics
2011-Present	Member, Eastern North American Region, International Biometric Society
2010-Present	Member, American Statistical Association
2009-Present	Member, American Society of Human Genetics

2009-Present Communication Committee Member, International Genetic Epidemiology Society

Honors

2012 Program in Quantitative Genomics Stellar Abstract Award, Harvard University
2012 Travel Award, 14th Meeting of New Researchers in Statistics and Probability
2012 Program in Quantitative Genomics Travel Award, Harvard University
2009 Dissertation Year Fellowship, University of California, Los Angeles

C. Contributions to Science

1. Development of statistical and computational tools. Large-scale and high-dimensional data are being generated at an unprecedented rate. In my 10 years of research, I have devoted myself to develop quantitative methods and software to facilitate using these large-scale datasets. In my previous research, I have addressed some challenges of utilizing familial data for gene mapping and made significant contributions to the field of genetic studies using family designs. Given the complexity of the design and scale of the genomic data, analysis tools either rely on simplistic assumptions or suffer from computational bottleneck. I have built regularization models for combinatorial process to improve the interpretability of these genomics data. Methods I developed reduced the computational time from days to hours with superior statistical power. Free user-friendly software packages were provided for each method I developed. My current research focuses on developing tools for metagenomics data and next generation sequencing (NGS) data.
    a. Hu L, Lv W, **Zhou JJ**, Zhou H. MM Algorithms for Variance Component Estimation and Selection in Logistic Linear Mixed Model. Stat Sin. 2019;29(3):1585-1605. PMCID: PMC7286582.
    b. Zhai J, Knox K, Twigg HL 3rd, Zhou H, **Zhou JJ**. Exact variance component tests for longitudinal microbiome studies. Genet Epidemiol. 2019 Apr;43(3):250-262. PMCID: PMC6416054.
    c. **Zhou JJ**, Hu T, Qiao D, Cho MH, Zhou H. Boosting gene mapping power and efficiency with efficient exact variance component tests of single nucleotide polymorphism sets. Genetics. 2016 Nov;204(3):921-931. PMCID: PMC5105869.
    d. Doubleday K, Zhou H, Fu H, **Zhou JJ**. An Algorithm for Generating Individualized Treatment Decision Trees and Random Forests. J Comput Graph Stat. 2018;27(4):849-860. 2018 Jun 14. PMCID: PMC7286561.

2. Identification of risk factors underly the development of diabetes complications. I have devoted myself to studying clinical and biological aspects of diabetes and its complications in the past five years. Taking advantage of my quantitative background, my group has conducted several secondary analyses of clinical trials. The findings highlighted the importance of intraindividual glycemic variability as an independent risk factor to diabetes complications. Together, they allow me to move closer to my career goal: at the interface of statistics, genetics, and biomedical informatics and better utilize “big” health-related data for personalized diabetes care.
    a. **Zhou JJ**, Koska J, Bahn G, Reaven P. Fasting Glucose Variation Predicts Microvascular Risk in ACCORD and VADT. J Clin Endocrinol Metab. 2021 Mar 25;106(4):1150-1162. PMCID: PMC7993576.
    b. **Zhou JJ,** Schwenke DC, Bahn G, Reaven P; VADT Investigators. Glycemic Variation and Cardiovascular Risk in the Veterans Affairs Diabetes Trial. Diabetes Care. 2018 Oct;41(10):2187-2194. 2018 Aug 6. PMCID: PMC6150432.
    c. **Zhou JJ**, Koska J, Bahn G, Reaven P. Glycaemic variation is a predictor of all-cause mortality in the Veteran Affairs Diabetes Trial. Diab Vasc Dis Res. 2019 Mar;16(2):178-185. PMCID: PMC7380497.

3. Identification of genetic determinants of complex diseases. Besides developing quantitative tools, I have made substantial efforts to understand genetic factors underlying complex diseases utilizing advanced computational tools and methodologies. We are the first to estimate heritability of COPD and related phenotypes using a GWAS study of 10,000 individuals.
    a. **Zhou JJ**, Cho MH, Castaldi PJ, Hersh CP, Silverman EK, Laird NM. Heritability of chronic obstructive pulmonary disease and related phenotypes in smokers. Am J Respir Crit Care Med. 2013 Oct 15;188(8):941-7. PMCID: PMC3826281.

b. Klimentidis YC, Arora A, Newell M, **Zhou JJ**, Ordovas JM, Renquist BJ, Wood AC. Phenotypic and Genetic Characterization of Lower LDL Cholesterol and Increased Type 2 Diabetes Risk in the UK Biobank. Diabetes. 2020 Oct;69(10):2194-2205 PMCID: PMC7506834.
c. **Zhou JJ**, Zhai J, Zhou H, Chen Y, Guerra S, Robey I, Weinstock GM, Weinstock E, Dong Q, Knox KS, Twigg HL 3rd. Supraglottic Lung Microbiome Taxa Are Associated with Pulmonary Abnormalities in an HIV Longitudinal Cohort. Am J Respir Crit Care Med. 2020 Dec 15;202(12):1727-1731. PMCID: PMC7737582.

4. Applied Mathematics. Combinatorics and graph theory are new fields in modern mathematics. Its recent spectacular growth is motivated by computer science, for instance, for the construction and analysis of computational algorithms. In my earlier papers, I studied enumeration, one of the most basic and important aspects of combinatorics. Some of the counting procedures in enumerative combinatorics are widely used in phylogenetic studies. Genocchi numbers are widely used for enumeration. We are the first to introduce a q-analog of Genocchi numbers through a q-analog of Seidels triangle and showed that these q-Genocchi numbers have interesting combinatorial interpretations such as alternating pistols, alternating permutations, and skew Young tableaux.
    a. Yan G, Yang L, **Zhou JJ**. The Zrank conjecture and restricted Cauchy matrix. Linear Algebra and its Applications. 2005; 411:371-385.
    b. Zeng J, **Zhou JJ**. Applications of Waring's formula to some identities of Chebyshev polynomials. Fibonacci Quarterly. 2006; 44.2:117-120.
    c. Zeng J, **Zhou JJ**. A q-analog of the Seidel generation of Genocchi numbers. European Journal of Combinatorics. 2006; 27:364-381.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/47795663/?sort=date&direction=ascending

OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 09/30/2024)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Allan Mackenzie-Graham, Ph.D.**

eRA COMMONS USER NAME (credential, e.g., agency login): MACKENZIEG2

POSITION TITLE: **Associate Professor, Neurology**

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training)

INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of California, Los Angeles, CA	B.S.	12/1996	Neuroscience
University of California, Los Angeles, CA	Ph.D.	04/2006	Neuroscience
University of California, Los Angeles, CA	Post-doc	06/2008	Neurology
University of California, Los Angeles, CA	Post-doc	06/2010	Neurology

A. Personal Statement

My primary interests are in the mechanisms underlying neurodegeneration and how to ameliorate it therapeutically. I have a broad background in neuroscience, imaging, and histology and I apply all of these skills to the end of understanding neurodegeneration in the normal aging process and neurological disease, specifically multiple sclerosis (MS) and experimental autoimmune encephalomyelitis (EAE), the most commonly used animal model of MS. My research involves the analysis of mouse brain magnetic resonance imaging (MRI) using voxel-based morphometry (VBM) and Clear Lipid-exchanged Acrylamide-hybridized Rigid Imaging-compatible Tissue-hYdrogel (CLARITY) imaging using atlasing techniques to evaluate the structural changes that occur in the brain as the result of disease and treatment. We have recently published this work in the Multiple Sclerosis Journal (Meyer 2109). In parallel, my lab studies localized gray matter changes using VBM in patients with MS. We strive to understand the relationship between gray matter atrophy and specific clinical disabilities in order to identify treatments to stop gray matter loss and prevent disability. This work was published in JAMA Neurology (MacKenzie-Graham 2016), Brain & Behavior (MacKenzie-Graham 2018), and Annals of Clinical and Translational Neurology (Voskuhl 2022).

I am very excited about working with Dr. Voskuhl on this groundbreaking proposal, Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach. The proposal leverages my lab's strengths in MRI acquisition, processing, and analysis, as well as our extensive collaborative history with Dr. Voskuhl, comprising many papers and grants over the years.

Citations I would like to highlight

1. Meyer CE, Gao JL, Cheng JY, Oberoi MR, Johnsonbaugh H, Lepore S, Kurth F, Thurston MJ, Itoh N, Patel KR, Voskuhl RR, **MacKenzie-Graham A**. (2019) Axonal Damage in Spinal Cord Is Associated with Gray Matter Atrophy in Sensorimotor Cortex in Experimental Autoimmune Encephalomyelitis. Mult Scler. 2019 Mar 7:1352458519830614. doi: 10.1177/1352458519830614. PMID: 30843756
2. Meyer CE, Kurth F, Lepore S, Gao JL, Johnsonbaugh H, Oberoi MR, Sawiak SJ, **MacKenzie-Graham A**. (2017) In Vivo Magnetic Resonance Images Reveal Neuroanatomical Sex Differences Through the Application of Voxel-Based Morphometry in C57BL/6 Mice. NeuroImage 163:197-205. PMCID: PMC5716897
3. Voskuhl RR, Patel K, Paul F, Gold SM, Scheel M, Kuchling J, Cooper G, Asseyer S, Chien C, Brandt AU, Meyer CE, **MacKenzie-Graham A.** (2020) Sex Differences in Brain Atrophy in Multiple Sclerosis. Biol Sex Differ. 2020 Aug 28;11(1):49. doi: 10.1186/s13293-020-00326-3. PMID: 32859258 PMCID: PMC7456053
4. **MacKenzie-Graham A**, Kurth F, Itoh Y, Wang HJ, Montag MJ, Elashoff R, Voskuhl RR. (2016) Disability-Specific Atlases of Gray Matter Loss in Relapsing-Remitting Multiple Sclerosis. JAMA Neurology 73(8):944-53. PMID: 27294295, PMCID: PMC6415681

Ongoing and completed projects I would like to highlight

NIH R01 NS121761 (MacKenzie-Graham/Shattuck MPI) 04/01/2022-03/31/2027

A Toolkit for Analysis and Visualization of Preclinical Rodent Neuroimaging Experiments

Goal: The goal of this project is to develop an open-source suite of software for the processing, analysis, and

visualization of rodent brain imaging data, which will enhance the ability of neuroscience researchers to perform preclinical studies on rodent models. This software will provide advanced capabilities for analyzing multimodal imaging data, including imagery from magnetic resonance imaging and optical microscopy studies, with the goal of improving understanding of processes and mechanisms underlying neurological diseases and disorders and their potential treatment.
Role: Multiple Principal Investigator

NIH R21NS121806 (MacKenzie-Graham PI) 04/01/21-09/30/2022
The Mechanism of Gray Matter Atrophy in Experimental Autoimmune Encephalomyelitis
Goal: To determine the role of oxidative stress in gray matter atrophy in EAE.
Role: Principal Investigator

NIH R01HD100298 (MacKenzie-Graham/Arnold/Lerch MPIs) 04/01/2020-03/31/2025
Coupling Neuroimaging with CLARITY and Single-Cell Genomics to Dissect Sex Differences in the Developing Brain
Goal: This project establishes sex-biasing effects of sex hormones and sex chromosomes on localized brain regions across the entire brain at specific times of life and investigates cellular and molecular mechanisms operating in a sex-specific manner at salient sites of sexual differentiation.
Role: Multiple Principal Investigator

Conrad N. Hilton Foundation #18394 (Voskuhl PI) 07/01/19-06/30/22
Disability-Specific Disease Modifying Treatments (DMTs) in Multiple Sclerosis (MS)
Goal: Investigation of disability-specific treatments in EAE, MS, and brain aging.
Role: Co-Investigator

NIH R01NS086981 (MacKenzie-Graham PI) 03/01/15-02/28/20
Bringing CLARITY to EAE
Goal: To determine the neuropathologies underlying gray matter atrophy in EAE.
Role: Principal Investigator

National Multiple Sclerosis Society #PP-1805-31001 (Gold PI) 11/1/18-10/31/19
UCLA Subcontract with Charité – Universitätsmedizin Berlin
Sex Differences in Neurodegeneration in CIS and Early Stage MS
Goal: Assess sex-specific disability progression and brain atrophy using an existing MS dataset in Berlin.
Role: Co-Investigator (UCLA Subcontract with Charité – Universitätsmedizin Berlin)

B. Positions, Scientific Appointments, and Honors

Employment

2017-present	Associate Professor, Brain Mapping Center, Neurology, UCLA, Los Angeles, CA
2015-present	Joint appointment in Physics and Biology in Medicine IDP, UCLA, Los Angeles, CA
2015-present	Joint appointment in Neuroscience IDP, UCLA, Los Angeles, CA
2010-2017	Assistant Professor, Brain Mapping Center, Neurology, UCLA, Los Angeles, CA
2008-2010	Postdoctoral Scholar (Jeffry Alger mentor), Neurology, UCLA, Los Angeles, CA
2006-2008	Postdoctoral Scholar (Arthur Toga mentor), Neurology, UCLA, Los Angeles, CA
1998-2006	Graduate Student (Arthur Toga mentor), Neuroscience, UCLA, Los Angeles, CA
1995-1998	Staff Research Associate, Neurology, UCLA, Los Angeles, CA

Other Experience and Professional Memberships

2019	ad hoc reviewer, NIH Peer Review Committee: CHHD-R
2019	ad hoc reviewer, NIH Peer Review Committee: CNBT
2018	ad hoc reviewer, NIH Peer Review Committee: MEDI
2018-present	Organization for the Study of Sex Differences, Member
2016-present	International Society for Neurochemistry, Member
2015-present	American Society for Neurochemistry, Member
2011-present	International Society for Magnetic Resonance in Medicine, Member
2012-2016	Laboratory of Neuroendocrinology, Minority Training Committee, Chair
2010-present	Laboratory of Neuroendocrinology, Member
1999-present	Society for Neuroscience, Member

Honors

2009 Mazziotta Award: Postdoctoral Scholar
2008-2011 NMSS Postdoctoral Fellow, National Multiple Sclerosis Society
1999-2003 METPAC Fellow, Minority Conference Fellowship Program, Society for Neuroscience

C. Contribution to Science

1. My laboratory studies the structural changes that occur in the central nervous system as the result of aging and disease, specifically, the relationship between GM atrophy and the neuropathologies that underlie it. We use cross-modality correlation to uncover these associations. The studies below document a strong correlation between GM atrophy measured by MRI and neuronal loss as measured by histology in EAE. Our early findings demonstrated that gray matter atrophy in the cerebellum and Purkinje cell loss were strongly associated in mice with EAE. More recently, we used CLARITY to observe a very strong correlation between not only neuronal loss and gray matter atrophy in the cerebral cortex, but also between axonal transection in the spinal cord and gray matter atrophy in the cerebral cortex. This work was the first use of the CLARITY technique in an animal model of disease.

    a. Meyer CE, Gao JL, Cheng JY, Oberoi MR, Johnsonbaugh H, Lepore S, Kurth F, Thurston MJ, Itoh N, Patel KR, Voskuhl RR, **MacKenzie-Graham A**. (2019) Axonal Damage in Spinal Cord Is Associated with Gray Matter Atrophy in Sensorimotor Cortex in Experimental Autoimmune Encephalomyelitis. Mult Scler. 2019 Mar 7:1352458519830614. doi: 10.1177/1352458519830614. PMID: 30843756
    b. Spence RD, Kurth F, Itoh N, Mongerson CRL, Wailes SH, Peng MS, **MacKenzie-Graham AJ**. (2014) Bringing CLARITY to Gray Matter Atrophy. NeuroImage 101:625-32 PMCID: PMC4437539
    c. **MacKenzie-Graham A**, Tiwari-Woodruff SK, Sharma G, Aguilar C, Vo KT, Strickland LV, Morales L, Fubara B, Martin M, Jacobs RE, Johnson GA, Toga AW, Voskuhl RR (2009) Purkinje Cell Loss in Experimental Autoimmune Encephalomyelitis. NeuroImage, 48(4):637-651. PMCID: PMC2754586
    d. **MacKenzie-Graham A,** Tinsley MR, Shah KP, Aguilar C, Strickland LV, Boline J, Martin M, Morales L, Shattuck DW, Jacobs RE, Voskuhl RR, Toga AW. (2006) Cerebellar Cortical Atrophy in Experimental Autoimmune Encephalomyelitis. Neuroimage 32(3):1016-23. PMID: 16806982

2. We are particularly interested in how to prevent, ameliorate, and/or repair damage to the CNS. In collaboration with Dr. Rhonda Voskuhl from the UCLA MS Program and with the intellectual support of the Laboratory of Neuroendocrinology (LNE), we have studied the effects of sex hormones, namely estriol and testosterone, on gray matter atrophy in EAE and MS, respectively. Both estriol and testosterone are promising treatments for MS. In a testosterone-treatment trial in men with MS, we found not only a decrease in gray matter atrophy after just six months, but also a localized increase in gray matter concentration after 12 months of treatment. We have also observed gray matter preservation by MRI and decreased myelin disruption by diffusion tensor imaging (DTI) in EAE mice treated with estrogen. Recently, we studied the association between voxelwise gray matter atrophy and clinical disability, discovering that gray matter loss in clinically eloquent regions are correlated with the paced auditory serial addition test (PASAT), 9-hole peg test (9-HPT), and the bowel and bladder subscale of the Kurtzke expanded disability status scale (EDSS).

    a. Voskuhl R, Kuhle J, Siddarth P, Itoh N, Patel K, **MacKenzie-Graham A**. (2022) Decreased Neurofilament Light Chain Levels In Estriol-Treated Multiple Sclerosis. Ann Clin Transl Neurol. 2022 Jun 29. doi:10.1002/acn3.51622. Online ahead of print. PMID: 35770318
    b. **MacKenzie-Graham A**, Brook J, Kurth F, Itoh Y, Meyer C, Montag MJ, Wang HJ, Elashoff R, Voskuhl RR. (2018) Estriol-Mediated Neuroprotection in Multiple Sclerosis Localized by Voxel-Based Morphometry. Brain Behav. 2018 Aug 24:e01086. doi: 10.1002/brb3.1086. PMID: 30144306, PMCID: PMC6160650
    c. **MacKenzie-Graham A**, Kurth F, Itoh Y, Wang HJ, Montag MJ, Elashoff R, Voskuhl RR. (2016) Disability-Specific Atlases of Gray Matter Loss in Relapsing-Remitting Multiple Sclerosis. JAMA Neurology 73(8):944-53. PMID: 27294295, PMCID: PMC6415681

d. Voskuhl RR, Wang H, Wu TC, Sicotte NL, Nakamura K, Kurth F, Itoh N, Bardens J, Bernard JT, Corboy JR, Cross AH, Dhib-Jalbut S, Ford CC, Frohman EM, Giesser B, Jacobs D, Kasper LH, Lynch S, Parry G, Racke MK, Reder AT, Rose J, Wingerchuk DM, **MacKenzie-Graham AJ**, Arnold DL, Tseng CH, Elashoff R. (2015) Estriol Combined with Glatiramer Acetate for Women with Relapsing-Remitting MS: A Randomised, Placebo-Controlled, Phase 2 Trial. Lancet Neurology Jan;15(1):35-46. PMID: 26621682

3. My laboratory is also interested in understanding sex differences in the brain, particularly the contribution of sex chromosomes to structural differences, as our recent grant funding demonstrates (NIH R01HD100298 and NIH R21HD090637). Early in my career I developed a framework for evaluating differences in structural anatomy in the mouse. More recently, we have used VBM to visualize changes in both the mouse and human brains. For VBM in the mouse we developed species- and in vivo-specific tissue probability maps (TPMs) to provide more accurate tissue segmentation. Our results demonstrated distinct neuroanatomical regions that were sexually dimorphic in the adult C57BL/6 mouse brain. Similarly, we found sexual dimorphism in the pattern of GM loss in the brain during MS by comparing female MS patients with female healthy controls and male MS patients with male healthy controls.

   a. Voskuhl RR, Patel K, Paul F, Gold SM, Scheel M, Kuchling J, Cooper G, Asseyer S, Chien C, Brandt AU, Meyer CE, **MacKenzie-Graham A.** (2020) Sex Differences in Brain Atrophy in Multiple Sclerosis. Biol Sex Differ. 2020 Aug 28;11(1):49. doi: 10.1186/s13293-020-00326-3. PMID: 32859258 PMCID: PMC7456053
   b. Meyer CE, Kurth F, Lepore S, Gao JL, Johnsonbaugh H, Oberoi MR, Sawiak SJ, **MacKenzie-Graham A**. (2017) In Vivo Magnetic Resonance Images Reveal Neuroanatomical Sex Differences Through the Application of Voxel-Based Morphometry in C57BL/6 Mice. NeuroImage 163:197-205. PMCID: PMC5716897
   c. Kurth F, **Mackenzie-Graham A**, Toga AW, Luders E. (2014) Shifting Brain Asymmetry: The Link Between Meditation and Structural Lateralization. Social Cognitive and Affective Neuroscience 10(1):55-61 PMID: 24643652
   d. **MacKenzie-Graham A**, Lee EF, Dinov I, Bota M, Shattuck DW, Ruffins S, Yuan H, Konstantinidis F, Pitiot A, Ding Y, Hu G, Jacobs RE, Toga AW (2004) A Multimodal, Multidimensional Atlas of the C57BL/6 Mouse Brain. Journal of Anatomy 204:93-102. PMCID: PMC1571243

4. As part of my doctoral training, I learned how to use sophisticated MRI analysis techniques to study natural variability in mice. In my first postdoctoral fellowship, I learned how to measure the effect of disease on brain morphology using MRI and in my second fellowship I learned how to collect MR images and correlate them with neuropathological changes. I successfully managed the Mouse Atlas Project (MAP) and served as the primary liaison and scientific advisor for the Laboratory of Neuro Imaging (LONI) to the Mouse Biomedical Informatics Research Network (MBIRN). A significant aspect of this work was the development of a mechanism for documenting data provenance for the documentation and validation of multiple kinds of imaging data.

   a. **MacKenzie-Graham A**, Payan A, Dinov I, Van Horn JD, Toga AW. (2008) Neuroimaging Data Provenance Using the LONI Pipeline Workflow Environment. In: Lecture Notes in Computer Science: International Provenance and Annotation Workshop 2008, Freire J, Koop D, and Moreau L (Eds). Springer-Verlag, pp 4145:208-220. LNCS 4145: 148–161.
   b. **MacKenzie-Graham A**, Van Horn JD, Payan A, Neu SC, Crawford KL, Toga AW (2008) Provenance in Neuroimaging. NeuroImage, 42(1):178-95. PMCID: 2664747
   c. **MacKenzie-Graham A**, Lee EF, Dinov ID, Yuan H, Jacobs RE, Toga AW. (2007) Multimodal, Multidimensional Models of Mouse Brain. Epilepsia, 48(Suppl. 4):75-81. PMCID: PMC3192853
   d. **MacKenzie-Graham A**, Jones ES, Shattuck DW, Dinov I, Bota M, Toga AW. (2003) The Informatics of a C57BL/6J Mouse Brain Atlas. Neuroinformatics 1:397-410. PMID: 15043223

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http://www.ncbi.nlm.nih.gov/sites/myncbi/allan.mackenzie-graham.1/bibliography/40421703/public/?sort=date&direction=ascending

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BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Prabha Siddarth

eRA COMMONS USER NAME (credential, e.g., agency login): siddarth2

POSITION TITLE: Research Statistician

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Madras, Madras, India	B.Sc.	06/1982	Chemistry
Indian Institute of Technology, Madras, India	M.Sc.	06/1984	Chemistry
Indian Institute of Technology, Madras, India	Ph.D.	06/1988	Chemistry
University of California, Los Angeles	M.S.	06/1999	Biostatistics

A. Personal Statement

I am a Research Statistician in the Department of Psychiatry and Biobehavioral Sciences at the University of California, Los Angeles (UCLA). As a biostatistician, I have extensive experience in experimental design, statistical analysis, and integration of complex multimodal data from translational, genomic, imaging and observational longitudinal studies as well as behavioral intervention trials, specifically in the area of neurological disorders. I have contributed significantly to research in behavioral, psychiatric and physiological aspects of depression, aging, cognitive functioning and Alzheimer's disease using multimodal imaging, and my work, which has appeared in top-tier journals in psychiatry (e.g. PNAS, Archives of General Psychiatry, Brain, the American Journal of Psychiatry), is highly cited, giving me an h-index of 53 and an i-10-index of 128. I have also served as the statistician in a multi-site study of clinical, cognitive, language, neuropsychological and psychiatric evaluation of patients with non-epileptic seizures recruited from 5 tertiary medical centers. I have a longstanding productive collaborative relationship with many Principal Investigators both within UCLA and outside of UCLA and my involvement has included statistical consultation regarding design, data collection as well as data analysis for various papers, presentations at scientific conferences, and participation in writing manuscripts. Further, I have also collaborated with many other investigators in clinical trials and other longitudinal studies and have recently published a paper with the PI of the current proposal. In the current project, I will participate in the analysis, interpretation, and publication of findings. Some recent publications where my contributions have been critical to the success of the projects are highlighted below:

a. Voskuhl R, Kuhle J, **Siddarth P**, Itoh N, Patel K, MacKenzie-Graham A. Decreased neurofilament light chain levels in estriol-treated multiple sclerosis. Ann Clin Transl Neurol. 2022 Jun 29. doi: 10.1002/acn3.51622. Epub ahead of print. PMID: 35770318.
b. Lavretsky H, Laird KT, Krause-Sorio B, Heimberg BF, Yeargin J, Grzenda A, Wu P, Thana-Udom K, Ercoli LM, **Siddarth P**. A Randomized Double-Blind Placebo-Controlled Trial of Combined Escitalopram and Memantine for Older Adults With Major Depression and Subjective Memory Complaints. Am J Geriatr Psychiatry. 2020 Feb;28(2):178-190. PMCID: PMC6997044
c. **Siddarth P**, Li Z, Miller KJ, Ercoli LM, Merrill DA, Henning SM, Heber D, Small GW. Randomized placebo-controlled study of the memory effects of pomegranate juice in middle-aged and older adults. Am J Clin Nutr. 2020;111(1):170–177 .
d. **Siddarth P.** Sparse data and use of logistic regression. Epilepsia (2018) 59, 1085.

B. Positions, Scientific Appointments, and Honors

Employment

2008-present	Research Statistician	University of California, Los Angeles
2003-2008	Associate Research Statistician	University of California, Los Angeles
1999-2003	Assistant Research Statistician	University of California, Los Angeles
1997-1999	Statistician	University of California, Los Angeles
1994-1997	Adjunct Professor	University of British Columbia
1991-1993	Senior Postdoctoral Fellow	California Institute of Technology
1988-1991	Postdoctoral Fellow	California Institute of Technology

Honors

2020-Present	Editorial Board, Journal of Geriatric Psychiatry and Neurology
2013-Present	Associate Editor, Epilepsia
2010-Present	Statistics Editor, Journal of Pediatric Epilepsy
2007	Young Investigators' Award, International Epilepsy Congress, Singapore
1999	Fellow, Delta Omega Society
1998	Raymond D. Goodman Scholarship for academic excellence, UCLA
1991	NATO Advanced Study Institute Fellowship, Caltech
1986 – 1988	CSIR Senior Research Fellowship, IIT
1984 1986	Junior Research Fellowship, IIT

C. Contributions to Science

I am extremely active in collaborative work, and am involved in projects in diverse areas but my primary field of application is psychiatry. The following is a brief description of my most significant contributions to science.

1. Research Relating to Memory, Aging and Late-life Depression
   I am the principal statistician for the UCLA Longevity Center and the Late-Life Depression, Stress and Wellness Program. Research in these programs have focused on identifying neuroanatomical correlates of depression, Alzheimer's disease, mild cognitive impairment to elucidate disease mechanisms, and on identifying cerebral abnormalities indicating disease-related predisposition in unaffected individuals biologically at-risk. Early detection has focused on imaging techniques; in addition to the imaging studies, I have been active in designing research studies to investigate the efficacy of mind-body intervention interventions to ameliorate depressive symptoms, and arrest cognitive decline in older adults. In all these studies, I play a fundamental role in study design, grant writing, data analyses, manuscript preparation and discussion of future studies, and am the liaison to collaborative laboratories.

   a. **Siddarth P**, Funes CM, Laird KT, Ercoli L, Lavretsky H. Predictors of Cognitive Improvement Following Treatment for Late-Life Depression. J Geriatr Psychiatry Neurol. 2020 Mar 25:891988720915515.
   b. Laird KT, Lavretsky H, St Cyr N, **Siddarth P.** Resilience predicts remission in antidepressant treatment of geriatric depression. Int J Geriatr Psychiatry. 2018 Dec;33(12):1596-1603 PMCID: PMC6246780
   c. **Siddarth P**, Rahi B, Emerson ND, Burggren AC, Miller KJ, Bookheimer S, Lavretsky H, Dobkin B, Small G, Merrill DA. Physical Activity and Hippocampal Sub-Region Structure in Older Adults with Memory Complaints. J Alzheimers Dis. 2018 61, 1089-1096 PMCID: PMC6461048
   d. **Siddarth P**, Thana-udom K, Ojha R, Merrill DA, Dzierzewski J, Miller K, Small GW and Ercoli L. Sleep quality, neurocognitive performance, and memory self-appraisal in middle-aged and older adults with memory complaints. Int Psychogeriatr. 2020. PMID: 32985406 PMCID: PMC8004546

2. Research Relating to Pediatric Epilepsy and Schizophrenia
   In collaboration with Dr. Caplan, I have been able to demonstrate neuropsychiatric comorbidities and imaging abnormalities in children with epilepsy with average IQ scores, even in epilepsy syndromes previously thought to be "benign" and in childhood schizophrenia. This research has involved various complex imaging modalities, including deformation-based morphometry, diffusion tensor imaging and

proton magnetic resonance spectroscopy. As an example, using deformation-based morphometry (a method for identifying macroscopic anatomical differences among the brains of different groups of subjects by first spatially normalizing the structural magnetic resonance images of a number of subjects so that they all conform to the same stereotaxic space and then applying multivariate statistics to the ensuing parameters describing the estimated nonlinear deformations), we showed that children with absence epilepsy did not demonstrate the normal regional age-related changes involving a decrease in cortical thickness and increase in sulcal depth and that they used different brain regions to perform cognitive functions compared to healthy controls. Similarly, children with complex partial seizures also exhibited abnormal age related patterns of cortical thickness and sulcal depth in a diversity of regions. These findings have far-reaching implications for both the children with epilepsy and their health care providers. In all these publications, I played a fundamental role in the conceptualization, data analysis and manuscript preparation.

a. Tosun D, **Siddarth P**, Levitt J, Caplan R. Cortical Thickness and Sulcal Depth: Insights on Development and Psychopathology in Pediatric Epilepsy. BJPsych Open 2015 1, 129-35. PMCID: PMC4995587
b. Doss J, Caplan R, **Siddarth P**, Bursch B, Falcone T, Forgey M, Hinman K, Curt LaFrance W Jr, Laptook R, Shaw R, Weisbrot D, Willis M, Plioplys S. Risk factors for learning problems in youth with psychogenic non-epileptic seizures. 2017 Epilepsy Behav. 70(Pt A):135-139.
c. Jones JE, **Siddarth P**, Almane D, Gurbani S, Hermann BP, Caplan R. Identification of risk for severe psychiatric comorbidity in pediatric epilepsy. Epilepsia 2016 57, 1817-1825. PMCID: PMC5868343
d. Lin JJ, **Siddarth P**, Riley JD, Gurbani SG, Ly R, Yee VW, Levitt JG, Toga AW, Caplan R. Neurobehavioral comorbidities of pediatric epilepsies and thalamic structural abnormalities. Epilepsia. 2013 **54**, 2116. PMCID: PMC4259153.

3. Other Research Projects
We have recently started a collaborative effort with the Gallup organization to investigate risk factors for memory problems and depressive symptoms. I have spearheaded the data analyses and manuscript preparation for these projects. These projects comprise data from tens of thousands of subjects (N is approximately 40,000) and the analyses have consequently been challenging and have required development of sophisticated data analytical techniques. I am also the principal statistician for a recently concluded multi-site project to investigate neural and psychosocial mechanisms as well as interventions for non-epileptic seizures in children and adolescents. This multi-site study involves collaborators from Children's Memorial Hospital, Chicago, Children's National Medical center, Washington, D.C., University of Pittsburgh Medical Center, University of Indiana, Stanford University and UCLA. I also spearheaded a recent project with UCLA Recreation, collecting and analyzing data provided by 281 volunteer participants in an employee wellness program, demonstrating a clear link between improvement in physical health and improvements in mental health, quality of life, stress, and energy.

a. Small GW, **Siddarth P**, Ercoli LM, Chen ST, Merrill DA, Torres-Gil F Healthy behavior and memory reports in young, middle-aged, and older adults. Int Psychogeriatr. (2013) **25**, 981.
b. Chen ST, **Siddarth P**, Ercoli LM, Merrill DA, Torres-Gil F, Small GW Modifiable Risk Factors for Alzheimer's Disease and Subjective Memory Impairment Across Age Groups. PLoS One. (2014) 9(6):e98630. PMCID: PMC4045888.
c. Plioplys S, Doss J, **Siddarth P**, Bursch B, Falcone T, Forgey M, Hinman K, LaFrance WC Jr, Laptook R, Shaw RJ, Weisbrot DM, Willis MD, Caplan R. Risk factors for comorbid psychopathology in youth with psychogenic nonepileptic seizures. Seizure (2016) 38, 32-7.
d. Emerson ND, Merrill DA, Shedd K, Bilder RM, **Siddarth P**. Effects of an employee exercise programme on mental health. Occup Med (Lond). 2016 Aug 23 kqw120. doi: 10.1093/occmed/kqw120

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/prabha.siddarth.2/bibliography/public

Name: Voskuhl, Rhonda Renee
E-Commons ID: VOSKUHL2

OTHER SUPPORT – Project/Proposal

1. ACTIVE

Project/Proposal Title	**Non-invasive Imaging of Brain Infiltrating T Lymphocytes in a Mouse Model of Experimental Autoimmune Encephalomyelitis with PET**
Major Goals	To image inflammation in vivo in EAE
Status of Support	Active
Project Number	R01NS112287
Name of PD/PI	Clark, Peter M
Source of Support	NIH-NINDS National Institute of Neurological Disorders and Stroke
Primary Place of Performance	University of California, Los Angeles
Project/Proposal Support Start Date	5/15/2019
Project/Proposal Support End Date	2/29/2024
Annual Direct Costs	$218,750
Person Months Per Budget Period	**Year** / **Cal** / **Acad** / **Sum** **2023** 0.60 **2024** 0.60

Project/Proposal Title	**Novel Estrogen Receptor Beta Ligand Treatment for Neuroprotection**
Major Goals	Preclinical studies of a novel ER beta ligand for development as a treatment for MS
Status of Support	Active
Project Number	20205124
Name of PD/PI	Voskuhl, Rhonda Renee
Source of Support	Yuyu Pharma, Inc. (Korea, Republic of)
Primary Place of Performance	University of California, Los Angeles
Project/Proposal Support Start Date	1/16/2021
Project/Proposal Support End Date	7/16/2023
Annual Direct Costs	$48,800
Person Months Per Budget Period	**Year** / **Cal** / **Acad** / **Sum** **2023** 1.20

Name: Voskuhl, Rhonda Renee
E-Commons ID: VOSKUHL2

Project/Proposal Title	**Neuroprotection in MS: A Cell-Specific and Region-Specific Transcriptomics Approach**
Major Goals	Understanding neurodengerative mechanisms in preclinical model of MS
Status of Support	Active
Project Number	R01NS109670
Name of PD/PI	Voskuhl, Rhonda Renee
Source of Support	NIH-NINDS National Institute of Neurological Disorders and Stroke
Primary Place of Performance	University of California, Los Angeles
Project/Proposal Support Start Date	9/30/2018
Project/Proposal Support End Date	5/31/2023
Annual Direct Costs	$284,984
Person Months Per Budget Period	**Year** / **Cal** / **Acad** / **Sum** **2023** / 3.60 / /

Project/Proposal Title	**The Mechanism of Gray Matter Atrophy in Experimental Autoimmune Encephalomyelitis**
Major Goals	To determine the role of oxidative stress in gray matter atrophy in EAE.
Status of Support	Active
Project Number	R21NS121806
Name of PD/PI	Mackenzie-Graham, Allan
Source of Support	NIH-NINDS National Institute of Neurological Disorders and Stroke
Primary Place of Performance	University of California, Los Angeles
Project/Proposal Support Start Date	4/1/2021
Project/Proposal Support End Date	9/30/2022
Annual Direct Costs	$125,000
Person Months Per Budget Period	**Year** / **Cal** / **Acad** / **Sum** **2022** / 0.60 / /

2. PENDING

None

3. IN-KIND CONTRIBUTIONS / FOREIGN SUPPORTS

None

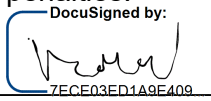
Name: Voskuhl, Rhonda Renee
E-Commons ID: VOSKUHL2

4. OVERLAP

None

5. PI Certification

I, PD/PI or other senior/key personnel, certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

DocuSigned by:

7ECE03ED1A9E409...

Signature

June 28, 2022

Date

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rhonda	R.	Voskuhl	MD	PD/PI	203,700.00	6.6			112,035.00	43,133.00	155,168.00
2 .	Dr.	Yuichiro		Itoh	PhD	Co-Investigator	107,900.00	4.2			37,765.00	18,240.00	56,005.00
3 .	Dr.	Jin		Zhou	PhD	Co-Investigator	160,000.00	0.6			8,000.00	3,080.00	11,080.00
4 .	Dr.	Allan		MacKenzie-Graham	PhD	Co-Investigator	137,900.00	1.8			20,685.00	7,964.00	28,649.00
5 .	Dr.	Prabha		Siddarth	PhD	Co-Investigator	153,697.00	0.6			7,685.00	3,712.00	11,397.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **262,299.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
1	Graduate Students	6			36,971.00	1,479.00	38,450.00
	Undergraduate Students						
	Secretarial/Clerical						
1	Senior Lab Technician	12			74,500.00	40,081.00	114,581.00
1	MRI Lab Technician	3.6			15,485.00	8,331.00	23,816.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**176,847.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**439,146.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	
Total Travel Cost	**3,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 1**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,426.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Animals	45,000.00
9. Sequencing Core facility	25,000.00
10. Mitochondrial function / Synaptosome Core	8,000.00
11. MRI in mice	25,000.00
12. DOMSTAT	3,000.00
13. Tuition Fees	17,857.00
14. Technology Infrastructure Fees (TIF)	1,556.00
Total Other Direct Costs	**149,839.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**591,985.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Research On Campus	56	574,128.00	321,512.00
		Total Indirect Costs	**321,512.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Janet Turner, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**913,497.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	913,497.00

L. Budget Justification*	File Name:
	Budget_Justification_RV1071243866.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2024 **End Date*:** 03-31-2025 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rhonda	R.	Voskuhl	MD	PD/PI	203,700.00	6.6			112,035.00	43,133.00	155,168.00
2 .	Dr.	Yuichiro		Itoh	PhD	Co-Investigator	107,900.00	4.2			37,765.00	18,240.00	56,005.00
3 .	Dr.	Jin		Zhou	PhD	Co-Investigator	160,000.00	0.6			8,000.00	3,080.00	11,080.00
4 .	Dr.	Allan		MacKenzie-Graham	PhD	Co-Investigator	137,900.00	1.8			20,685.00	7,964.00	28,649.00
5 .	Dr.	Prabha		Siddarth	PhD	Co-Investigator	153,697.00	0.6			7,685.00	3,712.00	11,397.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **262,299.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
1	Graduate Students	6			36,971.00	1,479.00	38,450.00
	Undergraduate Students						
	Secretarial/Clerical						
1	Senior Lab Technician	12			74,500.00	40,081.00	114,581.00
1	MRI Lab Technician	3.6			15,485.00	8,331.00	23,816.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**176,847.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**439,146.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Tracking Number: GRANT13677549
Funding Opportunity Number: RFA-NS-22-038 . Received Date: 2022-07-08T17:54:10.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2024 **End Date*:** 03-31-2025 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	
Total Travel Cost	**3,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2024 **End Date*:** 03-31-2025 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,426.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Animals	45,000.00
9. Sequencing Core facility	25,000.00
10. Mitochondrial function / Synaptosome Core	8,000.00
11. MRI in mice	25,000.00
12. DOMSTAT	3,000.00
13. Tuition Fees	17,857.00
14. Technology Infrastructure Fees (TIF)	1,556.00
Total Other Direct Costs	**149,839.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**591,985.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Research On Campus	56	574,128.00	321,512.00
		Total Indirect Costs	**321,512.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Janet Turner, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**913,497.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	913,497.00

L. Budget Justification*	File Name:
	Budget_Justification_RV1071243866.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2025 **End Date*:** 03-31-2026 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rhonda	R.	Voskuhl	MD	PD/PI	203,700.00	6.6			112,035.00	43,133.00	155,168.00
2 .	Dr.	Yuichiro		Itoh	PhD	Co-Investigator	107,900.00	4.2			37,765.00	18,240.00	56,005.00
3 .	Dr.	Jin		Zhou	PhD	Co-Investigator	160,000.00	0.6			8,000.00	3,080.00	11,080.00
4 .	Dr.	Allan		MacKenzie-Graham	PhD	Co-Investigator	137,900.00	1.8			20,685.00	7,964.00	28,649.00
5 .	Dr.	Prabha		Siddarth	PhD	Co-Investigator	153,697.00	0.6			7,685.00	3,712.00	11,397.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **262,299.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
1	Graduate Students	6			36,971.00	1,479.00	38,450.00
	Undergraduate Students						
	Secretarial/Clerical						
1	Senior Lab Technician	12			74,500.00	40,081.00	114,581.00
1	MRI Lab Technician	3.6			15,485.00	8,331.00	23,816.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**176,847.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**439,146.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2025 **End Date*:** 03-31-2026 **Budget Period: 3**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	
Total Travel Cost	**3,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2025 **End Date*:** 03-31-2026 **Budget Period: 3**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,426.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Animals	45,000.00
9. Sequencing Core facility	25,000.00
10. Mitochondrial function / Synaptosome Core	8,000.00
11. MRI in mice	25,000.00
12. DOMSTAT	3,000.00
13. Tuition Fees	17,857.00
14. Technology Infrastructure Fees (TIF)	1,556.00
Total Other Direct Costs	**149,839.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**591,985.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Research On Campus	56	574,128.00	321,512.00
		Total Indirect Costs	**321,512.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Janet Turner, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**913,497.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	913,497.00

L. Budget Justification*	File Name:
	Budget_Justification_RV1071243866.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2026 **End Date*:** 03-31-2027 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rhonda	R.	Voskuhl	MD	PD/PI	203,700.00	6.6			112,035.00	43,133.00	155,168.00
2 .	Dr.	Yuichiro		Itoh	PhD	Co-Investigator	107,900.00	4.2			37,765.00	18,240.00	56,005.00
3 .	Dr.	Jin		Zhou	PhD	Co-Investigator	160,000.00	0.6			8,000.00	3,080.00	11,080.00
4 .	Dr.	Allan		MacKenzie-Graham	PhD	Co-Investigator	137,900.00	1.8			20,685.00	7,964.00	28,649.00
5 .	Dr.	Prabha		Siddarth	PhD	Co-Investigator	153,697.00	0.6			7,685.00	3,712.00	11,397.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **262,299.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
1	Graduate Students	6			36,971.00	1,479.00	38,450.00
	Undergraduate Students						
	Secretarial/Clerical						
1	Senior Lab Technician	12			74,500.00	40,081.00	114,581.00
1	MRI Lab Technician	3.6			15,485.00	8,331.00	23,816.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**176,847.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**439,146.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Tracking Number: GRANT13677549 Funding Opportunity Number: RFA-NS-22-038 . Received Date: 2022-07-08T17:54:10.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2026 **End Date*:** 03-31-2027 **Budget Period: 4**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	
Total Travel Cost	**3,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2026 **End Date*:** 03-31-2027 **Budget Period: 4**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,426.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Animals	45,000.00
9. Sequencing Core facility	25,000.00
10. Mitochondrial function / Synaptosome Core	8,000.00
11. MRI in mice	25,000.00
12. DOMSTAT	3,000.00
13. Tuition Fees	17,857.00
14. Technology Infrastructure Fees (TIF)	1,556.00
Total Other Direct Costs	**149,839.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**591,985.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Research On Campus	56	574,128.00	321,512.00
		Total Indirect Costs	**321,512.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Janet Turner, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**913,497.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	913,497.00

L. Budget Justification*	File Name:
	Budget_Justification_RV1071243866.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2027 **End Date*:** 03-31-2028 **Budget Period: 5**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rhonda	R.	Voskuhl	MD	PD/PI	203,700.00	6.6			112,035.00	43,133.00	155,168.00
2 .	Dr.	Yuichiro		Itoh	PhD	Co-Investigator	107,900.00	4.2			37,765.00	18,240.00	56,005.00
3 .	Dr.	Jin		Zhou	PhD	Co-Investigator	160,000.00	0.6			8,000.00	3,080.00	11,080.00
4 .	Dr.	Allan		MacKenzie-Graham	PhD	Co-Investigator	137,900.00	1.8			20,685.00	7,964.00	28,649.00
5 .	Dr.	Prabha		Siddarth	PhD	Co-Investigator	153,697.00	0.6			7,685.00	3,712.00	11,397.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **262,299.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
1	Graduate Students	6			36,971.00	1,479.00	38,450.00
	Undergraduate Students						
	Secretarial/Clerical						
1	Senior Lab Technician	12			74,500.00	40,081.00	114,581.00
1	MRI Lab Technician	3.6			15,485.00	8,331.00	23,816.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**176,847.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**439,146.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2027 **End Date*:** 03-31-2028 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	
Total Travel Cost	**3,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT13677549 Funding Opportunity Number: RFA-NS-22-038 . Received Date: 2022-07-08T17:54:10.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2027 **End Date*:** 03-31-2028 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,426.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Animals	45,000.00
9. Sequencing Core facility	25,000.00
10. Mitochondrial function / Synaptosome Core	8,000.00
11. MRI in mice	25,000.00
12. DOMSTAT	3,000.00
13. Tuition Fees	17,857.00
14. Technology Infrastructure Fees (TIF)	1,556.00
Total Other Direct Costs	**149,839.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**591,985.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Research On Campus	56	574,128.00	321,512.00
		Total Indirect Costs	**321,512.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Janet Turner, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**913,497.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	913,497.00

L. Budget Justification*	File Name:
	Budget_Justification_RV1071243866.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 6

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2028 **End Date*:** 03-31-2029 **Budget Period: 6**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rhonda	R.	Voskuhl	MD	PD/PI	203,700.00	6.6			112,035.00	43,133.00	155,168.00
2 .	Dr.	Yuichiro		Itoh	PhD	Co-Investigator	107,900.00	4.2			37,765.00	18,240.00	56,005.00
3 .	Dr.	Jin		Zhou	PhD	Co-Investigator	160,000.00	0.6			8,000.00	3,080.00	11,080.00
4 .	Dr.	Allan		MacKenzie-Graham	PhD	Co-Investigator	137,900.00	1.8			20,685.00	7,964.00	28,649.00
5 .	Dr.	Prabha		Siddarth	PhD	Co-Investigator	153,697.00	0.6			7,685.00	3,712.00	11,397.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name: **Total Senior/Key Person** **262,299.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
1	Graduate Students	6			36,971.00	1,479.00	38,450.00
	Undergraduate Students						
	Secretarial/Clerical						
1	Senior Lab Technician	12			74,500.00	40,081.00	114,581.00
1	MRI Lab Technician	3.6			15,485.00	8,331.00	23,816.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**176,847.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**439,146.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 6

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2028 **End Date*:** 03-31-2029 **Budget Period: 6**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	
Total Travel Cost	**3,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 6

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2028 **End Date*:** 03-31-2029 **Budget Period: 6**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,426.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Animals	45,000.00
9. Sequencing Core facility	25,000.00
10. Mitochondrial function / Synaptosome Core	8,000.00
11. MRI in mice	25,000.00
12. DOMSTAT	3,000.00
13. Tuition Fees	17,857.00
14. Technology Infrastructure Fees (TIF)	1,556.00
Total Other Direct Costs	**149,839.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**591,985.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Research On Campus	56	574,128.00	321,512.00
		Total Indirect Costs	**321,512.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Janet Turner, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**913,497.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	913,497.00

L. Budget Justification*	File Name:
	Budget_Justification_RV1071243866.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 7

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2029 **End Date*:** 03-31-2030 **Budget Period: 7**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rhonda	R.	Voskuhl	MD	PD/PI	203,700.00	6.6			112,035.00	43,133.00	155,168.00
2 .	Dr.	Yuichiro		Itoh	PhD	Co-Investigator	107,900.00	4.2			37,765.00	18,240.00	56,005.00
3 .	Dr.	Jin		Zhou	PhD	Co-Investigator	160,000.00	0.6			8,000.00	3,080.00	11,080.00
4 .	Dr.	Allan		MacKenzie-Graham	PhD	Co-Investigator	137,900.00	1.8			20,685.00	7,964.00	28,649.00
5 .	Dr.	Prabha		Siddarth	PhD	Co-Investigator	153,697.00	0.6			7,685.00	3,712.00	11,397.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **262,299.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
1	Graduate Students	6			36,971.00	1,479.00	38,450.00
	Undergraduate Students						
	Secretarial/Clerical						
1	Senior Lab Technician	12			74,500.00	40,081.00	114,581.00
1	MRI Lab Technician	3.6			15,485.00	8,331.00	23,816.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**176,847.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**439,146.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: RFA-NS-22-038 . Received Date: 2022-07-08T17:54:10.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 7

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2029 **End Date*:** 03-31-2030 **Budget Period: 7**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	
Total Travel Cost	**3,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT13677549 Funding Opportunity Number: RFA-NS-22-038 . Received Date: 2022-07-08T17:54:10.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 7

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2029 **End Date*:** 03-31-2030 **Budget Period: 7**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,426.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Animals	45,000.00
9. Sequencing Core facility	25,000.00
10. Mitochondrial function / Synaptosome Core	8,000.00
11. MRI in mice	25,000.00
12. DOMSTAT	3,000.00
13. Tuition Fees	17,857.00
14. Technology Infrastructure Fees (TIF)	1,556.00
Total Other Direct Costs	**149,839.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**591,985.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Research On Campus	56	574,128.00	321,512.00
		Total Indirect Costs	**321,512.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Janet Turner, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**913,497.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	913,497.00

L. Budget Justification*	File Name:
	Budget_Justification_RV1071243866.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 12/31/2022

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 8

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Enter name of Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2030 **End Date*:** 03-31-2031 **Budget Period: 8**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Rhonda	R.	Voskuhl	MD	PD/PI	203,700.00	6.6			112,035.00	43,133.00	155,168.00
2 .	Dr.	Yuichiro		Itoh	PhD	Co-Investigator	107,900.00	4.2			37,765.00	18,240.00	56,005.00
3 .	Dr.	Jin		Zhou	PhD	Co-Investigator	160,000.00	0.6			8,000.00	3,080.00	11,080.00
4 .	Dr.	Allan		MacKenzie-Graham	PhD	Co-Investigator	137,900.00	1.8			20,685.00	7,964.00	28,649.00
5 .	Dr.	Prabha		Siddarth	PhD	Co-Investigator	153,697.00	0.6			7,685.00	3,712.00	11,397.00

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **262,299.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
1	Graduate Students	6			36,971.00	1,479.00	38,450.00
	Undergraduate Students						
	Secretarial/Clerical						
1	Senior Lab Technician	12			74,500.00	40,081.00	114,581.00
1	MRI Lab Technician	3.6			15,485.00	8,331.00	23,816.00
3	**Total Number Other Personnel**					**Total Other Personnel**	**176,847.00**
						Total Salary, Wages and Fringe Benefits (A+B)	**439,146.00**

RESEARCH & RELATED Budget {A-B} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 8

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2030 **End Date*:** 03-31-2031 **Budget Period: 8**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	3,000.00
2. Foreign Travel Costs	
Total Travel Cost	**3,000.00**

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 8

UEI*: RN64EPNH8JC6

Budget Type*: ● Project ❍ Subaward/Consortium

Organization: The Regents of the University of California, Los Angeles

Start Date*: 04-01-2030 **End Date*:** 03-31-2031 **Budget Period: 8**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	24,426.00
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
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8. Animals	45,000.00
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13. Tuition Fees	17,857.00
14. Technology Infrastructure Fees (TIF)	1,556.00
Total Other Direct Costs	**149,839.00**

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	**591,985.00**

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Research On Campus	56	574,128.00	321,512.00
		Total Indirect Costs	**321,512.00**

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) DHHS, Janet Turner, 415-437-7820

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	**913,497.00**

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	913,497.00

L. Budget Justification*	File Name:
	Budget_Justification_RV1071243866.pdf

RESEARCH & RELATED Budget {F-K} (Funds Requested)

BUDGET JUSTIFICATION

The annual direct costs requested in this R35 were calculated by Dr. Alisa Schaefer, NINDS, NIH, on June 2, 2021 based on the 4-year average of direct costs of my current award numbers R01NS096748 and R01NS109670 multiplied by 1.2. The annual direct cost for this R35 is $591,985.50 per year.

FY	PI Name	Type	Project Num	Awd Dir Cost	FY 2017	FY 2018	FY 2019	FY 2020	FY 2021	average FY18-21	average * 1.2
2022	VOSKUHL, RHONDA R	5	R01NS109670-05	$284,984	$277,783	$562,767	$562,767	$562,767	$284,984	$493,321.25	$591,985.50
2021	VOSKUHL, RHONDA R	5	R01NS109670-04	$284,984							
2020	VOSKUHL, RHONDA R	5	R01NS096748-05	$277,783							
2020	VOSKUHL, RHONDA R		R01NS109670-03	$284,984							
2019	VOSKUHL, RHONDA R	5	R01NS096748-04	$277,783							
2019	VOSKUHL, RHONDA R		R01NS109670-02	$284,984							
2018	VOSKUHL, RHONDA R	1	R01NS109670-01	$284,984							
2018	VOSKUHL, RHONDA R	5	R01NS096748-03	$277,783							
2017	VOSKUHL, RHONDA R	5	R01NS096748-02	$277,783							

PERSONNEL

Actual salaries (or NIH cap) and UCLA's composite benefit rate were utilized in this multi-year project.

SENIOR/KEY PERSONNEL

Rhonda Voskuhl, M.D., Principal Investigator (6.60 calendar months each year). Dr. Voskuhl will be responsible for research direction which drives the selection of the production of mice of all genotypes, MS disease models, and overall organization. All basic mouse experiments are considered in the context of MS clinical observations and unmet need. In addition, Dr. Voskuhl will use human MS imaging, transcriptomics and immunohistochemistry to guide and prioritizes work in mouse models. Within preclinical work, Dr. Voskuhl will apply the results of changes in gene expression primarily using chronic EAE to identify cell-specific, region-specific and sex-specific targets. She will employ the cuprizone model as needed depending on the question. She will be primarily responsible for directing experimental implementation as well as coordinating interpretation of transcriptomic results for prioritization of mechanistic studies to pursue. This will include experimental planning, analyses, and progress to publications. She will directly oversee work by her senior lab technician, Ms. Noriko Itoh, in charge of immunohistochemistry and will work closely with the graduate student on both scientific issues and career development goals. Dr. Voskuhl will assure that administrative issues are managed, that deadlines are met (e.g., regulatory approvals, findings properly disseminated to the scientific community), and that fiscal matters are properly executed. She will direct the trajectory of the research and be responsible for writing of manuscripts with assistance from collaborators.

Yuichiro Itoh, Ph.D. Co-Investigator (4.20 calendar months each year). Dr. Itoh will oversee breeding strategies and generation of cohorts of CNS cell-specific RiboTag mice and selective deletion of conditional knockouts in each CNS cell. He will get RNA sequencing data from the UCLA Sequencing Core and proceed to do RNA sequencing and gene expression pathway enrichment analyses. He will also design mice for epigenetic studies. He has carried out these studies in our publications. Dr. Itoh will also be in charge of single nuclei RNA sequencing as well as analyses in human MS snRNA-seq data (in collaboration with Dr. Jin Zhou of DOMStat). Results in human MS will guide preclinical work on top differentially expressed gene pathways in EAE for genetic and pharmacologic knock out and knock down, respectively. Dr. Itoh will work closely with Dr. Voskuhl and Dr. Zhou during these analyses regarding interpretation and further experimentation. Dr. Itoh will also assist with writing of manuscripts particularly in the area of gene expression and pathway analyses.

Jin Zhou, Ph.D., Co-Investigator (0.6 calendar months each year). Associate Professor, Dept of Medicine Statistics Core (DOMStat). Dr. Zhou will carry out transcriptomics analyses which integrate gene expression data across CNS cell types, CNS regions, both sexes, and across aging stages. She will assess interactions between these variables within the mouse data. Dr. Zhou will also be in charge of methylation statistical analyses, as well as integrating methylome data with transcriptome data. Dr. Zhou will mine existing human scRNA-seq datasets (in collaboration with Dr. Itoh) to help guide further mouse studies. She will work with Dr. Siddarth to integrate transcriptomics data with region-specific cellular and regional brain volume data. She has full access to facilities in the DOMStat Core (see Letter of Support from DOMStat Director, Dr. David Elashoff).

Allan MacKenzie-Graham, Ph.D. Co-Investigator (1.8 calendar months each year). Dr. MacKenzie-Graham will

be in charge of all neuroimaging acquisition, analysis, and interpretation (MRI). As faculty of the UCLA Brain Mapping Center, he has full access to the dedicated small animal MRI scanner. He will directly oversee work by the part time MRI neuroimaging technician. Dr. MacKenzie-Graham will provide neuroimaging data for Dr. Siddarth, for her to do statistical analyses correlating changes in gene expression with changes in localized gray matter atrophy. Dr. MacKenzie-Graham will also be in charge of CLARITY analysis for 3D neuropathology. Clarity neuropathology will also be correlated with localized gray matter atrophy. This will be done in collaboration with Dr. Voskuhl (PI) and with Dr. Siddarth. Dr. MacKenzie-Graham and Dr. Voskuhl have an ongoing collaboration investigating region-specific and sex-specific substructure atrophy using human MS datasets sent from Dr. Freidemannn Paul's group at Charite, Univ. of Berlin to UCLA. Dr. MacKenzie-Graham will lead the human image analyses, while working with Dr. Voskuhl and Dr. Paul. He will assist with writing of manuscripts particularly in the area of neuroimaging.

Prabha Siddarth, Ph.D. Co-Investigator (0.6 calendar months each year). Senior Statistician, UCLA Semel Institute Statistics Core (SiStat). Dr. Siddarth will carry out statistical analyses between quantitative expression of key genes of focus at the protein level by immunohistochemistry in each region with corresponding regional substructure brain volumes, in each sex and at each age. This will include regressions, multimodality correlations, and predictive probabilities. It will also include between groups comparisons by age, sex, and age by sex interactions. Dr. Siddarth will work with Dr. Zhou as they integrate gene neuropathology and neuroimaging statistics with transcriptomics statistics. As Semel Institute faculty, she has full access to the UCLA Semel Institute Statistics Core (SiStat). She will also assist with writing of manuscripts particularly in the area of statistical analyses.

This team of investigators has an extensive track record of successful collaboration with many shared publications and grants over the last several years.

OTHER PERSONNEL

Graduate student (GSR), 6.0 calendar months each year). The graduate student (Diego Cortez-Delgado currently) with work closely with Dr. Voskuhl to be mentored in cell-specific, region-specific, and sex-specific research using transcriptomics followed by determination of causality through gene deletion in the cell identified by gene expression pathway analysis. This trainee will learn hands on lab techniques from Ms. Itoh, and is expected to become increasingly independent. He will learn genetic engineering mouse design from Dr. Itoh and transcriptome analyses from Dr. Itoh and Dr. Zhou. The graduate student will be heavily involved in manuscript writing and will apply for graduate student fellowships based on the project. Notably, the overall project is highly ambitious, requiring Ms. Itoh and this GSR to focus on different cell types, pathways, sex differences, and aging aspects. This creates parallel work which is well supervised. Upon attaining his degree, this GSR will be replaced by another during the planned 8 year duration of this award.

Noriko Itoh, M.S., Senior Lab Technician, (12.0 calendar months each year). Under the supervision of Dr. Voskuhl, Ms. Itoh will be responsible for breeding colonies, genotyping, EAE induction, and treatment. She will sacrifice and perfuse all mice for collection of CNS tissues. Ms. Itoh will be responsible for tissue acquisition, obtaining RNAs from cell specific RiboTag mice, validation of HA labeling and cell-specific enrichment, as well as validation of changes in gene expression by RT-qPCR and immunohistochemistry. She will also do clinical EAE scoring and EAE neuropathology as well as mitochondrial & synaptosome experiments in the dedicated UCLA core. She will provide care to EAE mice as per veterinarian recommendations and ARC guidelines. Ms. Itoh maintain ARC for approvals and continuations.

MRI Lab Technician, (3.6 calendar months each year). Under the supervision of Dr. MacKenzie-Graham, the MRI lab technician will acquire MRI scans of all cohorts of mice in the Brain Mapping Center, then carry out image processing and analyses of all raw image data for localized gray matter atrophy using atlas-based morphometry under his direction.

Benefit rates are calculated at 38.5% for HCOMP Faculty, 48.3% for Other Academics, 4% for GSR, and 53.8% for Non-exempt. The fringe benefit rates used have been proposed to DHHS.

Travel

Domestic travel of two investigators to scientific conference each year (within the U.S.). $3,000 per year.Travel

costs for each: $750 for airfare, $600 for three nights lodging, and $150 for food and taxi.

Other Costs

Lab reagents: $24,426 per year
This includes funds for RNA isolations, PCR for genotyping, qPCRs for expression analysis at the RNA level, antibodies for immunohistochemistry, EAE induction, EAE and placebo treatments.

Animals: DLAM (mouse vivarium): $45,000 per year
Extensive mouse colonies will be needed to support the study of transcriptomics in astrocytes, oligodendrocytes, microglia, and neurons, in both females and males, and at different life stages. Also double-label transcriptomics in 2 cells within the same mice and cell-specific gene deletion mice will be done.
Sequencing Core facility: $25,000 per year
Extensive RNA sequencing will be needed to determine gene expression in astrocytes, oligodendrocytes, microglia, and neurons, in both females and males, and at different life stages during disease as compared to healthy controls.

Mitochondrial function / Synaptosome Core: $8,000 per year
Core services are needed for respirometry assays by SeaHorse Analyzer as an outcome of mitochondrial function in neurons as a functional correlate of neuropathology.

MRI in mice: $25,000 per year

Atlas based morphometry analysis of in vivo MRIs in both females and males, and at different ages during EAEas compared to healthy controls will localize the region of gray matter atrophy and the impact of cell-specific knockouts and pharmacologic treatments.

DOMStat $3,000 per year: Core Data Management and statistical analysis staff to support Dr. Zhou and Dr. Siddarth.

Tuition Fees $17,857 per year: The university policy is graduate student researcher working at 25% or greater in a lab is eligible for tuition/remission fees. Funds are requested to offset UCLA tuition fees and health insurance costs for the listed graduate student. These funds will be used to warrant that the graduate student researcher can focus the efforts on this project.

Technology Infrastructure Fees (TIF): Funding is requested for teleconferences and telecommunications, as UCLA charges a technology infrastructure fee of $43.96/calendar month per employee for communications andtelephone services. TIF pays for campus communication services on the basis of a monthly accounting of actual usage data. TIF is a charge for campus network, backbone, internal connection, hardware, wireless services, etc. These mandatory costs are charged as direct costs and are not recovered as indirect costs. We are requesting $1,586 each year.

Facilities and Administrative Costs: Indirect Costs are based on the institutions federally negotiated agreement dated 10/12/2018. Effective 7/1/19 our rate becomes provisional. Awards using provisional rates must be adjusted once a new F&A rate agreement is negotiated and approved by the cognizant agency for indirect costs. MTDC is excluding student tuition/remission costs.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		2,098,392.00
Section B, Other Personnel		1,414,776.00
Total Number Other Personnel	24	
Total Salary, Wages and Fringe Benefits (A+B)		3,513,168.00
Section C, Equipment		
Section D, Travel		24,000.00
1. Domestic	24,000.00	
2. Foreign		
Section E, Participant/Trainee Support Costs		
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other		
6. Number of Participants/Trainees		
Section F, Other Direct Costs		1,198,712.00
1. Materials and Supplies	195,408.00	
2. Publication Costs		
3. Consultant Services		
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations		
8. Other 1	360,000.00	
9. Other 2	200,000.00	
10. Other 3	64,000.00	
11. Other 4	200,000.00	
12. Other 5	24,000.00	
13. Other 6	142,856.00	
14. Other 7	12,448.00	
15. Other 8		
16. Other 9		
17. Other 10		
Section G, Direct Costs (A thru F)		4,735,880.00
Section H, Indirect Costs		2,572,096.00

Section I, Total Direct and Indirect Costs (G + H)	7,307,976.00
Section J, Fee	
Section K, Total Costs and Fee (I + J)	7,307,976.00

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

Expiration Date: 09/30/2024

1. Vertebrate Animals Section

Are vertebrate animals euthanized? ● Yes ○ No

If "Yes" to euthanasia

Is the method consistent with American Veterinary Medical Association (AVMA) guidelines?

● Yes ○ No

If "No" to AVMA guidelines, describe method and provide scientific justification

2. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period *Anticipated Amount ($) *Source(s)

PHS 398 Cover Page Supplement

3. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ○ Yes ● No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, check the box indicating that one from the registry will be used:

Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s) (Example: 0004):

4. Human Fetal Tissue Section

*Does the proposed project involve human fetal tissue obtained from elective abortions? ○ Yes ● No

If "yes" then provide the HFT Compliance Assurance

If "yes" then provide the HFT Sample IRB Consent Form

5. Inventions and Patents Section (Renewal applications)

*Inventions and Patents: ○ Yes ○ No

If the answer is "Yes" then please answer the following:

*Previously Reported: ○ Yes ○ No

6. Change of Investigator/Change of Institution Section

❑ Change of Project Director/Principal Investigator

Name of former Project Director/Principal Investigator

Prefix:

*First Name:

Middle Name:

*Last Name:

Suffix:

❑ Change of Grantee Institution

*Name of former institution:

PHS 398 Research Plan

OMB Number: 0925-0001
Expiration Date: 09/30/2024

Introduction	
1. Introduction to Application (for Resubmission and Revision applications)	
Research Plan Section	
2. Specific Aims	
3. Research Strategy*	R35_Research_Strategy1071243917.pdf
4. Progress Report Publication List	
Other Research Plan Section	
5. Vertebrate Animals	Vertebrate_Animals1071122660.pdf
6. Select Agent Research	
7. Multiple PD/PI Leadership Plan	
8. Consortium/Contractual Arrangements	
9. Letters of Support	Letters_Of_Support1071243833.pdf
10. Resource Sharing Plan(s)	Resource_Sharing_Plan_R351071243743.pdf
11. Authentication of Key Biological and/or Chemical Resources	Auth_Key_Reagent_R351071243731.pdf
Appendix	
12. Appendix	

A new approach to a major unmet need. Multiple sclerosis (MS) is an autoimmune and neurodegenerative disease with inflammatory lesions, demyelination, axonal damage, glial activation and synaptic loss. There are acute relapses and accumulation of permanent disabilities. There are over 20 disease modifying treatments (DMTs) targeting cells and mechanisms in the immune system, with robust effects on relapses. There remains a need for DMTs that target cells in central nervous system (CNS) to halt neurodegeneration and repair disabilities. The CNS is a highly complex target organ of the autoimmune attack in MS. I hypothesize that neuroprotective treatments in MS will not work using a "one size fits all" approach using Phase 3 trials with a composite of disabilities (Expended Disabilities Status Scale, EDSS) and whole brain atrophy as outcomes. Three clinical observations are clues to a new approach: **1) MS patients are heterogenous regarding which disabilities are predominant, 2) being female versus male impacts disability worsening, and 3) aging aligns with disability progression.** We will use a cell-specific, region-specific, and sex-specific approach to discover optimal neurodegenerative treatment targets for distinct disabilities in MS women and men. Beyond this R35, future clinical trials in MS will target a specific disability as the primary outcome measure with corresponding regional MRI abnormalities as the biomarker, and enrollment will be tailored for sex and age.

Overview: Our preclinical work begins (clinical observations) and ends (clinical trials) with MS patients, **Fig. 1.** Also, at the laboratory bench, human MS data guide preclinical lead prioritization and provide validation at three steps (Fig. 1, asterisks). This R35 will 1) Extend our recent work in astrocytes (1-3) and oligodendrocytes (4, 5) to microglia and neurons, with cell:cell interactions revealed in mice double-labelled to study gene expression changes in two distinct cell types in the same region in the same mouse, and 2) Determine if there is an effect of **sex** and/or **age** on the most differentially expressed cell-specific and region-specific pathways. This R35 takes our research to the next level: Identifying sex by age interactions in cell-specific and region-specific transcriptomics, neuropathology, and regional atrophy on MRI.

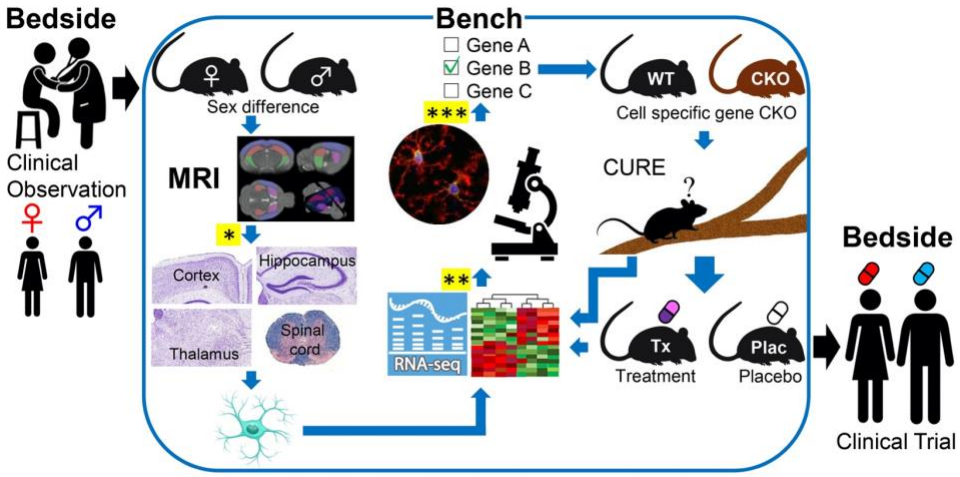

Fig. 1. Bedside to Bench to Bedside research: A region-specific, cell-specific, and sex-specific approach to neurodegeneration in MS. Clinical observations of sex differences are investigated at the preclinical level then translated back to the clinic as trials designed for each sex. Bench investigations entail *in vivo* MRI for region-specific atrophy, neuropathology of each region, RNA-sequencing of each CNS cell from each region, immunohistochemistry validation of top genes in highly differentially expressed pathways, conditional knockout (CKO) of target genes in each CNS cell to reverse phenotype, and knockdown of target genes with pharmacologic treatment (Tx) to reverse phenotype. The effect of genetic (CKO vs WT) and/or pharmacologic (treatment vs placebo) intervention on reversal of gene expression is determined using the same cell-specific and region-specific approach in each sex.
Human MS data guide preclinical research at 3 checkpoints (yellow highlighted asterisks, left of arrows):
* MRI in females and males with MS revealing sex differences in regions of atrophy will prioritize regions in EAE with atrophy.
** snRNA-seq analyses in females and males with MS revealing gene pathways of interest will prioritize gene pathways in EAE.
*** immunohistochemistry in females and males using MS postmortem tissues will validate immunohistochemistry in EAE.
Informative substitutions to the use of female versus male mice in the beginning (upper left), include: i) use of gonadectomized versus gonadally intact mice to reveal activational effects of sex hormones; ii) use of Four Core Genotype mice to reveal sex chromosome effects versus developmental sex hormone effects; and iii) use of young versus old mice to reveal the effect of aging. Use of more than one of these interventions in the same experiment will reveal sex hormone by age interactions or sex chromosome by age interactions.

A cell-specific and region-specific approach: Premise. Our disability-specific approach is based on the heterogeneity of disabilities in MS patients, and that distinct disabilities (walking, vision, cognition, coordination) align with different CNS regions. Even in healthy brain, a given CNS cell type differs in gene expression from one brain region to another for neurons (6), microglia (7), astrocytes (8, 9), and oligodendrocytes (10, 11). Mechanisms driving neurodegeneration underlying distinct disabilities in MS are unlikely to be identical across the CNS. So too, treatments to reverse neurodegeneration are unlikely to be identical across the CNS.

My lab has extensive experience in determining CNS cell-specific and region-specific gene expression changes in MS preclinical models (1, 2, 4, 12). We hypothesized that there would be regional differences in gene expression in response to injury during neurodegenerative disease and were the first to show it in chronic experimental autoimmune encephalomyelitis (EAE) in C57BL/6 mice (2). To avoid effects of *in vitro* cell isolation

on gene expression (13), we used *in vivo* RiboTag technology (14). Our cell-specific and region-specific transcriptomics approach identified the following candidate neuroprotective treatment targets: Spinal cord astrocytes have decreased expression of cholesterol synthesis pathway genes during EAE. In adults, cholesterol is synthesized by astrocytes and transported out via ATP-binding cassette transporter (ABCA1) to apolipoprotein E (ApoE) (15) to oligodendrocytes to make myelin (15, 16) to neurons for synaptic plasticity (17, 18). While damage in EAE is due to the autoimmune attack, we posited that failure of remyelination and synaptic plasticity is due to decreased cholesterol synthesis in astrocytes (2). Treatment with an ABCA1 agonist improved walking and reduced spinal cord pathology (2). This was confirmed by others (19). Optic nerve astrocytes have increased expression of complement pathway genes during optic neuritis in EAE (1), which we validated in MS using human postmortem tissues (2). This suggested targeting complement in optic neuritis in MS (1), which was confirmed by others (20). Also, higher C3 expression in females (1) suggested potential sex differences in efficacy of treatments targeting complement (21). Corpus callosum oligodendrocytes have increased expression of cholesterol synthesis pathway genes in oligodendrocytes during remyelination (4). Estrogen receptor beta (ERβ) ligand treatment recapitulated the promyelinating effect of estriol in the blood of pregnant mothers. It increased cholesterol synthesis gene expression in oligodendrocytes and enhanced remyelination in cuprizone & EAE models (4, 5). $CD4^+$ T lymphocytes: *Kdm6a*, an X chromosome gene, increased neuroinflammatory pathway signaling in $CD4^+$ T cells. Knockout of *Kdm6a* in $CD4^+$ T cells reversed the transcriptome and ameliorated EAE (22). **Studies in MS tissues have guided our preclinical studies (2, 4, 22, 23).**

A sex-specific approach: Premise. Our sex-specific approach in MS is based on sex differences in MS. Females are more susceptible to MS (24-27), but males show faster disability progression and worse gray matter atrophy (24, 26, 28-33). Sex differences in the healthy brain exist from mice to humans (34-39), providing evidence for effects of sex hormones and/or sex chromosomes. There are sex differences in substructure volumes even when accounting for differences in brain size (34, 36-38, 40-48). There are also sex differences in the brain at the cellular, molecular, and functional levels (49-54). Thus, mechanisms of neurodegeneration are unlikely to be identical in females and males. The study of sex differences capitalizes on a clinical observation, disentangling it at the laboratory bench, then translating findings to the clinic as a novel treatment trial (26). The importance of sex as a biologic variable (SABV) has been recognized by the NIH (55, 56). In this R35, identifying the effect of sex on the most differentially expressed cell-specific and region-specific pathways can lead to disability-specific neuroprotective treatments tailored for each sex.

I am a leader in the study of sex differences in the immune system and the CNS (26, 32, 33). Like other autoimmune diseases with a female bias, MS susceptibility is thought to be due to sex differences in immune responses (57, 58). We disentangled sex hormone and sex chromosome effects in EAE using the Four Core Genotypes (FCG) model to compare XX versus XY sex chromosome complements in the absence of the confound of a difference in sex hormones (59-61). We then determined whether differences in XX versus XY are due to X-gene dosage effects, parental imprinting of X genes, or Y gene effects (22, 62, 63). We also showed how sex hormone and sex chromosome effects can be complementary or compensatory in function (59, 64). For example, in EAE the XX genotype is proinflammatory in T lymphocytes, while estrogens at a level and type consistent with pregnancy are neuroprotective (26, 32, 65). This neuroprotection in EAE extends beyond spinal cord to include cerebral cortex, hippocampus and cerebellum (5, 66-68), and it is dependent on dose, timing, estrogen type (estradiol, estriol), and estrogen receptor (ER) ligation (ERα, ERβ) (5, 32, 66, 69, 70).

Sex differences in neurodegeneration during aging. Gray matter atrophy and disability progression are worse in MS men from young adulthood to midlife, median age < 50 years (71-73). In contrast, older women have worsening of their MS disabilities after menopause (74-80). Loss of neuroprotective estradiol with menopause is consistent with cognitive difficulties in healthy women with menopause, quantified by objective cognitive testing (81-87) and termed “brain fog” (81, 82, 84, 88-91). Alzheimer’s disease (AD) is more common in females, which is not accounted for by longevity (92-94). Women ages > 60 years have a higher rate of progression from Mild Cognitive Impairment (MCI) to AD and faster rates of brain atrophy. In contrast, at ages < 60 years, women are not at higher risk for MCI, and men have higher rates of progression from MCI to AD (94). Loss of sex hormones during menopause and andropause aligns with cognitive decline and increased AD risk (95-97). Similar negative effects of menopause and andropause may be due to testosterone’s conversion to estradiol in brain by aromatase. Decreased levels of either hormone during aging reduces estrogen receptor ligation in brain (98). In MS men, worse cognitive decline correlates with lower testosterone levels (99), and testosterone treatment reduced brain atrophy in a pilot trial by the PI (100, 101). In a placebo-controlled clinical trial by the PI (69), treatment with estriol, a natural ERβ ligand, reduced cerebral cortex atrophy and improved cognition (69, 102).

Cognitive improvement correlated with cerebral cortex sparing and estriol blood level. Serum neurofilament light chain (sNfL) levels were decreased by estriol treatment, and this correlated with less neuroaxonal injury (103).

Sex by age interactions: Hypothesis. Aging is a risk factor for the transition from the inflammatory MS phase to the neurodegenerative phase (28, 104). During health in mice and humans, aging aligns with brain atrophy, neurodegeneration, and cognitive decline. **I hypothesize that the effect of biologic sex during the lifespan is complex, with sex hormones and sex chromosomes contributing differently based on the timing of the loss of neuroprotective sex hormones during andropause versus menopause.** Andropause starts at age 30 with gradual decline of testosterone to old age (Fig. 2, blue). Menopause starts later (ages 46-52) with an abrupt decline in hormones (Fig. 2, red). At 75 to 90 years, loss of neuroprotective sex hormones in both sexes may unmask underlying effects of sex chromosomes (XX vs XY) that persist across the lifespan (Fig. 2, green). Here, we will determine whether sex differences in cell-specific and region-specific gene expression during aging are due to effects of sex hormones and/or sex chromosomes and identify the hormone receptor and/or sex chromosome gene responsible.

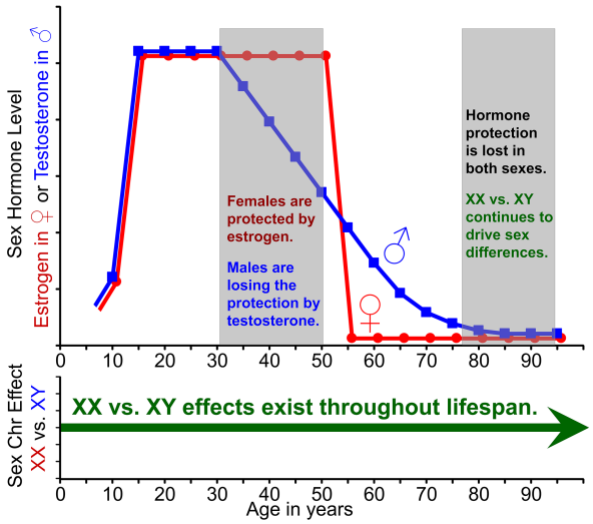

Fig. 2. Sex hormone and sex chromosome effects during aging: Neurodegeneration in males is worse before midlife, with females worse after midlife.

Preliminary data: A sex hormone by age interaction. Understanding the effect of brain aging during health can provide insights into the effect of brain aging during MS. Healthy menopausal women experience cognitive difficulties at menopause. Treatments are needed that target cognition in healthy menopausal women and target disability worsening in MS menopausal women. We recently discovered a sex difference in brain substructure atrophy in healthy aging mice by *in vivo* MRI (Fig. 3) and found a sex difference in the effect of gonadectomy on cognitive function at midlife (Fig. 4a). Ovariectomy induced cognitive deficits (Fig. 4b), astrocyte activation (Fig. 4c), synaptic loss and dorsal hippocampal atrophy in females at midlife, but not young age. Deletion of ERβ in astrocytes in midlife females recapitulated the effect of ovariectomy on cognitive deficits and dorsal hippocampal atrophy (Fig 5). Thus, ligation of ERβ in astrocytes was identified as a target to prevent hippocampal-dependent cognitive deficits and dorsal hippocampal atrophy in healthy females at midlife (3).

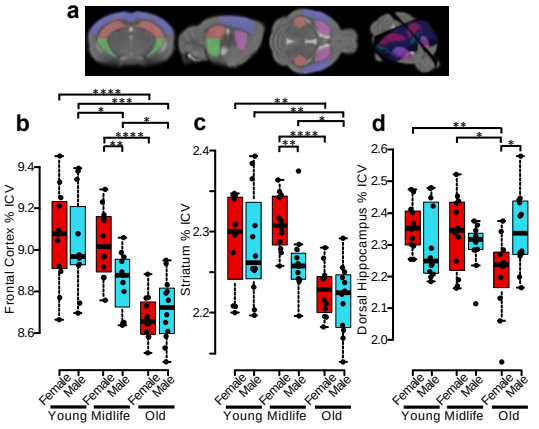

Fig. 3. In contrast to males (blue) who have gradual frontal cortex and striatum volume loss with aging, females (red) have substructure volume preservation from young age (3-4 months) to midlife (12-14 mo), followed by abrupt volume loss from midlife to old age (20-22 mo). a) substructure delineations; volumes expressed as % intracranial volume (ICV) in **b)** frontal cortex, **c)** striatum, **d)** dorsal hippocampus. red (females), blue (males). * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$.

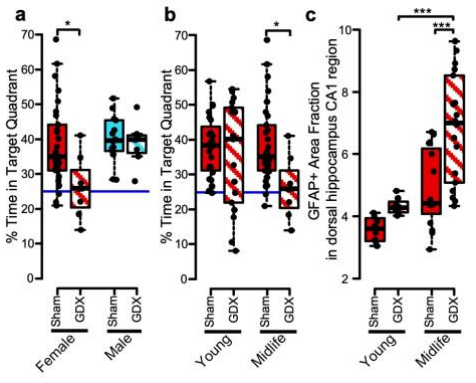

Fig. 4. Gonadectomy of females, but not males, worsens hippocampal-dependent cognition and increases astrocyte activation at midlife (12-14 mo), but not at young (3-4 mo) ages, revealing a sex hormone by age interaction. a,b) % time in target quadrant (Morris Water Maze); **c)** reactive astrocytosis (GFAP staining). red (females), blue (males); gonadally intact (solid), GDX (stripe).* $p < 0.05$; ** $p < 0.01$.

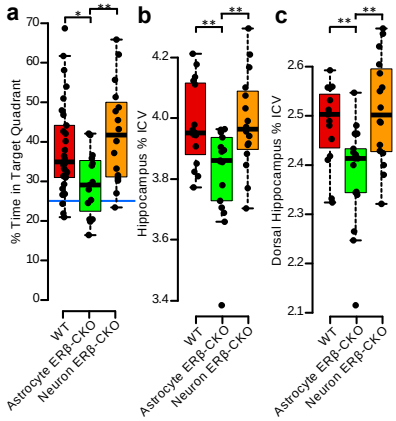

Fig. 5. Selective deletion of ERβ in astrocytes, but not neurons, induces hippocampal-dependent cognitive impairment and dorsal hippocampus atrophy at midlife in gonadally intact females. a) % time in TQ, **b)** whole hippocampal volumes, **c)** dorsal hippocampal volumes. red (WT), green (astrocyte ERβ CKO), orange (neuron ERβ CKO). * $p < 0.05$; ** $p < 0.01$.

We and others find that aging mice have worse walking and microglia activation in spinal cord during active and adoptive EAE (105). Here, we will identify age by EAE interactions in microglia (and astrocytes) in cord and also hippocampus, cerebral cortex, striatum, and cerebellum in each sex to find optimal targets.

Preliminary data: X chromosome gene. *Kdm6a* is a gene on the X chromosome that escapes X-inactivation and is expressed higher in XX (females) than XY (males) (22). KDM6A regulates expression of autosomal and sex chromosome genes by encoding for a histone demethylase that removes repressive trimethylation on histone H3 lysine 27 (H3K27me3) to expose chromatin for transcription (106, 107). When we selectively deleted *Kdm6a* in $CD4^+$ T lymphocytes, it reduced walking disability and neuropathology in spinal cord. The transcriptome in the CKO showed downregulation of expression of Neuroinflammation Signaling Pathway genes in $CD4^+$ T lymphocytes (22). This demonstrated that *Kdm6a* is proinflammatory in $CD4^+$ T lymphocytes during EAE, consistent with XX dosage increasing susceptibility of females to MS. Here, we will extend our approach to microglia. To make microglia-specific *Kdm6a* knockout mice, $Kdm6a^{f/f}$ (floxed/floxed) mice were crossed with *Tmem119*-Cre/ERT2 mice, and tamoxifen drove gene deletion. Data in *Tmem119*-Cre:RiboTag mice validated HA labelling specifically in microglia (Fig. 6a,b), and the microglial *Kdm6a* CKO showed increased H3K27me3 levels in microglia (Fig. 6c,d). Selective deletion of *Kdm6a* in microglia ameliorated clinical EAE in C57BL/6 mice (Fig. 6, right). Here, the effect of deletion of *Kdm6a* in microglia will be determined for pathology in spinal cord, hippocampus, cerebral cortex, striatum, cerebellum, and optic nerve. Whether substructure atrophy is reduced will be ascertained. The effect of the *Kdm6a* CKO on the microglial transcriptome will be revealed. Prioritization of validation of RNA-Seq candidates will be guided by analyses of data from human MS postmortem tissues examining the microglia transcriptome. The deleterious effect of *Kdm6a* in T cells and microglia in EAE contrasts with a report that *Kdm6a* is protective in the human amyloid precursor protein (hAPP) mouse model of Alzheimer's disease (108). Different outcomes may be due to a deleterious effect *Kdm6a* in the MS model versus a protective effect of *Kdm6a* in the AD model. Alternatively, differences may be due to targeting *Kdm6a* in microglia in spinal cord in MS versus neurons in hippocampus in AD. This underscores the importance of using a region-specific and sex-specific approach in each disease model.

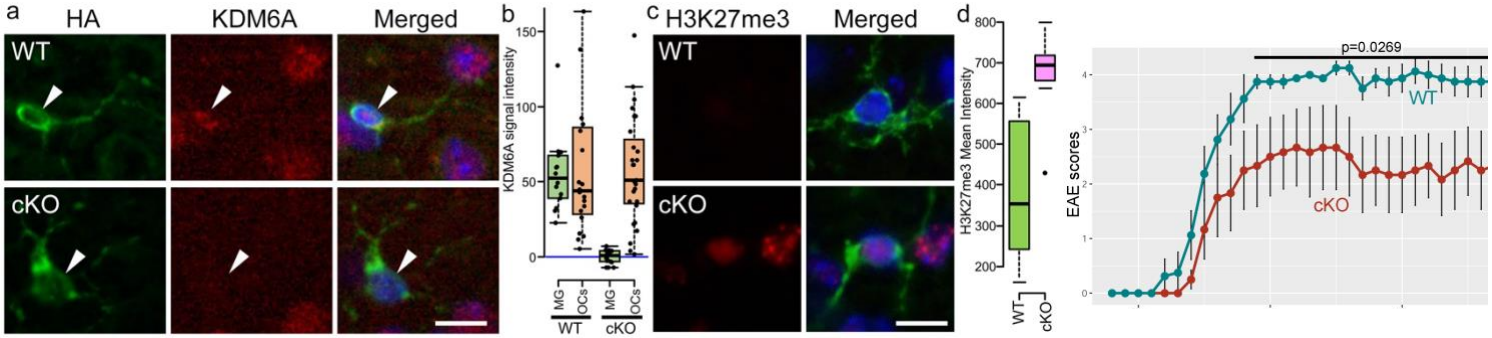

Fig. 6. Knockout of *Kdm6a* in microglia in *Tmem119*-Cre:RiboTag mice. In microglial *Kdm6a* cKO vs WT mice **a)** KDM6A was decreased. KDM6A (red), HA labelled microglia (green), DAPI (blue). **b)** quantification ($p < 0.0001$). **c)** H3K27me3 was increased in CKO. H3K27me3 (red), HA labelled microglia (green), DAPI (blue). **d)** quantification ($p < 0.001$). Tissues: dorsal hippocampus.
Right: *Kdm6a*-microglial-CKO mice have less severe EAE. $Kdm6a^{f/f}$-$Tmem119^{cre/ERT2+/-}$ (CKO) and $Kdm6a^{f/f}$-$Tmem119^{cre/ERT2-/-}$ (WT) mice were tamoxifen treated. (i.p. injection for 5 days). Eight weeks later, EAE was induced. CKO n=8, WT n=6 mice. All females. p-values, repeated measures ANOVA. The experiment was repeated, and again showed a significant CKO vs WT difference.

Details of Proposed Research Program in Fig. 1. We will identify treatment targets that are sex-specific, region-specific and cell-specific. Use of cell-specific RiboTag mice (14) on the C57BL/6 background permits deep sequencing of cells in the CNS in MS mouse models. Cell-specific gene deletion determines causality.
Preclinical models of MS: MS entails autoimmunity, CNS inflammation, glial activation, demyelination, and axonal damage, with minimal remyelination, in spinal cord, corpus callosum and optic nerve. There is also glial activation and synaptic damage in cerebral cortex, hippocampus, striatum, thalamus, and cerebellum, with substructure atrophy on MRI and retinal thinning on OCT. Our prior rationale for using chronic cuprizone treatment was to model the axonal damage and incomplete remyelination that occurs in MS (4), as opposed to lysolecithin or acute cuprizone models with minimal axonal damage and near complete remyelination. Chronic EAE (MOG 35-55 peptide in C57BL/6 mice) entails autoimmunity, CNS inflammation, demyelination, and axonal damage, with minimal remyelination in spinal cord (2, 5, 22, 109). It also affects corpus callosum (110-114) and optic nerve (1, 20, 115-127). Further, chronic EAE induces neuropathology in cerebral cortex (66, 109, 110, 128-133), hippocampus (67, 132, 134-147), striatum (141, 148-152), thalamus (153, 154), and cerebellum (66, 68, 128, 132, 155-157). Gray matter pathology in EAE entails microglial and astrocyte activation, synaptic loss and dysfunction, and substructure atrophy by MRI. Pathologies and atrophy progress over time from acute to chronic

EAE even after walking scores plateau at high values. MS patients also accumulate pathologies and atrophy after EDSS scores plateau at high values. EAE impairs walking, vision, cognition, and coordination, as it affects spinal cord, optic nerve, retina, hippocampus, cerebral cortex, cerebellum and striatum. **Preclinical models are critical to mechanism and discovery. There is never a perfect animal model for any human disease, including MS. The model used is based on the question asked. Acute, relapsing EAE is the most widely used model to develop anti-inflammatory DMTs in MS. Chronic EAE is a model of neurodegeneration in MS, with more than one neuropathology in more than one region, all in the context of autoimmunity.**

Principle Component Analysis, Differential Expression Analyses, and Canonical Pathway Analysis will identify the most differentially enriched pathways in chronic EAE, as described by our group (1, 2, 4, 22, 158). Single nuclei RNA sequencing (snRNA-seq) from human postmortem tissues (159), as well as analyses of existing human MS datasets (160-165), will be used to prioritize DE gene expression pathways in the preclinical model for validation and functional causality experiments. Retrieved snRNA-seq data will be analyzed accordingly to the protocol (e.g., 10x Genomics or CEL2-seq). We will use Seurat package (v.3.2.0 and v. 4.0.2.) in R for clustering and differential analysis. We will require genes to be expressed in more than five cells, as described (162). Additional QCs will be applied, such as the % of neuroinflammatory genes > 5%, and the number of expressed genes > 2500 (potentially “Multiplet”) will be removed prior to downstream analyses. A global-scaling normalization method will be employed, and gene expression will be log-transformed. Other normalization methods will also be considered for sensitivity analysis. Louvain clustering will be used to group cells, and cell type clusters will be identified using canonical marker genes. Non-linear dimensional reduction techniques, such as tSNE and UMAP, will be adopted to visualize and explore these datasets. Differentially expressed genes between MS and control will be identified using the FindMarkers function in Seurat, with non-parametric Wilcoxon rank-sum tests and adjustment for multiple comparison testing. Gene Ontology analyses (166) will be performed with AmiGO (Fisher Exact Test with FDR correction). Immunohistochemistry in postmortem tissues from MS will validate immunohistochemistry in EAE (2, 4, 23). MRI in MS women and men will reveal sex differences in regions of atrophy and prioritize regions of atrophy in EAE, as described, in collaboration with Dr. Friedemann Paul (33). Here, we will use an existing larger, longitudinal MS dataset (280 subjects followed for up to 5 years) from Charité, Universitätsmedizin Berlin (F. Paul-Letter of Support). Together, this will provide rationale for design of a future clinical trial of a DMT in MS to prevent substructure atrophy and improve the corresponding disability. See our publications on disability-specific atrophy in MS (33, 102, 167).

Our publications of cell-specific and region-specific gene expression in astrocytes and oligodendrocytes (1, 2, 4, 22) provide proof-of-principle that our approach can discover targets for neuroprotection. Here, we will extend this approach to microglia and neurons. We will compare females versus males to ascertain if there are sex differences in cell-specific and region-specific transcriptomes in EAE versus healthy mice. We will compare young adult (3-4 months), midlife (12-14 months), and old (20-22 months) mice in each sex. By integrating the different transcriptomic datasets, we will be able to perform comprehensive analyses permitting discovery of interactions between cells, regions, sex, and age. To ensure analysis reproducibility and rigor for transcriptomics data analyses, we will incorporate careful quality control of raw sequences, read alignment, and quantifying gene and transcript expression for differential expression analyses (168). DESeq2 (169), a count-based statistically powerful and computationally efficient tool, will be used for differential expression analysis between sexes. We will aggregate gene expression levels for genes in each pathway using principal component loadings. In addition, we will test for sex by cell, sex by region and age interactions to report cell-specific and region-specific effects of disease. Gene-level differential expression analysis will also be conducted with a false discovery rate (FDR) of 10%. Canonical pathway enrichment analysis will identify additional disease-related pathway enrichment. A transcriptomics database including data on cell type, region, sex, and age will be interrogated and hosted through Amazon Web Services (AWS) configured for UCLA Health Sciences. User interface will be implemented and deployed as a Shiny app for results dissemination. Our extensive publications showing sex hormone and sex chromosome effects in MS preclinical models demonstrate our ability to determine which X chromosome gene and which hormone/receptor causally impacts the disease-related transcriptome, neuropathology, and atrophy.

Cell-Cell Interactions. Here, we will determine the relationship between the transcriptomes of astrocytes and neurons within the same mouse. Aldh1l1-EGFP/Rpl10a mice (astrocytes) will be crossed with NSEII-Cre RiboTag mice (neurons) to create double-labelled mice (Aldh1l1-EGFP/Rpl10a: NSEII-Cre RiboTag), with immunoprecipitation of astrocyte- and neuron-specific RNAs using antibodies (anti-EGFP for astrocytes, anti-HA for neurons). We will determine which gene expression pathway changes in astrocytes correspond with changes in neurons during EAE by quantifying gene co-expressions of pathway pairs between astrocytes and neurons. Statistically efficient and computationally fast partial least square (PLS) regression will be adopted to evaluate the relationship between the two gene expression matrices for distinct pathways between the two cell

types (170). Statistical significance will be assessed by permutation test. We will control experiment-wide FDR at 10%. Sample size is based on preliminary data and number of comparisons. The same analysis will be conducted for two timepoints in EAE, early (day 12) and late (day 40), to reveal how cell-cell gene expression interactions evolve during disease. Tissues will be collected from 6 regions (motor cortex, hippocampus, striatum, cerebellum, optic nerve, and spinal cord) to determine regional differences in cell-cell interactions.

Not only can astrocytes modulate the neuronal synaptosome directly (8), they can also influence synapses indirectly though interactions of complement on astrocytes with complement receptor on microglia, which in turn affects phagocytosis of synapses (171, 172). We will cross Aldh1l1-EGFP/Rpl10a mice (astrocytes) with Tmem119-Cre RiboTag mice (microglia) to create double-labelled mice (Aldh1l1-EGFP/Rpl10a: Tmem119-Cre RiboTag mice). Immunoprecipitation of astrocyte and microglia specific RNAs will use antibodies (anti-EGFP for astrocytes, anti-HA for microglia) and RNA sequencing will reveal the transcriptome in each cell, in the same region. This will be done in EAE vs healthy controls. Statistical analyses (as above) will determine which gene expression pathway changes in astrocytes correspond with changes in microglia during early and late EAE.

Astrocyte-neuronal interactions and astrocyte-microglial interactions in each region will be contrasted between females versus males as well as between young (3-4 months) versus midlife (12-14 months) versus old (20-22 months). The effect of sex and age will be determined with modified query of the database, here accounting for the correlation measured within the same mouse. In particular, a random effect model (e.g., *duplicateCorrelation* function within limma package (173)) will be adopted to analyze repeated measured gene expressions. This will reveal how molecular signatures of these two cells change within a given mouse by region, in each sex, at each age, during EAE as compared to healthy controls. This will identify candidate treatments to halt or repair neurodegeneration within specific regions in each sex at the most optimal age.

Cross-modality correlations between neuropathology and neuroimaging. In a separate cohort of mice, *in vivo* brain MRIs will be collected (34, 128) and analyzed using atlas-based morphometry (ABM) to determine the degree of atrophy in cerebral cortex (109), hippocampus (134), striatum (109), and cerebellum (157, 174) during EAE. Imaged mice will undergo CLARITY for 3D neuropathology of intact tissues using the right half of brain (109, 175). MRI/CLARITY studies will use double transgenic mice (GFAP-TdTomato and Thy1-YFP) to show the relationship between astrocytes (GFAP) and synaptic density, dendritic arborizations, and neuronal number (Thy1). Co-registration of MRI data with CLARITY data from the same mice will reveal the neuropathology of astrocytes and neurons within regions of atrophy. Immunohistochemistry of sections of the other half of brain will assess microglial and astrocyte activation and synaptic density in gray matter, as well as glial activation, axonal damage and loss, and demyelination in white matter (176-178). Double-label immunohistochemistry will quantify expression of target genes identified by transcriptomics in the context of neuropathology. Relationships between regional atrophy and neuropathologies will entail regression analyses, as described (66, 68, 109, 128, 134, 157).

Epigenetics. To address mechanisms underlying gene expression changes, cell-specific epigenetics analysis (histone modifications and DNA methylation) will be done using Sun1-tagged INTACT mice (B6;129-Gt(ROSA)26Sor$^{tm5(CAG-Sun1/sfGFP)Nat}$/J) crossed with CNS cell-specific Cre mice. We will determine disease related epigenetics changes in WT mice as well as the effect of selectively deleting *Kdm6a* on H3K27me3 modification. Using methylSig (179), we will identify differentially methylated cytosines (DMCs) or regions (DMRs) of at least 15% change and control for FDR (10%), as we previously published (63). We will annotate DMCs and DMRs using UCSC Genome Browser's annotations for CpG islands, promoters, and other regions (180). For each DMCs and DMRs, we will calculate the correlation between DNA methylation and gene expression in the context of annotations (181). Notably, from INTACT mice, we will isolate 1) nuclear RNA for gene expression, 2) DNA for methylation, and 3) chromatin for histone modification.

Candidate treatments. Metformin occupies the same set of residues within the catalytic pocket of KDM6A which is involved in H3K27me3 binding and demethylation, thereby blocking KDM6A's effect on histone demethylase activity (107). Metformin has anti-aging properties (182-187) and protects in MS models (188-193). In contrast to effects on oligodendrocytes (188), we will focus on metformin's actions on *Kdm6a* in microglia (Fig. 1). While metformin is attractive due to repurposing, we will also test the more specific *Kdm6a* inhibitor, GSK-J4 (194). Our studies suggest that ERβ ligation in astrocytes prevents cognitive decline, dorsal hippocampal atrophy and neuropathology in healthy aging (3), while ERβ ligation in oligodendrocytes and CD11c^{+} cells induces remyelination in MS models (4, 5). The PI is an inventor on novel ERβ ligands patented and optioned by UCLA. Additional neurodegenerative targets will be discovered here in distinct CNS regions of females and males to generate additional candidate treatments optimal for distinct disabilities and tailored for MS women and men. **This R35 combines expertise in two RO1s, one using a region-specific, cell-specific approach (NS109670) and the other using a sex-specific approach (NS096748), to discover interactions. It also determines the effect of aging on these interactions. This body of work is ideally suited for an R35.**

PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001
Expiration Date: 09/30/2024

Use of Human Specimens and/or Data

Does any of the proposed research in the application involve human specimens and/or data *	● Yes ❍ No
Provide an explanation for any use of human specimens and/or data not considered to be human subjects research.	Human_Subjects1071243793.pdf
Are Human Subjects Involved	❍ Yes ● No
Is the Project Exempt from Federal regulations?	❍ Yes ❍ No
Exemption Number	❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8
Other Requested Information	

Human Subjects:

No human subjects will be recruited, followed, or treated in this proposal.

Existing clinical and imaging data from human subjects of the University of Berlin were previously de-identified and transferred to UCLA. Proposed experiments will examine this existing dataset in place currently at UCLA.

Human postmortem tissues have been previously used in this group's publications. The tissues are de-identified and no additional informed consent is necessary for their use. Over the course of the 8 year R35, publicly available postmortem tissue datasets will be used.

Vertebrate Animals Section

1. Description of Procedures

Provide a concise description of the proposed procedures to be used that involve vertebrate animals. Identify the species, strains, ages, sex, and total number of animals by species to be used. If dogs or cats are proposed, provide the source of the animals. Note, for applications with due dates on or after May 25, 2016: (1) the method of euthanasia is eliminated from the VAS and is addressed in the FORMS-D Cover Page Supplement or PHS Fellowship Supplemental forms; (2) a description of veterinary care is no longer required; and (3) the justification for the number of animals has been eliminated from the VAS and should now be addressed in the Research Strategy as part of experimental design.

All experiments involve mice of the C57BL/6 background.

For each cell-specific-RiboTag mouse cohort, there will be n=15 mice per group, at 3 ages (Young, Midlife, Old) and 2 sexes (female, male) with two disease states (EAE/Health), this will require n=180 total mice (15x3x2x2=180). This cohort (n=180) of mice will have mice n=15 mice removed at each age (Young, Midlife, Old) from each sex (female, male) for EAE or Healthy control to assess brain atrophy and neuropathology outcomes.

The *in vivo* translatome of each cell type will be determined by using RiboTag mice crossed with CNS cell-specific promotor driven, tamoxifen inducible lines. Tamoxifen or vehicle treatment at age 1.5 months (by i.p. injection on 5 consecutive days). Gene expression will be determined during young adulthood (3-4 months) and midlife (12-14 months) and old (20-22 months) in a cell-specific, region-specific and sex-specific manner).

For cell-specific target gene deletion (for example, *Kdm6a* CKO and WT mice) experiments: there will be sample size of n=15 in each group, 2 ages (3mo, 18 mo), 2 genotypes (CKO, WT), 2 sexes (female, male) and 2 clinical states (health, EAE), this experiment will require a total of 240 mice. Brain MRI will be done 40 days after EAE induction (including in age matched healthy controls), and tissues will be collected from CNS regions as described for neuropathology.

Pharmacologic treatment (metformin for example) versus placebo treatment will determine the effect of treatment on disease (clinical, regional brain atrophy, and neuropathology). Treatment of cell-specific RiboTag mice will reveal how the treatment impacts cell-specific gene expression in vivo. For example, metformin will also be used in *Kdm6a*-cell specific CKO crossed with RiboTag mice to reveal how the *Kdm6a* CKO affects the cell-specific translatome. Two weeks after the last tamoxifen injection (age 2 months), daily treatment with 100 mg metformin or control i.p. injections will begin.

Note that over the course of this 8 year grant, optimal gene deletion targets and pharmacologic treatments will evolve, so all cannot be predicted at present, however the same approach as described above for *Kdm6a* and metformin will be used.

No dogs or cats.

2. Justifications

Provide justification that the species are appropriate for the proposed research. Explain why the research goals cannot be accomplished using an alternative model (e.g., computational, human, invertebrate, in vitro).

The murine models of aging are widely used for assessing neurodegeneration. The C57BL/6 mouse is particularly useful in light of the genetic modifications and reagents that exist. To date, there is no other phylogenetically lower species which models these aspects. Additionally, in vitro and computer models do not mimic the complexity of mammalian physiology, so information from these models would not as fully recapitulate aging. Our ultimate goal is to lay a foundation for the future that will use the model to develop and test novel therapeutic strategies in patients.

The murine models of MS are widely used for assessing neuroinflammation. Our ultimate goal is to use the model to develop novel therapeutic strategies for MS patients. If we do not test these agents in the murine MS model first, clinical trials in MS proposals will not be funded due to lack of "preclinical data". New treatments must be effective at minimum in mice with EAE first before translating to humans. Finally, conditional knocks of *Kdm6a* in mice will allow us to understand the role of sex chromosomes in neuroinflammation.

3. Minimization of Pain and Distress

Describe the interventions to minimize discomfort, distress, pain, and injury. These include analgesia, anesthesia, sedation, palliative care, and humane endpoints.

Mice are cared for by a licensed veterinarian (Division of Laboratory Animal Medicine, UCLA). With regard to pain and distress, EAE mice will be monitored in accord with UCLA DLAM guidelines.

With regard to pain and distress, all mice without EAE are in Category A, while all mice induced to have EAE are in Category C regardless of how mild their disease is. EAE is characterized by temporary paralysis, with no evidence of pain based on the human demyelinating CNS disease multiple sclerosis. Mice with EAE are checked twice daily and this data is recorded for each mouse. Mice with severe EAE, grade 3 or 4 are housed separately from mice with less severe EAE to avoid competition for food and hydration as well as to avoid harm of the weaker mice by the stronger mice. If during a particular time period, the mice become too weak to reach the water supply, apples are routinely added to cages and subcutaneous injections of PBS are given when needed.

The procedures which require **anesthesia** include the following.

Active EAE induction: Mice are first anesthesized with 2-3% isoflurane gas mixed with oxygen using a vaporizer (Summit, Model:PAM). The injections to induce EAE are then given.

Upon completion of experiments or if EAE should become severe enough to produce a moribund state, mice are **euthanized** by isoflurane inhalation using a nose cone.

Mice will undergo brain MRIs *in vivo* in a 7 T Bruker spectrometer under isoflurane anesthesia. Prior to imaging the mice will be brought to a plane of anesthesia where they are not responsive to a toe pinch and then placed in a head restraint within the imaging cradle. If the animal appears to be dehydrated, a 0.5 mL bolus of sterile saline solution will be administered subcutaneously. The imaging cradle will be maintained at 37° C and respiration will be monitored continuously during the scan. If the animal appears to be in distress (very slow or very fast respiration), the imaging session will be aborted, the mouse removed from the head restrain and imaging cradle and also anesthesia. Mice will recover from anesthesia on a warming pad and will be monitored continuously until conscious and then returned to their cage.

Upon completion of experiments, mice are **euthanized** by isoflurane inhalation using a nose cone.

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UNIVERSITY OF CALIFORNIA, LOS ANGELES **UCLA**

BERKELEY • DAVIS • IRVINE • LOS ANGELES • MERCED • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

OFFICE OF CONTRACT AND GRANT ADMINISTRATION
10889 WILSHIRE BOULEVARD, SUITE 700
LOS ANGELES, CALIFORNIA 90095-1406

PHONE: (310) 794-0102
FAX: (310) 794-0631

July 8, 2022

Chief Grants Management Officer
National Institute of Neurological Disorders and Stroke (NINDS)
ChiefGrantsManagementOfficer@ninds.nih.gov

Dear Chief Grants Management Officer,

On behalf of The Regents of the University of California, I am pleased to submit and support the enclosed proposal:

Title:	Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach
Principal Investigator:	Rhonda Voskuhl, MD
Project Period:	04/01/2023 through 03/31/2031
Amount Requested:	$7,307,976

The University is aware of and accept the condition that other NINDS research awards must be relinquished as a condition of receiving the NINDS Research Program Award (RPA). If awarded, Dr. Voskuhl will devote 6.60 person months to the RPA throughout the duration of the award period.

If you have any questions or require additional information, please contact us at your convenience.

Sincerely,

Digitally signed by
Jessica Kim
Date: 2022.07.08
08:26:35 -07'00'

Jessica Kim
Senior Contract and Grant Analyst
UCLA Office of Contract & Grant Administration
10889 Wilshire Boulevard, Suite 700
Los Angeles, CA 90095-1406
Phone: 310-983-3673
Jessica.Kim@research.ucla.edu

DEPARTMENT OF NEUROLOGY
DAVID GEFFEN SCHOOL OF MEDICINE AT UCLA

Reed Neurological Research Center
710 Westwood Plaza
Los Angeles, CA 90095-1769
(310) 825-5521
Fax: (310) 825-1730

July 6, 2022

Dear Colleagues,
It is pleasure to write this letter of support for Dr. **Rhonda Voskuhl** for her R35 application. As Chair of Neurology, I have worked closely with Rhonda in her Departmental and scientific leadership and building of an impressive multiple sclerosis program. As physician-scientist, I have collaborated with Rhonda in her scientific studies, and know her bench and clinical research and its impact. Dr. Voskuhl has pioneered several important directions in MS research, translated these into clinical trials and has mentored young faculty toward successful careers.

Rhonda is a leader in the field of sex differences in disease, showing sex chromosome and sex hormone effects in autoimmunity and neurodegeneration. This work started with the innovative sex chromosome models in mice, and findings in both MS and lupus in an effect on disease pathogenesis. She then identified a specific gene that mediated the susceptibility to autoimmune disease on the X chromosome. This work was published in high impact journals and rigorously pursued the research issues of sex chromosome effects down to the molecular level. Along the way, and in a particularly surprising set of findings, Rhonda's lab showed that the XY chromosome complement leads to enhanced neurodegenerative disease in the same model systems in which XX leads to an increase in autoimmune disease. This work has clear implications for MS clinically.

Rhonda Voskuhl used similarly innovative approaches to identify cell-specific and region-specific differences in transcriptomics in the CNS response to injury. I remember very well when these studies started to really take off. Rhonda had the ideas that MS pathogenesis would involve key components from astrocyte signaling and responses, and initiated a collaboration with Dr. Michael Sofroniew to pursue this idea. At the time Michael had developed astrocyte-specific transcriptional profiling that was not widely available in the field, and was studying spinal cord injury. Rhonda's initiative took these tools in studies of MS, and identified several important astrocyte metabolic and signaling pathways that associate with disease severity or progression. In further studies, some of these molecular pathways in astrocytes and also in oligodendrocytes, segregate by brain region in the MS model. These findings suggest novel treatments that might target distinct effects of damage and secondary disabilities aligned by brain region in multiple sclerosis.

A particularly strong example of Rhonda's role in the MS field and impact as a physician-scientist is in her work in estrogen effects in this disease. She characterized the effects of selective estrogen receptor pathway signaling in MS, and identified estrogen receptors as promising targets—specifically in astrocytes, then in oligodendrocytes. As with her other work, these studies were published in high impact journals, and were done in parallel projects in her lab to those noted above. Rhonda took this emerging estrogen story and moved it toward the clinic with estriol—a molecule that was deliberately chosen because it is the estrogen unique to pregnancy, a time of protection in MS, as well as being inexpensive and readily available across global economic strata. Rhonda developed a multi-site clinical trial to test estriol. She applied quantitative brain imaging and found a difference in effect by disability measure and brain region. In recent work, she has developed patterns of regional brain atrophy together with serum neurofilament light chain as biomarkers for further clinical trials.

In the course of this work, Rhonda has patented many of the approaches, such as one set of patents that is licensed pertaining to estriol treatment of cognitive decline in menopausal women and another group which entails use of estrogen receptor beta selective ligand treatment of multiple sclerosis. This has had the important effect of stimulating pharmaceutical company interest in moving these therapies forward on a larger scale.

In the midst of this scientific work, Dr. Voskuhl has run the MS clinical program at UCLA, and mentored many MS fellows. She has recruited two very talented junior faculty to UCLA, Kevin Patel and Elaine Su, to grow specific aspects of the MS program in imaging and clinical trial approaches. Rhonda is a strong leader in the Department, and a voice for bench-to-bedside clinical translation, in setting up infrastructure and faculty mentoring that will facilitate basic and clinical research.

In short, Rhonda Voskuhl is an excellent candidate for the R35 program for her superb and wide-ranging research, leadership of her field, identification of new biological principles in autoimmunity and neurodegenerative diseases and growth of the field through mentorship and a vision for translational science.

S. Thomas Carmichael, M.D., Ph.D.
Professor and Chair
Frances Stark Chair
Department of Neurology
David Geffen School of Medicine at UCLA

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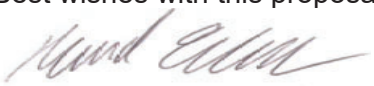
STATISTICS CORE
UCLA DEPARTMENT OF MEDICINE
DAVIDGEFFENSCHOOL OF MEDICINE AT UCLA
1100 GLENDON SUITE 1820
LOS ANGELES, CALIFORNIA90024

June 26th, 2022

Dear Rhonda,

I am writing to express my support for your NINDS NIH R35 application entitled. "Neurodegeneration underlying distinct disabilities in multiple sclerosis using a cell-specific, region-specific, and sex-specific approach." As the Director of Department of Medicine Statistics Core (DOMStat), I am committed to providing the resources needed for statistical analyses of your gene expression data. Dr. Jin Zhou, Associate Professor Department of Medicine Statistics Core, has substantial expertise in genetics and genomics. As you know, UCLA is a leader in genomics research, and Dr. Zhou's experience in metagenomics data analysis makes her a good fit for your proposal. She is available to collaborate with you on this interesting project integrating transcriptomics analyses across brain cell types, regions, sex, and age. The level of her involvement would be commensurate with Dr. Zhou being a Co-Investigator, and we could add additional staff statisticians as needed from DOMStat.

Best wishes with this proposal,



David Elashoff, Ph.D.
Professor, Departments of Medicine, Biostatistics and Computational Medicine
Director, Department of Medicine Statistics Core
Leader, UCLA CTSI Biostatistics, Epidemiology and Research Design Program
University of California-Los Angeles
Phone: 310-384-8744
Email: delashoff@mednet.ucla.edu

CHARITÉ

Charité | Campus Buch | Lindenberger Weg 80 | 13125 Berlin

Rhonda Voskuhl, M.D.
Jack H. Skirball Chair
Professor, UCLA Dept. of Neurology
Director, UCLA Multiple Sclerosis Program
Laurie D. and Steven C. Gordon
Neuroscience Research Building
Room 475D
635 Charles E. Young Drive South
Los Angeles, CA 90095

Experimental and Clinical Research Center – ECRC- eine Kooperation von MDC und Charité

Kommissarischer Direktor

Univ.-Prof. Dr. Friedemann Paul

friedemann.paul@charite.de

Unser Zeichen:
Tel. 030 450- 540002
Fax 030 450- 540900

July 4, 2022

Dear Rhonda,

This is a Letter of Support for your R35 grant to NINDS, NIH entitled, "Neurodegeneration underlying distinct disabilities in multiple sclerosis using a cell-specific, region-specific, and sex-specific approach". Given that this grant application includes both an MS model for preclinical research as well as MS human data for clinical research, its human MS aspect aligns well with the going collaboration between my team at Charité, Universitätsmedizin Berlin and your team at the University of California, Los Angeles (UCLA).

As you know, I am fully supportive of our ongoing collaboration which has entailed transfer of data from an existing dataset of MS patients at Charité, Universitätsmedizin Berlin to UCLA. Dr. Allan MacKenzie-Graham of your group is determining region-specific and sex-specific gray matter atrophy in female and male MS patients using data from my existing longitudinal dataset of very high quality clinical and imaging data collected from 280 subjects (112 female MS patients and 99 male MS patients matched for age and disease duration, plus 43 female healthy controls and 26 male healthy controls also matched for age) followed for up to five years by my MS group at Charité – Universitätsmedizin Berlin.

Our collaboration has been successful, with initial cross-sectional findings in a smaller dataset published ("Sex differences in brain atrophy in multiple sclerosis", *Biology of Sex Differences*, 11:49, 2020). I am enthusiastic as we expand our collaboration into regional differences in sex differences in our ongoing larger, longitudinal study, with ultimate integration of findings in human MS with sex-specific, region-specific, and cell-specific differences in gene expression and neuropathology in the most widely used MS animal model, experimental autoimmune encephalomyelitis (EAE).

Best wishes for success in your R35 grant application, which is central to a precision medicine approach to better understand neurodegeneration in MS.

Sincerely,

Friedemann Paul, MD

Data Sharing Plan:

The proposed research will include data from genome wide transcriptome analysis of specific CNS cell types in chronic EAE, health, and aging from both sexes (female and male) of mice. Data generated from use of the chronic cuprizone model will also be shared. Select groups will also have methylome data available.

For data sharing purpose, all high throughput data will be deposited in GEO (Gene Expression Omnibus, NCBI) database and will be publicly available.

Mice created during the course of this grant through crosses and breeding will be made available to other researchers upon request.

At this point, it is difficult to predict precisely what types of discoveries made during analyses of such sequences may have intellectual property implications. If the results produced within this proposal have potential as a biomarker or targeted drug therapy, we will discuss the intellectual property issues with a representative from the UCLA Office of Intellectual Property. Regarding patentable inventions, the title will belong to UCLA, with nonexclusive, royalty-free license to the Government per 37 CFR 401.14, “Patent Rights (Small Business Firms and Nonprofit Organizations)”.

Voskuhl Authentication of Key Reagents:

This grant does not use cell lines or specialty chemicals.

Antibodies and other biologics are commercially available and commercially validated.

Experiments involving Cre-loxP recombination using Ribotag mice to HA label RNAs from each cell type are generated with mice currently commercially available (Jackson labs). As outlined in our research plan, all mice have been and will continue to be validated by genotyping and immunohistochemistry. Also, cell-specific RNA enrichment is validated using double label immunofluorescence immunostaining and qPCR for enrichment of targeted cell type and de-enrichment of other cell types (as described in our previous publications).

EXHIBIT C

Department of Health and Human Services
National Institutes of Health
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Notice of Award
FAIN# R35NS132150
Federal Award Date
05/08/2023

Recipient Information

1. Recipient Name
UNIVERSITY OF CALIFORNIA, LOS ANGELES
10889 WILSHIRE BLVD STE 700

LOS ANGELES, CA 90024

2. Congressional District of Recipient
36

3. Payment System Identifier (ID)
1956006143A1

4. Employer Identification Number (EIN)
956006143

5. Data Universal Numbering System (DUNS)
092530369

6. Recipient's Unique Entity Identifier
RN64EPNH8JC6

7. Project Director or Principal Investigator
RHONDA R VOSKUHL, MD
Professor
rvoskuhl@ucla.edu
310-206-4636

8. Authorized Official
Lydia McHam

Federal Agency Information

9. Awarding Agency Contact Information
Kerry Gastley

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
kerry.gastley@nih.gov
(240) 276-5472

10. Program Official Contact Information
URSULA UTZ
Program Director
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
utzu@ninds.nih.gov
301-496-1431

Federal Award Information

11. Award Number
1R35NS132150-01

12. Unique Federal Award Identification Number (FAIN)
R35NS132150

13. Statutory Authority
42 USC 241 42 CFR 52

14. Federal Award Project Title
Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach

15. Assistance Listing Number
93.853

16. Assistance Listing Program Title
Extramural Research Programs in the Neurosciences and Neurological Disorders

17. Award Action Type
New Competing

18. Is the Award R&D?
Yes

Summary Federal Award Financial Information

19. Budget Period Start Date 05/15/2023 **– End Date** 04/30/2024	
20. Total Amount of Federal Funds Obligated by this Action	$876,448
20 a. Direct Cost Amount	$568,236
20 b. Indirect Cost Amount	$308,212
21. Authorized Carryover	$0
22. Offset	
23. Total Amount of Federal Funds Obligated this budget period	$876,448
24. Total Approved Cost Sharing or Matching, where applicable	$0
25. Total Federal and Non-Federal Approved this Budget Period	$876,448
26. Project Period Start Date 05/15/2023 **– End Date** 04/30/2031	
27. Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period	$876,448

28. Authorized Treatment of Program Income
Additional Costs

29. Grants Management Officer - Signature
Aaron Kinchen

30. Remarks

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Notice of Award

OUTSTANDING INVESTIGATOR GRANTS
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

SECTION I – AWARD DATA – 1R35NS132150-01

Principal Investigator(s):
RHONDA R VOSKUHL, MD

Award e-mailed to: awards@research.ucla.edu

Dear Authorized Official:

The National Institutes of Health hereby awards a grant in the amount of $876,448 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF CALIFORNIA LOS ANGELES in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Neurological Disorders And Stroke of the National Institutes of Health under Award Number R35NS132150. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please direct questions to the Federal Agency contacts.

Sincerely yours,

Aaron Kinchen
Grants Management Officer
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Additional information follows

Cumulative Award Calculations for this Budget Period (U.S. Dollars)

Salaries and Wages	$300,563
Fringe Benefits	$120,964
Personnel Costs (Subtotal)	$421,527
Materials & Supplies	$23,446
Travel	$2,880
Other	$103,242
Tuition Remission	$17,141
Federal Direct Costs	$568,236
Federal F&A Costs	$308,212
Approved Budget	$876,448
Total Amount of Federal Funds Authorized (Federal Share)	$876,448
TOTAL FEDERAL AWARD AMOUNT	$876,448
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$876,448

SUMMARY TOTALS FOR ALL YEARS (for this Document Number)		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
1	$876,448	$876,448
2	$913,497	$913,497
3	$913,497	$913,497
4	$913,497	$913,497
5	$913,497	$913,497
6	$913,497	$913,497
7	$913,497	$913,497
8	$913,497	$913,497

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

Payment System Identifier: 1956006143A1
Document Number: RNS132150A
PMS Account Type: P (Subaccount)
Fiscal Year: 2023

IC	CAN	2023	2024	2025	2026	2027	2028	2029	2030
NS	8472428	$876,448	$913,497	$913,497	$913,497	$913,497	$913,497	$913,497	$913,497

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: UTZU NE / **OC**: 41021 / **Released**: Kinchen, Aaron 04/28/2023
Award Processed: 05/08/2023 12:07:35 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 1R35NS132150-01

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – STANDARD TERMS AND CONDITIONS – 1R35NS132150-01

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VII Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to obtain a unique entity identifier (UEI) and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a UEI requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R35NS132150. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

Recipients must administer the project in compliance with federal civil rights laws that prohibit discrimination on the basis of race, color, national origin, disability, age, and comply with applicable

conscience protections. The recipient will comply with applicable laws that prohibit discrimination on the basis of sex, which includes discrimination on the basis of gender identity, sexual orientation, and pregnancy. Compliance with these laws requires taking reasonable steps to provide meaningful access to persons with limited English proficiency and providing programs that are accessible to and usable by persons with disabilities. The HHS Office for Civil Rights provides guidance on complying with civil rights laws enforced by HHS. See https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html and https://www.hhs.gov/.

- Recipients of FFA must ensure that their programs are accessible to persons with limited English proficiency. For guidance on meeting the legal obligation to take reasonable steps to ensure meaningful access to programs or activities by limited English proficient individuals, see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html and https://www.lep.gov.
- For information on an institution's specific legal obligations for serving qualified individuals with disabilities, including providing program access, reasonable modifications, and to provide effective communication, see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html.
- HHS funded health and education programs must be administered in an environment free of sexual harassment; see https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html. For information about NIH's commitment to supporting a safe and respectful work environment, who to contact with questions or concerns, and what NIH's expectations are for institutions and the individuals supported on NIH-funded awards, please see https://grants.nih.gov/grants/policy/harassment.htm.
- For guidance on administering programs in compliance with applicable federal religious nondiscrimination laws and applicable federal conscience protection and associated anti-discrimination laws, see https://www.hhs.gov/conscience/conscience-protections/index.html and https://www.hhs.gov/conscience/religious-freedom/index.html.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:

Additional Costs

SECTION IV – NS SPECIFIC AWARD CONDITIONS – 1R35NS132150-01

Clinical Trial Indicator: No

This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

STANDARD TERMS AND CONDITIONS OF AWARD

This award provides funding in response to NS22-038. These funds are to be administered in accordance with the guidelines described in this specific funding opportunity.

The funds in this award shall not be used to pay the salary of an individual at a rate in excess of Executive Level II. Please see the Salary Cap Summary (FY 1990 - Present) for rates and effective dates.

In accordance with the NINDS Funding Strategy, NINDS does not provide funds for inflationary increases. Where applicable, future years have been adjusted.

DELAYED START DATE

This award includes funding for twelve (12) months of support. The competing budget period is awarded for less than twelve (12) months. Future year budget periods will begin on May 1. Allowable preaward costs may be charged to this award.

FOREIGN COMPONENT

This award includes collaboration with Dr. Freiderman Paul in Germany. This site has been NINDS approved. No additional foreign performance sites may be added to this project without the written prior approval of the National Institute for Neurological Disorders and Stroke. Contact the assigned Grants Management Specialist if the collaboration changes.

SHARING PLAN

The recipient is required to follow the Data Sharing plan included in dated 2/7/2023. Any change requires prior approval from the NINDS.

INFORMATION

This award has been issued at 95.99% of the adjusted requested level* for the 01 year to reflect overlapping support from the following grant:
R01NS109670-05 through 5/31/2023

*Adjusted requested level: The requested level of support with adjustments made in accordance with the budget narrative in the summary statement and applicable grant policies.

GRADUATE STUDENT COMPENSATION

In accordance with the NIH Grants Policy Statement section 2.3.7.9, total direct costs (salary, fringe benefits and tuition remission) for graduate students are provided at a level not to exceed the NIH maximum allowable amount (zero level of the Ruth L. Kirschstein National Research Service Award stipend in effect at the time of the competing award). Support recommended for future years that exceeds the allowable amount has been adjusted accordingly.

R35 TERMS OF AWARD

1. This competing award has been made at the council-recommended direct cost level.
2. The PI/PD must maintain a minimum effort of 6 person months for the duration of the RPA award. Any modification of research effort on the RPA as a percent of total effort requires prior approval from NINDS.
3. A permanent change of PI/PD will not be allowed.
4. An R35 PI/PD can be awarded a new NINDS grant only if it has been identified as being in an exempted category (see Part 2. Section 1 in the FOA: http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-19-037.html). PI/PDs are strongly encouraged to contact their NINDS Program Officer for consultation prior to submission.
5. If the PI/PD wishes to relinquish their R35 award, they should, through their organization, inform NINDS program and grants management staff so that an orderly close out can occur.
6. The use of the eRA Research Performance Progress Report (RPPR) Module for submitting Type 5 Progress Reports is required for all awards with start dates on or

after October 17, 2014. See Guide Notice: NOT-OD-15-014 http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-014.html

7. As noted in the FOA, http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-19-037.html (See Section VI, Award Administration Information, Subsection 3, Reporting) the RPPR instructions are modified as follows:
    a. Under Section 6.2 B.1, What are the major goals of the project? Note that the goals of the program of research supported by the RPA are broader than the specific aims of a single project and should be appropriately described. If the goals of the RPA have changed, complete section B.1.a. Provide a rationale for the changes in the context of the originally proposed research program and further contributions to the field, and an explanation of how the research continues to fit within NINDS mission interests.
    b. Under Section B.2, in addition to the instructions, emphasize how the work continues to be innovative and of high impact.
    c. Under section D.2.c. additional information, indicate if there have been changes in Other Support. In addition to the revised Other Support page, include an explanation of the relationship of the new awards to the activities supported by the RPA.
8. Six months prior to the end of the -05-budget period, the following should be submitted concurrently with the year four RPPR in order to request the three additional years of funding:
    a. A letter co-signed by the Business Official and Principal Investigator requesting an additional three years of support; and
    b. A one-to-two-page description of the overall research accomplishments during the previous 4.5 years that justifies continuation of the research program for the final three years.

The NINDS in consultation with the NINDS Advisory Council will review these documents. A Notice of Award will be issued extending the award for three additional years contingent upon a successful administrative review and approval by the NINDS and the NINDS Council.

SPREADSHEET SUMMARY
AWARD NUMBER: 1R35NS132150-01

INSTITUTION: UNIVERSITY OF CALIFORNIA LOS ANGELES

Budget	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
Salaries and Wages	$300,563	$313,126	$313,126	$313,126	$313,126	$313,126	$313,126	$313,126
Fringe Benefits	$120,964	$126,020	$126,020	$126,020	$126,020	$126,020	$126,020	$126,020
Personnel Costs (Subtotal)	$421,527	$439,146	$439,146	$439,146	$439,146	$439,146	$439,146	$439,146
Materials & Supplies	$23,446	$24,426	$24,426	$24,426	$24,426	$24,426	$24,426	$24,426
Travel	$2,880	$3,000	$3,000	$3,000	$3,000	$3,000	$3,000	$3,000
Other	$103,242	$107,556	$107,556	$107,556	$107,556	$107,556	$107,556	$107,556
Tuition Remission	$17,141	$17,857	$17,857	$17,857	$17,857	$17,857	$17,857	$17,857
TOTAL FEDERAL DC	$568,236	$591,985	$591,985	$591,985	$591,985	$591,985	$591,985	$591,985

TOTAL FEDERAL F&A	$308,212	$321,512	$321,512	$321,512	$321,512	$321,512	$321,512	$321,512
TOTAL COST	$876,448	$913,497	$913,497	$913,497	$913,497	$913,497	$913,497	$913,497

Facilities and Administrative Costs	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
F&A Cost Rate 1	56%	56%	56%	56%	56%	56%	56%	56%
F&A Cost Base 1	$550,379	$574,128	$574,128	$574,128	$574,128	$574,128	$574,128	$574,128
F&A Costs 1	$308,212	$321,512	$321,512	$321,512	$321,512	$321,512	$321,512	$321,512

EXHIBIT D

National Institutes of Health
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Notice of Award
FAIN# R35NS132150
Federal Award Date
04/24/2024

Recipient Information

1. Recipient Name
UNIVERSITY OF CALIFORNIA, LOS ANGELES
10889 WILSHIRE BLVD STE 700
LOS ANGELES, CA 90024

2. Congressional District of Recipient
36

3. Payment System Identifier (ID)
1956006143A1

4. Employer Identification Number (EIN)
956006143

5. Data Universal Numbering System (DUNS)
092530369

6. Recipient's Unique Entity Identifier
RN64EPNH8JC6

7. Project Director or Principal Investigator
RHONDA R VOSKUHL, MD
Professor
rvoskuhl@mednet.ucla.edu
310-206-4636

8. Authorized Official
Jessica Kim
jessica.kim@research.ucla.edu

Federal Agency Information

9. Awarding Agency Contact Information
Kerry Gastley

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
kerry.gastley@nih.gov
(240) 276-5472

10. Program Official Contact Information
URSULA UTZ
Program Director
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
utzu@ninds.nih.gov
301-496-1431

Federal Award Information

11. Award Number
5R35NS132150-02

12. Unique Federal Award Identification Number (FAIN)
R35NS132150

13. Statutory Authority
42 USC 241 42 CFR 52

14. Federal Award Project Title
Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach

15. Assistance Listing Number
93.853

16. Assistance Listing Program Title
Extramural Research Programs in the Neurosciences and Neurological Disorders

17. Award Action Type
Non-Competing Continuation

18. Is the Award R&D?
Yes

Summary Federal Award Financial Information	
19. Budget Period Start Date 05/01/2024 **– End Date** 04/30/2025	
20. Total Amount of Federal Funds Obligated by this Action	$894,212
20 a. Direct Cost Amount	$574,224
20 b. Indirect Cost Amount	$319,988
21. Authorized Carryover	
22. Offset	
23. Total Amount of Federal Funds Obligated this budget period	$894,212
24. Total Approved Cost Sharing or Matching, where applicable	$0
25. Total Federal and Non-Federal Approved this Budget Period	$894,212
26. Project Period Start Date 05/15/2023 **– End Date** 04/30/2031	
27. Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period	$1,775,705

28. Authorized Treatment of Program Income
Additional Costs

29. Grants Management Officer - Signature
Aaron Kinchen

30. Remarks

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Notice of Award

OUTSTANDING INVESTIGATOR GRANTS
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

SECTION I – AWARD DATA – 5R35NS132150-02

Principal Investigator(s):
RHONDA R VOSKUHL, MD

Award e-mailed to: awards@research.ucla.edu

Dear Authorized Official:

The National Institutes of Health hereby awards a grant in the amount of $894,212 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF CALIFORNIA LOS ANGELES in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Neurological Disorders And Stroke of the National Institutes of Health under Award Number R35NS132150. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please direct questions to the Federal Agency contacts.

Sincerely yours,

Aaron Kinchen
Grants Management Officer
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Additional information follows

Cumulative Award Calculations for this Budget Period (U.S. Dollars)

Salaries and Wages	$303,732
Fringe Benefits	$122,239
Personnel Costs (Subtotal)	$425,971
Materials & Supplies	$23,693
Travel	$2,910
Other	$104,329
Tuition Remission	$17,321
Federal Direct Costs	$574,224
Federal F&A Costs	$319,988
Approved Budget	$894,212
Total Amount of Federal Funds Authorized (Federal Share)	$894,212
TOTAL FEDERAL AWARD AMOUNT	$894,212
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$894,212

SUMMARY TOTALS FOR ALL YEARS (for this Document Number)		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
2	$894,212	$894,212
3	$922,109	$922,109
4	$922,109	$922,109
5	$922,109	$922,109
6	$922,109	$922,109
7	$922,109	$922,109
8	$922,109	$922,109

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

Payment System Identifier:	1956006143A1
Document Number:	RNS132150A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2024

IC	CAN	2024	2025	2026	2027	2028	2029	2030
NS	8472428	$894,212	$922,109	$922,109	$922,109	$922,109	$922,109	$922,109

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: UTZU NE / **OC**: 41025 / **Released**: Kinchen, Aaron 04/23/2024
Award Processed: 04/24/2024 12:17:13 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R35NS132150-02

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – STANDARD TERMS AND CONDITIONS – 5R35NS132150-02

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final

progress report when applicable.

f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VII Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to obtain a unique entity identifier (UEI) and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a UEI requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R35NS132150. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

Recipients must administer the project in compliance with federal civil rights laws that prohibit discrimination on the basis of race, color, national origin, disability, age, and comply with applicable conscience protections. The recipient will comply with applicable laws that prohibit discrimination on the basis of sex, which includes discrimination on the basis of gender identity, sexual orientation, and pregnancy. Compliance with these laws requires taking reasonable steps to provide meaningful access to persons with limited English proficiency and providing programs that are accessible to and usable by persons with disabilities. The HHS Office for Civil Rights provides guidance on complying with civil rights laws enforced by HHS. See https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html and https://www.hhs.gov/.

- Recipients of FFA must ensure that their programs are accessible to persons with limited English proficiency. For guidance on meeting the legal obligation to take reasonable steps to ensure meaningful access to programs or activities by limited English proficient individuals, see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html and https://www.lep.gov.
- For information on an institution's specific legal obligations for serving qualified individuals with disabilities, including providing program access, reasonable modifications, and to provide effective communication, see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html.
- HHS funded health and education programs must be administered in an environment free of sexual harassment; see https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html. For information about NIH's commitment to supporting a safe and respectful work environment, who to contact with questions or concerns, and what NIH's expectations are for institutions and the individuals supported on NIH-funded awards, please see

https://grants.nih.gov/grants/policy/harassment.htm.

- For guidance on administering programs in compliance with applicable federal religious nondiscrimination laws and applicable federal conscience protection and associated anti-discrimination laws, see https://www.hhs.gov/conscience/conscience-protections/index.html and https://www.hhs.gov/conscience/religious-freedom/index.html.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – NS SPECIFIC AWARD CONDITIONS – 5R35NS132150-02

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

FUNDING

This award has been issued at 97% of the level indicated on the previous Notice of Award. Upward adjustments to awarded levels will be considered after our FY 2024 appropriations are enacted.

STANDARD TERMS AND CONDITIONS OF AWARD

This award provides funding in response to NS22-038. These funds are to be administered in accordance with the guidelines described in this specific funding opportunity.

The funds in this award shall not be used to pay the salary of an individual at a rate in excess of Executive Level II. Please see the Salary Cap Summary (FY 1990 - Present) for rates and effective dates.

In accordance with the NINDS Funding Strategy, NINDS does not provide funds for inflationary increases. Where applicable, future years have been adjusted.

FOREIGN COMPONENT

This award includes collaboration with Dr. Freiderman Paul in Germany. This site has been NINDS approved. No additional foreign performance sites may be added to this project without the written prior approval of the National Institute for Neurological Disorders and Stroke. Contact the assigned Grants Management Specialist if the collaboration changes.

SHARING PLAN

The recipient is required to follow the Data Sharing plan included in dated 2/7/2023. Any change requires prior approval from the NINDS.

R35 TERMS OF AWARD

1. This competing award has been made at the council-recommended direct cost level.
2. The PI/PD must maintain a minimum effort of 6 person months for the duration of the RPA award. Any modification of research effort on the RPA as a percent of total effort requires prior approval from NINDS.
3. A permanent change of PI/PD will not be allowed.

4. An R35 PI/PD can be awarded a new NINDS grant only if it has been identified as being in an exempted category (see Part 2. Section 1 in the FOA: http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-19-037.html). PI/PDs are strongly encouraged to contact their NINDS Program Officer for consultation prior to submission.
5. If the PI/PD wishes to relinquish their R35 award, they should, through their organization, inform NINDS program and grants management staff so that an orderly close out can occur.
6. The use of the eRA Research Performance Progress Report (RPPR) Module for submitting Type 5 Progress Reports is required for all awards with start dates on or after October 17, 2014. See Guide Notice: NOT-OD-15-014 http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-014.html
7. As noted in the FOA, http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-19-037.html (See Section VI, Award Administration Information, Subsection 3, Reporting) the RPPR instructions are modified as follows:
    1. Under Section 6.2 B.1, What are the major goals of the project? Note that the goals of the program of research supported by the RPA are broader than the specific aims of a single project and should be appropriately described. If the goals of the RPA have changed, complete section B.1.a. Provide a rationale for the changes in the context of the originally proposed research program and further contributions to the field, and an explanation of how the research continues to fit within NINDS mission interests.
    2. Under Section B.2, in addition to the instructions, emphasize how the work continues to be innovative and of high impact.
    3. Under section D.2.c. additional information, indicate if there have been changes in Other Support. In addition to the revised Other Support page, include an explanation of the relationship of the new awards to the activities supported by the RPA.
8. Six months prior to the end of the -05-budget period, the following should be submitted concurrently with the year four RPPR in order to request the three additional years of funding:
    1. A letter co-signed by the Business Official and Principal Investigator requesting an additional three years of support; and
    2. A one-to-two-page description of the overall research accomplishments during the previous 4.5 years that justifies continuation of the research program for the final three years.

The NINDS in consultation with the NINDS Advisory Council will review these documents. A Notice of Award will be issued extending the award for three additional years contingent upon a successful administrative review and approval by the NINDS and the NINDS Council.

SPREADSHEET SUMMARY
AWARD NUMBER: 5R35NS132150-02

INSTITUTION: UNIVERSITY OF CALIFORNIA LOS ANGELES

Budget	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
Salaries and Wages	$303,732	$313,126	$313,126	$313,126	$313,126	$313,126	$313,126
Fringe Benefits	$122,239	$126,020	$126,020	$126,020	$126,020	$126,020	$126,020
Personnel Costs (Subtotal)	$425,971	$439,146	$439,146	$439,146	$439,146	$439,146	$439,146
Materials & Supplies	$23,693	$24,426	$24,426	$24,426	$24,426	$24,426	$24,426
Travel	$2,910	$3,000	$3,000	$3,000	$3,000	$3,000	$3,000
Other	$104,32	$107,55	$107,55	$107,55	$107,55	$107,55	$107,55

	9	6	6	6	6	6	6
Tuition Remission	$17,321	$17,857	$17,857	$17,857	$17,857	$17,857	$17,857
TOTAL FEDERAL DC	$574,224	$591,985	$591,985	$591,985	$591,985	$591,985	$591,985
TOTAL FEDERAL F&A	$319,988	$330,124	$330,124	$330,124	$330,124	$330,124	$330,124
TOTAL COST	$894,212	$922,109	$922,109	$922,109	$922,109	$922,109	$922,109

Facilities and Administrative Costs	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
F&A Cost Rate 1	57%	57.5%	57.5%	57.5%	57.5%	57.5%	57.5%
F&A Cost Base 1	$46,409	$574,128	$574,128	$574,128	$574,128	$574,128	$574,128
F&A Costs 1	$26,453	$330,124	$330,124	$330,124	$330,124	$330,124	$330,124
F&A Cost Rate 2	57.5%						
F&A Cost Base 2	$510,495						
F&A Costs 2	$293,535						

EXHIBIT E

National Institutes of Health
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Notice of Award
FAIN# R35NS132150
Federal Award Date
06/02/2025

Recipient Information

1. Recipient Name
UNIVERSITY OF CALIFORNIA, LOS ANGELES
10889 WILSHIRE BLVD STE 700
LOS ANGELES, CA 90024

2. Congressional District of Recipient
36

3. Payment System Identifier (ID)
1956006143A1

4. Employer Identification Number (EIN)
956006143

5. Data Universal Numbering System (DUNS)
092530369

6. Recipient's Unique Entity Identifier
RN64EPNH8JC6

7. Project Director or Principal Investigator
RHONDA R VOSKUHL, MD
Professor
rvoskuhl@mednet.ucla.edu
310-206-4636

8. Authorized Official
Jessica Kim
jessica.kim@research.ucla.edu

Federal Agency Information

9. Awarding Agency Contact Information
Kerry Gastley

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
kerry.gastley@nih.gov
(240) 276-5472

10. Program Official Contact Information
URSULA UTZ
Program Director
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE
utzu@ninds.nih.gov
301-496-1431

Federal Award Information

11. Award Number
5R35NS132150-03

12. Unique Federal Award Identification Number (FAIN)
R35NS132150

13. Statutory Authority
42 USC 241 42 CFR 52

14. Federal Award Project Title
Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach

15. Assistance Listing Number
93.853

16. Assistance Listing Program Title
Extramural Research Programs in the Neurosciences and Neurological Disorders

17. Award Action Type
Non-Competing Continuation

18. Is the Award R&D?
Yes

Summary Federal Award Financial Information	
19. Budget Period Start Date 05/01/2025 **– End Date** 04/30/2026	
20. Total Amount of Federal Funds Obligated by this Action	$922,109
20 a. Direct Cost Amount	$591,985
20 b. Indirect Cost Amount	$330,124
21. Authorized Carryover	
22. Offset	
23. Total Amount of Federal Funds Obligated this budget period	$922,109
24. Total Approved Cost Sharing or Matching, where applicable	$0
25. Total Federal and Non-Federal Approved this Budget Period	$922,109
26. Project Period Start Date 05/15/2023 **– End Date** 04/30/2031	
27. Total Amount of the Federal Award including Approved Cost Sharing or Matching this Project Period	$2,697,814

28. Authorized Treatment of Program Income
Additional Costs

29. Grants Management Officer - Signature
Cheryl Y. Wall

30. Remarks

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Notice of Award

OUTSTANDING INVESTIGATOR GRANTS
Department of Health and Human Services
National Institutes of Health

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

SECTION I – AWARD DATA – 5R35NS132150-03

Principal Investigator(s):
RHONDA R VOSKUHL, MD

Award e-mailed to: awards@research.ucla.edu

Dear Authorized Official:

The National Institutes of Health hereby awards a grant in the amount of $922,109 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to UNIVERSITY OF CALIFORNIA LOS ANGELES in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award, including the "Terms and Conditions," is acknowledged by the recipient when funds are drawn down or otherwise requested from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Neurological Disorders And Stroke of the National Institutes of Health under Award Number R35NS132150. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please direct questions to the Federal Agency contacts.

Sincerely yours,

Cheryl Y. Wall
Grants Management Officer
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Additional information follows

Cumulative Award Calculations for this Budget Period (U.S. Dollars)

Salaries and Wages	$313,126
Fringe Benefits	$126,020
Personnel Costs (Subtotal)	$439,146
Materials & Supplies	$24,426
Travel	$3,000
Other	$107,556
Tuition Remission	$17,857
Federal Direct Costs	$591,985
Federal F&A Costs	$330,124
Approved Budget	$922,109
Total Amount of Federal Funds Authorized (Federal Share)	$922,109
TOTAL FEDERAL AWARD AMOUNT	$922,109
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$922,109

SUMMARY TOTALS FOR ALL YEARS (for this Document Number)		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
3	$922,109	$922,109
4	$922,109	$922,109
5	$922,109	$922,109
6	$922,109	$922,109
7	$922,109	$922,109
8	$922,109	$922,109

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

Payment System Identifier:	1956006143A1
Document Number:	RNS132150A
PMS Account Type:	P (Subaccount)
Fiscal Year:	2025

IC	CAN	2025	2026	2027	2028	2029	2030
NS	8472428	$922,109	$922,109	$922,109	$922,109	$922,109	$922,109

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: UTZU NE / **OC**: 41025 / **Released**: 05/30/2025
Award Processed: 06/05/2025 12:48:13 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R35NS132150-03

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – STANDARD TERMS AND CONDITIONS – 5R35NS132150-03

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VII Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

Carry over of an unobligated balance into the next budget period requires Grants Management Officer prior approval.

This award is subject to the requirements of 2 CFR Part 25 for institutions to obtain a unique entity identifier (UEI) and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a UEI requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R35NS132150. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

Recipients must administer the project in compliance with federal civil rights laws that prohibit discrimination on the basis of race, color, national origin, disability, age, and comply with applicable conscience protections. The recipient will comply with applicable laws that prohibit discrimination on the basis of sex, which includes discrimination on the basis of gender identity, sexual orientation, and pregnancy. Compliance with these laws requires taking reasonable steps to provide meaningful access to persons with limited English proficiency and providing programs that are accessible to and usable by persons with disabilities. The HHS Office for Civil Rights provides guidance on complying with civil rights laws enforced by HHS. See https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html and https://www.hhs.gov/.

- Recipients of FFA must ensure that their programs are accessible to persons with limited English proficiency. For guidance on meeting the legal obligation to take reasonable steps to ensure meaningful access to programs or activities by limited English proficient individuals, see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html and https://www.lep.gov.
- For information on an institution's specific legal obligations for serving qualified individuals with disabilities, including providing program access, reasonable modifications, and to provide effective communication, see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html.
- HHS funded health and education programs must be administered in an environment free of sexual harassment; see https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html. For information about NIH's commitment to supporting a safe and respectful work environment, who to contact with questions or concerns, and what NIH's expectations are for institutions and the individuals supported on NIH-funded awards, please see https://grants.nih.gov/grants/policy/harassment.htm.
- For guidance on administering programs in compliance with applicable federal religious nondiscrimination laws and applicable federal conscience protection and associated anti-

discrimination laws, see https://www.hhs.gov/conscience/conscience-protections/index.html and https://www.hhs.gov/conscience/religious-freedom/index.html.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

Recipient is compliant with Title IX of the Education Amendments of 1972, as amended, 20 U.S.C. §§ 1681 et seq., including the requirements set forth in Presidential Executive Order 14168 titled Defending Women From Gender Ideology Extremism and Restoring Biological Truth to the Federal Government, and Title VI of the Civil Rights Act of 1964, 42 U.S.C. §§ 2000d et seq., and Recipient will remain compliant for the duration of the Agreement.

- The above requirements are conditions of payment that go the essence of the Agreement and are therefore material terms of the Agreement.
- Payments under the Agreement are predicated on compliance with the above requirements, and therefore Recipient is not eligible for funding under the Agreement or to retain any funding under the Agreement absent compliance with the above requirements.
- Recipient acknowledges that this certification reflects a change in the government's position regarding the materiality of the foregoing requirements and therefore any prior payment of similar claims does not reflect the materiality of the foregoing requirements to this Agreement.
- Recipient acknowledges that a knowing false statement relating to Recipient's compliance with the above requirements and/or eligibility for the Agreement may subject Recipient to liability under the False Claims Act, 31 U.S.C. § 3729, and/or criminal liability, including under 18 U.S.C. §§ 287 and 1001.

SECTION IV – NS SPECIFIC AWARD CONDITIONS – 5R35NS132150-03

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

STANDARD TERMS AND CONDITIONS OF AWARD

This award provides funding in response to NS22-038. These funds are to be administered in accordance with the guidelines described in this specific funding opportunity.

The funds in this award shall not be used to pay the salary of an individual at a rate in excess of Executive Level II. Please see the Salary Cap Summary (FY 1990 - Present) for rates and effective dates.

In accordance with the NINDS Funding Strategy, NINDS does not provide funds for inflationary increases. Where applicable, future years have been adjusted.

FOREIGN COMPONENT
NINDS was notified that the foreign component is no longer active and all work is being completed at Stanford. This award includes collaboration with Dr. Freiderman Paul in Germany. This site has been NINDS approved. No additional foreign performance sites may be added to this project without the written prior approval of the National Institute for Neurological Disorders and Stroke. Contact the assigned Grants Management Specialist if the collaboration changes.

SHARING PLAN
The recipient is required to follow the Data Sharing plan included in dated 2/7/2023. Any change requires prior approval from the NINDS.

R35 TERMS OF AWARD

1. This competing award has been made at the council-recommended direct cost level.

2. The PI/PD must maintain a minimum effort of 6 person months for the duration of the RPA award. Any modification of research effort on the RPA as a percent of total effort requires prior approval from NINDS.
3. A permanent change of PI/PD will not be allowed.
4. An R35 PI/PD can be awarded a new NINDS grant only if it has been identified as being in an exempted category (see Part 2. Section 1 in the FOA: http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-19-037.html). PI/PDs are strongly encouraged to contact their NINDS Program Officer for consultation prior to submission.
5. If the PI/PD wishes to relinquish their R35 award, they should, through their organization, inform NINDS program and grants management staff so that an orderly close out can occur.
6. The use of the eRA Research Performance Progress Report (RPPR) Module for submitting Type 5 Progress Reports is required for all awards with start dates on or after October 17, 2014. See Guide Notice: NOT-OD-15-014 http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-014.html
7. As noted in the FOA, http://grants.nih.gov/grants/guide/rfa-files/RFA-NS-19-037.html (See Section VI, Award Administration Information, Subsection 3, Reporting) the RPPR instructions are modified as follows:
    a. Under Section 6.2 B.1, What are the major goals of the project? Note that the goals of the program of research supported by the RPA are broader than the specific aims of a single project and should be appropriately described. If the goals of the RPA have changed, complete section B.1.a. Provide a rationale for the changes in the context of the originally proposed research program and further contributions to the field, and an explanation of how the research continues to fit within NINDS mission interests.
    b. Under Section B.2, in addition to the instructions, emphasize how the work continues to be innovative and of high impact.
    c. Under section D.2.c. additional information, indicate if there have been changes in Other Support. In addition to the revised Other Support page, include an explanation of the relationship of the new awards to the activities supported by the RPA.
8. Six months prior to the end of the -05-budget period, the following should be submitted concurrently with the year four RPPR in order to request the three additional years of funding:
    a. A letter co-signed by the Business Official and Principal Investigator requesting an additional three years of support; and
    b. A one-to-two-page description of the overall research accomplishments during the previous 4.5 years that justifies continuation of the research program for the final three years.

The NINDS in consultation with the NINDS Advisory Council will review these documents. A Notice of Award will be issued extending the award for three additional years contingent upon a successful administrative review and approval by the NINDS and the NINDS Council.

SPREADSHEET SUMMARY
AWARD NUMBER: 5R35NS132150-03

INSTITUTION: UNIVERSITY OF CALIFORNIA LOS ANGELES

Budget	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
Salaries and Wages	$313,126	$313,126	$313,126	$313,126	$313,126	$313,126
Fringe Benefits	$126,020	$126,020	$126,020	$126,020	$126,020	$126,020
Personnel Costs (Subtotal)	$439,146	$439,146	$439,146	$439,146	$439,146	$439,146
Materials & Supplies	$24,426	$24,426	$24,426	$24,426	$24,426	$24,426
Travel	$3,000	$3,000	$3,000	$3,000	$3,000	$3,000
Other	$107,556	$107,556	$107,556	$107,556	$107,556	$107,556
Tuition Remission	$17,857	$17,857	$17,857	$17,857	$17,857	$17,857
TOTAL FEDERAL DC	$591,985	$591,985	$591,985	$591,985	$591,985	$591,985
TOTAL FEDERAL F&A	$330,124	$330,124	$330,124	$330,124	$330,124	$330,124
TOTAL COST	$922,109	$922,109	$922,109	$922,109	$922,109	$922,109

Facilities and Administrative Costs	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
F&A Cost Rate 1	57.5%	57.5%	57.5%	57.5%	57.5%	57.5%
F&A Cost Base 1	$574,128	$574,128	$574,128	$574,128	$574,128	$574,128
F&A Costs 1	$330,124	$330,124	$330,124	$330,124	$330,124	$330,124

EXHIBIT F

From: Lorsch, Jon (NIH/NIGMS) [E] <jon.lorsch@nih.gov>
Sent: Thursday, July 31, 2025 1:03 PM
To: Chancellor Julio Frenk
Cc: Memoli, Matthew (NIH/OD) [E]; Keveney, Sean (HHS/OGC)
Subject: Suspension Letter
Attachments: UCLA Suspsension Letter Jul 31 2025.pdf; 2025-07-21 UCLA Grants Suspended.xlsx

Chancellor Frenk,

Please see the letter attached, sent on behalf of NIH.

--
Jon Lorsch, Ph.D.
Acting Deputy Director for Extramural Research
National Institutes of Health

July 31, 2025

Dr. Julio Frenk
Chancellor
University of California – Los Angeles
2147 Murphy Hall
Los Angeles, CA 90095

Ref: Notice of Award Suspensions

Dr. Frenk:

Pursuant to 45 Code of Federal Regulations (CFR) § 75.371(c), this letter constitutes official notification that the U.S. Department of Health and Human Services (HHS), National Institutes of Health (NIH) is hereby suspending the attached list of grant awards to the University of California Los Angeles (UCLA). UCLA should immediately cease all activities on these award numbers. The purpose of this action is to address concerns reported and observed in UCLA programs and ensure compliance with applicable Federal statutes and regulations, and the terms and conditions of these Federal awards. This action is effective 7/31/2025.

Noncompliance:

NIH has identified the following specific examples of noncompliance:

- UCLA engages in racism, in the form of illegal affirmative action;
- UCLA fails to promote a research environment free of antisemitism and bias;
- UCLA discriminates against and endangers women by allowing men in women's sports and private women-only spaces.

With respect to admissions, although UCLA expressly disclaims reliance on race, NIH believes that UCLA's "holistic review" admissions process, which considers factors such as an applicant's neighborhood/zip code, family income, and school profile—and invites the disclosure of an applicant's race via personal statements—is a transparent attempt to engage in race-based admissions in all but name.[1] UCLA's surreptitious—and unlawful—prioritization of race over

[1] UCLA, Newsroom, FAQ: Supreme Court ruling on race-conscious college admissions, June 29, 2023, https://newsroom.ucla.edu/stories/faq-supreme-court-ruling-on-affirmative-action (last accessed July 28, 2025); UCLA, Newsroom, UCLA Experts: The Supreme Court's affirmative action decisions, June 2, 2023, https://newsroom.ucla.edu/advisories/ucla-experts-supreme-court-affirmative-action-decisions (last accessed July 28, 2025); UCLA, Newsroom, How UCLA has responded to Proposition 209, June 29, 2023, https://newsroom.ucla.edu/releases/how-ucla-has-responded-to-proposition-209 (last accessed July 28, 2025); *see generally* UCLA, Application Review Process for First-Years, https://admission.ucla.edu/apply/first-year/first-year-requirements/application-review-process (last accessed July 25, 2025).

merit has significantly disadvantaged white and Asian applicants and must end.[2] No one should be denied educational opportunities because of the color of their skin.

With respect to antisemitism, UCLA's own Task Force to Combat Antisemitism and Anti-Israeli Bias at UCLA revealed that Jewish students, faculty, and staff were subjected to threats, assaults, swastika graffiti, and hostile slogans during the 2024 pro-Palestinian encampment.[3] Shockingly, "there were 100 reports of individuals experiencing a physical attack or physical threat."[4] The report criticized UCLA's administration for tolerating such behavior under the guise of free speech, and determined that "cited events appear to (1) violate law, (2) violate University or campus rules or policies, or (3) likely contribute to a hostile campus climate for Jews and Israelis."[5] These findings were echoed by the Republican Staff Report on the U.S. House Committee on Education and the Workforce's year-long investigation into antisemitism on 11 university campuses, including University of California schools.[6] Regarding UCLA, the report provided extensive details regarding antisemitic and anti-Israeli demonstrations, disruptions, and violence on UCLA's campus in late April to early May 2024, ultimately finding that "UCLA officials stood by and failed to act as the illegal encampment violated Jewish students' civil rights and placed [the] campus at risk."[7] Such vile conduct is antithetical to the safe and welcoming environment necessary for effective research, for which UCLA receives millions of dollars in taxpayer funds through NIH grants.

Finally, NIH is seriously concerned that UCLA's policy of allowing males to compete in women's sports and utilize women-only facilities has created an unsafe environment for women that further threatens the integrity of the campus research environment.[8] NIH cannot sit idly by as a major grants recipient systemically marginalizes its female students, faculty, and staff by stripping away necessities, like safe and secure bathrooms[9], and extracurricular opportunities.

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[2] *See Students Against Racial Discrimination v. Regents of the University of California et al.*, No. 8:25-cv-00192 (C.D. Cal.), Am. Compl., Dkt. No. 26, ¶¶ 8-36 (describing changes to UC admissions policies and results thereof); *see also* Richard Sander, UCLA School of Law, The Consideration of Race in UCLA Undergraduate Admissions, Oct. 20, 2012, at 1, available at chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://scvtv.com/pdf/ucla022513sander.pdf (last accessed July 25, 2025) ("Holistic admissions by itself did not add anything to African-American admissions at UCLA; rather, it provided a cover for illegal discrimination by UCLA's admissions office. The only significant, tangible effect of holistic admissions at UCLA was a reduction in the proportion of academically gifted students – of all races – admitted by the university."); *id.* at 5 (summarizing conclusions of Sander's analysis).

[3] Antisemitism and Anti-Israeli Bias at UCLA, Oct. 16, 2024, chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.antisemitismreport.org/ (last accessed July 25, 2025).

[4] *Id.* at 1.

[5] *Id.* at 44.

[6] Republican Staff Report, Committee on Education and the Workforce, U.S. House of Representatives, Antisemitism on College Campuses Exposed, Oct. 31, 2024, at 24-30, available at chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://edworkforce.house.gov/uploadedfiles/10.30.24_committee_on_education_and_the_workforce_republican_staff_report_-_antisemitism_on_college_campuses_exposed.pdf (last accessed July 25, 2025) (detailing antisemitic activities at UCLA from late April to early May 2024).

[7] *Id.* at 24.

[8] *See generally* UCLA Gender Recognition Taskforce: Recommendations Report, 2020, available at https://ucla.app.box.com/s/21hdsdcnopsixi66x5fhcfcjblki243y (last accessed July 25, 2025).

[9] UCLA, Gender-Inclusive Restroom Map, updated July 2019, available at chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://lgbtq.ucla.edu/file/1500b7f1-7c6b-4c1b-9bbe-12674dd23f67 (last accessed July 28, 2025).

Requested Action:

Based on UCLA's failure to comply with federal requirements, policies, and procedures, NIH is suspending the above-referenced awards. NIH has considered UCLA's reliance interests in continued availability of funding under the attached list of grants and they are outweighed by the concerns identified above. This action is effective immediately as authorized under 45 CFR § 75.371 *Remedies for noncompliance*, and NIH Grants Policy Statement, Chapter 8.5.2. As such, UCLA must cease all activities on the awards and immediately discontinue drawing down funds from the Payment Management System (PMS) for any expenses incurred after receipt of this letter. For each award, please submit a draw request to PMS for any expenses that occurred prior to July 31, 2025, no later than COB August 31, 2025 with the appropriate justification.

Corrective Actions:

NIH is willing to work with UCLA to identify corrective actions to bring UCLA into compliance. UCLA must acknowledge in writing its willingness to discuss these corrective actions by August 15.

Assuming corrective actions are agreed upon by UCLA and NIH, NIH will determine whether UCLA has established effective internal control over its Federal awards by adopting procedures that provide NIH with a reasonable assurance that the organization will be managing its Federal awards in compliance with Federal statutes, regulations, and award terms and conditions. *See* 45 CFR § 75.303 (Internal controls).

Please note that under 45 CFR § 75.372 and 45 CFR § 75.373, NIH may move to terminate an award for reasons including if the recipient has failed to comply with the terms and conditions of an award.

We look forward to hearing from you. Please direct any questions or concerns to Sean R. Keveney, Acting General Counsel, U.S. Department of Health and Human Services.

Sincerely,

Jon R. Lorsch -S

Digitally signed by Jon R. Lorsch -S
Date: 2025.07.31 15:46:08 -04'00'

Signed on behalf of NIH

Unified Project Num	Title	Institution
1R21AA031366-01A1	Chronic alcohol effects on the biogenesis, distribution, and RNA content of astrocytic exosomes	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F32AA031405-01A1	Neuroepigenetic mechanisms of alcohol response	UNIVERSITY OF CALIFORNIA LOS ANGELES
2RF1AG013622-22	Molecular, Cellular and Circuit Mechanisms for Age-Related Deficits in Memory-Linking	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T35AG026736-20	UCLA Medical Student Training in Aging Research (MSTAR) Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
5P01AG036695-13	Molecular Regulation of Stem Cell Aging	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG037514-13	Role of Mitochondrial Homeostasis in Animal Aging	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R01AG037514-13S1	Role of Mitochondrial Homeostasis in Animal Aging	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG049157-08	Role of Intestinal Homeostasis in Organismal Aging	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R13AG056135-08	Organization for the Study of Sex Differences Annual Meeting	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG068116-03	Small molecule mimetics of Humanin that normalize neuronal p-Akt as novel therapeutics for AD	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K07AG068184-05	Academic Career Leadership Award in Aging	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08AG068372-05	The Implications of Insurance Benefit Design for Health and Disability Among Low Income Adults with Diabetes.	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG068633-05	The Impact of physician and health system factors on the quality of care for persons with Alzheimers disease and related dementias at the end of life	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG068667-06	Aging and Stem Cell Resilience	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG069924-04	Mitochondrial DNA Deletion Mutation Frequency as a Metric of Biologic Age	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG070895-04	Towards Treatment of Alzheimer's Disease by Targeting Pathogenic Tau and Beta-Amyloid Structures	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG071783-05	Epigenetic Reprogramming of Cellular Age	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG073377-04	Evaluating the p-Tau inhibition and neuroprotective effects of sAPPalpha using brain permeable small molecules	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG075206-04	Systematic analysis of functional 3' UTR genetic variants and their relevance to Alzheimer's Disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG075909-04	Microglial lysosomes and selective neuronal vulnerability	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R01AG075909-04S1	Microglial lysosomes and selective neuronal vulnerability	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG075955-05	Astrocyte and neuron brain-region and compartment-specific proteome dynamics in aging and Alzheimer's disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U01AG076804-04	Mapping Cellular Resolution Connectopathies in Aging and Alzheimers Disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30AG077832-03	Designing novel therapeutics for Alzheimer's disease using structural studies of tau	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG078950-04	Regulation and function of dsRNAs derived from retrotransposable elements in AD	UNIVERSITY OF CALIFORNIA LOS ANGELES
4R00AG080116-03	Functional Characterization of Tau Mutation and Post-translational Modifications	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21AG082041-02	Combining electron and nuclear magnetic resonance to track Alzheimers amyloid-beta oligomer-to-fibril conversion	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG082761-03	Nutrient signaling at ER-Mitochondrial contacts and age-related mitochondrial dysfunction	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG082764-03	Genomic Instability as A Driver of Stem Cell Exhaustion	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG083379-03	Mendelian imputation for family-based GWAS and association-by-proxy in diverse ancestries	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG084036-03	Sexual dimorphic cell type and connectivity atlases of the aging and AD mouse brains	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AG084823-02	LIFE-M 2.0: Data Infrastructure for Understanding the Longitudinal and Intergenerational Determinants of Health and Aging	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30AG086001-02	Role of interleukin-6 signaling on T cell potential of aged hematopoietic stem cells and thymic progenitors	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R24AG089055-02	Creating and disseminating resources for the genomics and omics of behavioral and social phenotypes	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R61AG090398-01	Hematopoietic Stem Cell-based CAR Macrophage for Alzheimers Disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01AG090773-01	Optimization and preclinical evaluation of brain permeant SE-CRISPR to edit ApoE4 after IV infusion in AD models	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21AG091113-01	Probing the Toxic Effects of Early Stage Tau Pathology on Microglial Modulation of Neuronal Circuits Using iPSC Hippocampal Assembloids	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21AG092008-01	Understanding the cellular time machine that enables rejuvenation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI162802-04	Transcriptional networks governing A. fumigatus virulence	LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER
5R21AI178352-02	Delineating host response to central venous catheter associated Candida albicans biofilm infections, and development of novel therapeutics to combat drug resistant biofilms	LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER
1R21AI187999-01A1	Mouse model of neonatal fungal colonization to study homeostasis and disease	LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER
5R01AI052217-21	Cell Surface Polymer Display in Gram-Positive Bacteria	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI094386-13	Genome structure, transcription and packaging of dsRNA viruses	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R01AI094386-13S1	Genome structure, transcription and packaging of dsRNA viruses	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI123360-08	Functional Analysis of Novel Components of the Toxoplasma Inner Membrane Complex	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI135631-05	Optimization and Advanced Proof-of-Concept Studies of a Listeria-vectored Multi-Antigenic Vaccine against Tuberculosis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI143730-05	Surface sensing, memory, and motility control in biofilm formation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI146615-05	Mechanism underlying regulation of Ca2+ signaling in local effector T cells	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U01AI148119-05	Mapping the effector response space of antibody combinations	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI148475-05	Identification of key players mediating internalization of Trichomonas vaginalis extracellular vesicles by host cells and parasite adherence and survival in vivo	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U19AI149504-05	(Attack)2: Genetic engineering of cellular and humoral immunity to cure HIV	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI151055-05	Composition, Atomic Structure and Function of the Francisella Type 6 Secretion System, a Distinct Subtype Essential for Phagosomal Escape, Intracellular Replication, and Virulence	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI153044-04	Statistical innovation to integrate sequences and phenotypes for scalable phylodynamic inference	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI155170-05	Structural biology of 7SK RNP and its interaction with HIV-1 Tat	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08AI155232-05	The Effect of Natural Killer Cell-Based Therapy on the HIV Reservoir	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI155856-05	THE RELAXIN RECEPTOR GR/RXFP1 SIGNALING IN LIVER TRANSPLANT ISCHEMIA-REPERFUSION INJURY AND THE INFLAMMATION RESOLUTION	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI158154-04	Develop broad-spectrum antiviral agents against COVID-19 based on innate immune response to SARS-CoV-2 infection	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI158704-05	Functional analysis of host and viral determinants for ZAP inhibition	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI161803-05	Natural killer cell engineering to target the HIV reservoir	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI161828-04	Molecular basis of heme scavenging by Gram-positive bacteria	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI163216-05	Developing three-dimensional antisense oligonucleotide drugs against COVID-19	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI167713-03	Using geospatial science to maximize the opportunity to access ART in Africa	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08AI168567-04	NFkB dynamics in the stimulus specificity of trained immunity	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21AI168952-02	Chemoenzymatic Synthesis of Darobactin Antibiotics	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21AI171702-02	Untangling the mechanisms of initiation and discontinuous RNA synthesis by COVID-19 RdRp	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI172410-03	Towards HIV eradication: New concepts and potent compounds for PKC-mediated latency reversal	UNIVERSITY OF CALIFORNIA LOS ANGELES
4R01AI172727-04	Induction of autophagy to enhance CAR-T cells in HIV cure approaches	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI173050-03	Targeting the transcriptional co-activators YAP and TAZ with statins to prevent solid organ transplant rejection by HLA donor specific antibodies	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI173214-03	Characterizing functional states of macrophages via their stimulus-responses	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI173496-03	The Role of lymphatic endothelium in the developing thymus	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI173769-03	Antibody-based therapeutic strategy for New World mammarenavirus hemorrhagic fever	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI174519-03	Sex Differences in NK Cells Mediated by X-linked UTX	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F31AI174799-02	Identifying the role of serotonin receptor 7 in regulating intestinal immune tolerance	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F32AI174816-03	Mechanosensory Behaviors of Skin-Penetrating Parasitic Nematodes	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI175183-02	Mechanisms of skin penetration in skin-penetrating parasitic nematodes	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI175831-03	Targeting host lipid metabolism to limit tissue damage in necrotizing fasciitis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21AI175920-02	Therapy for long-COVID in a preclinical model	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI176249-03	The role of BCL11B in T lineage fate during human thymopoiesis and pluripotent stem cell differentiation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21AI178355-02	Flagellar cAMP signaling in Trypanosoma brucei	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30AI179222-02	Oxygen sensation in human-parasitic skin-penetrating nematodes	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F31AI179235-01A1	Unraveling alphavirus neuroinvasion: Molecular insights from a stem cell based blood-brain barrier model	UNIVERSITY OF CALIFORNIA LOS ANGELES
7K08AI180370-02	Systems Antibody Immunology of the Malaria Sporozoite Vaccine	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21AI180896-02	Trypanosome cAMP signaling mediates parasite-vector interaction	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01AI181072-01A1	Mechanistic link between mitochondrial cristae integrity and Th1 responses	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30AI181449-02	Transcriptional regulation of NK cell metabolism and effector function by MEF2C	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI181579-02	Harnessing the Pathogenesis of CMV Against HIV	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21AI181743-02	In vivo CAR-T-cell HIV therapy using in vitro reconstituted virus-like particles	UNIVERSITY OF CALIFORNIA LOS ANGELES
1K08AI182485-01A1	Dynamic FOXP3 Expression in the Development of Regulatory T cells from Induced Pluripotent Stem Cells	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AI183978-02	Efficacy and Safety of AI-enabled PRS Regimen VI (Clofazimine, Bedaquiline and Pyrazinamide) as Ultra-Short Course Therapy of LTBI in Non-Human Primates in a setting mimicking HIV co-infection	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01AI185026-01A1	The IRF regulatory network in innate immune training of macrophages	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21AI185484-01A1	Identification by High Throughput Screening of inhibitors of the Mycobacterium tuberculosis ESX-1 and ESX-5 Type VII Secretion Systems – critical virulence determinants and novel drug targets	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01AI186079-01A1	Transcriptional Regulation of human natural killer cell function	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F32AI186416-01	Elucidating the role of IFN epsilon mediated type I IFN responses against Trichomonas vaginalis	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21AI187865-01A1	TIM-4 Signaling in NASH Liver Transplant Ischemia/Reperfusion Injury	UNIVERSITY OF CALIFORNIA LOS ANGELES

1R34AI188541-01	Hematopoietic Stem/Progenitor Cell-Based Chimeric Antigen Receptor Gene Therapy for HIV Infection	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F30AI191652-01	The Role of Xist in T Cell Activation and Female-Biased Autoimmunity	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AR063182-12	Disease Pathogenesis and Modification for CaV1.1-Associated Hypokalemic Periodic Paralysis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AR064582-15	Morphogenesis and function of somatosensory axon ensheathment by epidermal cells	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AR075768-05	Novel mechanisms regulating muscle growth and regeneration: elucidating the Klotho/Jmjd3/Wnt axis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AR078198-05	Pathophysiology of Myotonia and Periodic Paralysis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21AR078905-02	Predicting who will fracture: Exploration of machine learning in the observational Womens Health Initiative Study dataset.	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AR079470-04	Leveraging immune-fibroblast interactions for biomaterial induced skin regeneration	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AR081794-02	Menopause-related increase in gut leak and its relation to immune activation, bone density decline and fractures	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AR084245-02	Metabolic Control of Hair Follicle Stem Cell Homeostasis and Tumorigenesis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01AT010001-08	Engineering Yeast towards High Titer Production of Monoterpene Indole Alkaloid Natural Products	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21AT012694-02	Whole-body-level metabolic flux quantitation by machine learning	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21AT012814-02	Exploring the mechanisms underlying plant (poly)phenols bioactivity via integrating metabolomics and fluxomics	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA238736-02	Deciphering functions of the ATR-METTL3-BRCA1 Axis in genome instability and Tumorigenesis	LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER
5T32CA009142-45	Molecular Epidemiology Cancer Training Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA208642-08	Imaging mitochondrial heterogeneity in LKB1 mutant lung cancer	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA215185-08	Nutrient Regulation of Cancer Cell Growth	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA228157-05	The Role of Follicular CD8+ T Cells in Pathogenesis of AIDS-NHL.	UNIVERSITY OF CALIFORNIA LOS ANGELES
5P01CA236585-05	Chemoprevention and mechanisms of obesity-promoted pancreatic adenocarcinoma	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA237401-06	Investigating the heterogeneity of glucose transport in lung adenocarcinoma	UNIVERSITY OF CALIFORNIA LOS ANGELES
4R37CA240822-06	Elucidating the Role of Trop2 in Prostate Cancer	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R00CA248836-04	Functional Characterization of HER Family Variant Biology and Resistance in Cancer	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32CA251072-05	Patient-Centered Outcomes Research Training in Urologic and Gynecologic Cancers (PCORT UroGynCan)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA251872-05	Drivers of metabolic plasticity promote radiation resistance in glioblastoma multiforme	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R01CA251872-05S1	Drivers of metabolic plasticity promote radiation resistance in glioblastoma multiforme	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA253215-05	Targeting delivery of mAbs to CNS metastases	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA260886-04	Use of CTEP portfolio compounds to counteract phenotype conversion in GBM	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R01CA260886-04S1	Use of CTEP portfolio compounds to counteract phenotype conversion in GBM	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA262686-04	Exploiting public genomic and transcriptomic data to uncover cancer-RNA editing relationships	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA267721-04	In vivo imaging of mitochondria structure and function in therapy resistant lung tumors	UNIVERSITY OF CALIFORNIA LOS ANGELES
4DP2CA271301-04	Uncovering diverse genotype-phenotype relationships in prostate cancer	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA274978-03	Delineate the Role of GSTP1 in Advanced Prostate Cancer	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30CA278297-03	Engineering detours around the biologic barriers to allogeneic, iPSC-derived CAR T immunotherapy	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F32CA278619-03	Structural Insights into Leucine Transport for mTORC1 Activation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R50CA278913-02	NCI Research Specialist/Clinician Scientist Award for Urologic Oncology Research	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA279094-03	Multidimensional analyses to improve PSMA-RPT efficacy in mCRPC	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA281682-03	Utilizing Radiation-Induced Multi-potency to Increase the Efficacy of Radiotherapy	UNIVERSITY OF CALIFORNIA LOS ANGELES
7R01CA282496-02	Development of a 3D printed small animal intensity modulated radiation system	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01CA283736-01A1	Innovative mRNA vaccines to enhance the efficacy of T-cell transfer therapies against solid tumors	UNIVERSITY OF CALIFORNIA LOS ANGELES
1UH2CA286583-01A1	Impact of dietary lipids on pancreas cancer initiation and progression	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01CA287669-02	Testing ATAD2 as a new therapeutic target for advanced prostate cancer	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F31CA288105-01A1	Defining the role of NUDT5 in ovarian cancer	UNIVERSITY OF CALIFORNIA LOS ANGELES
1T32CA288354-01A1	Neuro-Oncology Translational Research Training Program (NOTR-TP)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21CA289085-02	Adipose Tissue Reprograms Acute Lymphoblastic Leukemia Cells to Facilitate CNS and Bone Invasion	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21CA289090-01A1	Identifying novel targets for cancer using high throughput deformability screening	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R37CA289813-01A1	TNF-alpha-armed TCR vectors to enhance adoptive cell therapy for solid tumors	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R03CA289852-02	Human brain organoids as a novel platform for evaluating effects of radiation in the CNS and screening for radiation mitigators	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01CA289908-01A1	Studying heterogeneity in [18F] FDG accumulation at the individual cell level using Betabox technology to better understand PET scans of patient tumors	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01CA292866-01A1	Investigating mitochondrial networks as a critical determinant of response to antibody drug conjugates in advanced NSCLC	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F31CA294887-01	Aberrant activation of epidermal growth factor receptor signaling drives programming of an immunosuppressive brain tumor microenvironment in glioblastoma	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F31CA295026-01	Deciphering Inv3/t(3;3) Myeloid Leukemia Vulnerabilities via Proteogenomics and N-terminal Proteomics	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30CA295084-02	Brain microenvironment-dependent lineage plasticity drives adaptation to targeted therapy in malignant gliomas	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DA035443-12	Amygdala Output Circuitry in Reward Encoding, Expectation, and Decision Making	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R25DA038167-11	Training Institutes for mobile health (mHealth) methodologies	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DA047870-07	Cortico-Amygdalar Substrates of Adaptive Learning	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DA051897-05	Integrative Modeling of HIV-Associated Neurocognitive Disorder in Human Brain Organoids	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DA052841-05	Define the effects and mechanism of THC and CBD on IFN-I mediated inflammation and immune dysfunction during HIV infection	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DA053752-04	Amygdala kappa opioid system involvement in opioid relapse in pain states	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K01DA054359-04	Real-world complexities in opioid use disorder treatment: understanding family comorbidity, high-risk medication use, and costs related to treatment adherence and health outcomes	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21DA054383-02	New brainstem targets for counteracting opioid induced apnea	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DA057084-03	Contribution of non-canonical dopamine pathways to model-based learning	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21DA057690-02	High Content Functional Neuroanatomy of Endogenous GPCRs	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DA058374-02	Do opposing amygdala-striatal pathways enable chronic stress to promote habit formation?	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DA058639-03	Maintaining opioid analgesia and preventing addiction with hypocretin antagonism	UNIVERSITY OF CALIFORNIA LOS ANGELES
7R25DA059073-03	Scientific Training in Addiction Research Techniques (START) for Gifted Future Investigators	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U01DA059695-02	Integrating genetic and circuit variation to identify genes involved in behaviors related to substance use disorder	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DA059873-02	Targeting autophagy to reduce inflammasome-mediated inflammation and immune dysfunction in HIV and methamphetamine use	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01DA060229-01A1	Linking the dopaminergic mechanisms of reinforcement learning and timing	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DA061057-02	Habenula Circuitry, Smoking, and Genomics	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F31DA062444-01	Functions and mechanisms of Crym-positive astrocytes in the nucleus accumbens	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DC016959-05	Tissue engineering to regenerate functional vocal fold after scarring or tissue loss	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DC019459-05	Peripheral vestibular hypofunction and neurosensory coding	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08DC019957-04	Prolonged Local Melatonin Delivery for Recurrent Laryngeal Nerve Neuropraxia	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R25DC020151-03	Enabling careers as surgeon-scientists in otolaryngology-head and neck surgery	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21DC020581-02	Shedding light on balance: Interrogating individual synapses within vestibular epithelia	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DC021489-02	Neural mechanisms of gas sensing in a human-infective worm	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F31DC022520-01	Behavioral and neural mechanisms of chemosensation in skin-penetrating parasitic nematodes	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE031382-04	Oral commensal fungi and structural immunity	LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER
2R01DE017382-16	Molecular Assembly on the Cell Surface of Actinomyces	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE019465-14	Pathophysiologic mechanisms during initiation of medication related osteonecrosis of the jaws	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE025015-11	Post-translocational protein folding in Gram-positive bacteria	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R01DE025015-11S1	Post-translocational protein folding in Gram-positive bacteria	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE025567-10	In situ atomic structures of the Kaposis sarcoma-associated herpesvirus portal-terminase complex and glycoproteins	UNIVERSITY OF CALIFORNIA LOS ANGELES
7R01DE029200-06	Molecular control of bone development and inflammation by FBXO11	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE029234-05	Osteoclast modulatory biomaterials for skull regeneration	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE029353-05	Dual roles of Nell-1 in craniofacial bones and brain through interaction with Cntnap4	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R25DE030117-05	Bruins in Genomics: Dental, Oral & Craniofacial Research Training Program (BIG DOC)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE030471-04	Mechanical regulation of transcription in dental epithelial stem cells through cell packing and tissue forces	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE030536-05	Regulation of Alveolar Bone Marrow MSC Senescence in Skeletal Aging and Periodontitis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T90DE030860-05	UCLA Dentist-Scientist and Oral Health-Researcher Training Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21DE031074-02	Targeting Grainyhead-Like 2 Suppresses Entry Factors of SARS-CoV-2 in Epithelial Cells of Oral Mucosa.	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R90DE031531-05	UCLA Dentist-Scientist and Oral Health-Researcher Training Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE031711-04	Hydrogel delivery of DBM and exosome mimetics for bone repair	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21DE031906-01A1	The role of CXCL10-CXCR3 axis in the compounding effects of diabetes mellitus in periodontitis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE032624-02	Role of the oral microbiome in driving local and systemic inflammation in HIV	UNIVERSITY OF CALIFORNIA LOS ANGELES

5K01DE032775-03	Oral microbiome establishment and development of Latinx Children at the US-Mexico border	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21DE032906-02	Metabolic modulation of Fusobacterium nucleatum virulence	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R21DE032906-02S1	Metabolic modulation of Fusobacterium nucleatum virulence	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R34DE033593-01	Interdisciplinary Clinical Advances and Research Excellence in TMDs (ICARE 4 TMDs) Collaborative	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DE033900-02	Assembly and function of outer membrane tubules in Fusobacterium nucleatum	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21DE034146-01	The function role of salivary piRNAs in oral wound healing	UNIVERSITY OF CALIFORNIA LOS ANGELES
1K08DE034493-01	Therapeutic Targeting of Apical Periodontal T-Cells in Chronic Oral Inflammation	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R03DE034516-01A1	Distinct roles of neural crest cell populations in cranial suture development and disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK136888-02	Spatiotemporal regulation of human islet organogenesis	LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER
5R01DK062357-20	HuR/HIF – SIRT1 Signaling Axis in Liver Transplant Rejuvenation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK077162-14	The Biology of NBCe1 in Health and Disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK082412-13	Chymotrypsin in pancreatitis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK117850-06	Systems Genetics Dissection of Non-alcoholic Steatohepatitis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK121557-05	REGULATION OF HUMAN HEMATOPOIETIC STEM CELL FATE VIA MLLT3 ISOFORMS	UNIVERSITY OF CALIFORNIA LOS ANGELES
7R01DK123327-05	Molecular regulation of gut lipid metabolism by mTOR and autophagy proteins	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK125354-05	Role of dynamin-related protein 1 in the regulation of metabolism and skeletal muscle mass	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K01DK127004-05	Iron and Pregnancy: Regulatory Mechanisms and Adverse Outcomes	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK127232-05	RNA modification in cardiometabolic disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK128898-04	Sex Differences in Postprandial Lipid Metabolism	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U2CDK129496-05	KUH-ART: Advanced Research Training in Kidney disease, Urology and Hematology	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK131111-04	Impaired autophagy, mitochondrial dysfunction, and inflammation in pancreatitis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK131493-03	Dysregulated cholesterol homeostasis, caused by lysosomal/autophagy dysfunction, mediates pancreatitis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK132319-03	Piezo-1 & 2's role in murine intestinal muscularis cells of the SIP syncytium	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01DK132735-01	Metabolic and epigenetic reprogramming of vital organs in SARS-CoV-2 induced systemic toxicity	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R01DK132735-01S1	Metabolic and epigenetic reprogramming of vital organs in SARS-CoV-2 induced systemic toxicity	UNIVERSITY OF CALIFORNIA LOS ANGELES
5TL1DK132768-05	Training Core	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K01DK133666-03	Dysregulation of inflammation resolution as therapeutic target for IBD	UNIVERSITY OF CALIFORNIA LOS ANGELES
7K01DK133670-04	Microbial drivers of metabolically unhealthy obese phenotype	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30DK134050-04	Regulation of hepatic lipid metabolism by novel protein BASIC	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08DK134868-03	Highly Elastic Biomaterial Development for Urethral Application	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08DK134872-02	Intestinal mitochondrial dysfunction and the gut-brain-immune axis in models of Parkinsons Disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK136073-03	Hypothalamic gating of the anorexic effects of estradiol	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK136150-03	Lipid storage and utilization in physiology and obesity	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08DK136706-02	Role of a Novel Methyltransferase in Liver Lipid Metabolism	UNIVERSITY OF CALIFORNIA LOS ANGELES
1K99DK138289-01A1	Regulation of intestinal lipid metabolism by type-3 immune cytokine	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08DK138316-02	Diversity generation in the gastrointestinal microbiome	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK138340-02	Bile acid-mediated control of lipid absorption and fatty liver disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F31DK138752-02	Dissecting the Role of Peroxisomal PEX Family Proteins in Hepatic Bile Acid and Lipid Metabolism	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01DK139605-02	GABAergic Cells in the Periaqueductal Gray Region Control Food-Seeking	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01DK142845-01	Interplay between brain oxytocin and CRF systems in stress-related visceral analgesia vs hyperalgesia: implications in IBS	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01DK143368-01	A sex-biased obesity gene on the X chromosome	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EB023052-04	Engineering a naturally derived and highly adhesive surgical sealant	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EB027172-06	Biocompatible fluorophores for shortwave infrared imaging	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EB032264-04	Accelerating the discovery and development of neurotracers via high-throughput radiochemistry	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21EB035280-02	Engineering biomimetic 3D printed urethral tissue constructs using elastin-based bioinks for urethroplasty	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U45ES006173-33	Hazardous Materials Worker Health and Safety Training (U45)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01ES029395-05	Role of Intestinal Microbiota in Dyslipidemia and Atherosclerosis Induced by Ambient Ultrafine Particles	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01ES032806-05	Interplay Between Macrophages, Lipid Oxidation and the Nrf2/HO-1 Axis in the Cardiometabolic Toxicity Induced by Ultrafine Particles	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R25ES033043-04	Occupational and Environmental Exposures and Work Practices for Nanomaterials and Electronic Products	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01ES033660-04	Novel Approaches for Improving Inflammation Resolution Following Chronic Exposure to Air Pollutants	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01ES033703-04	Dissecting the Role of Arachidonic Acid Metabolic Pathways Involved in Resolution Versus Progression of PM-Induced Cardiometabolic Toxicity	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01ES034251-03	Role of epigenetic crosstalks in directing locus sensitivity to arsenic	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K99ES034819-02	Impact of Biomass Burning Aerosol and Humic-like Substances on Iron Homeostasis and Atherosclerosis	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01ES036923-01	Nuclear moonlighting of arsenic metabolic enzymes and reprogramming-resistant epimutations	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY001844-48	Physiology of Photoreceptors	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY022979-13	A cell-type specific explanation of visual decision circuits.	UNIVERSITY OF CALIFORNIA LOS ANGELES
2R01EY023871-10A1	Origins of plasticity in the establishment of binocular vision	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY026031-09	Neural circuits for visual feature detection	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY026319-08	Metabolism and neuronal viability of the retina	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY029689-05	Vitreoretinal Surgery via Robotic Microsurgical System with Image Guidance, Force Feedback, Virtual Fixture, and Augmented Reality	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY032149-04	Interplay between AMPK and Hippo Signaling Regulates Ocular Antiviral Response to Zika virus infection	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY032561-05	Targeting epithelial membrane protein 2 (EMP2) in retinopathy of prematurity	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY032863-04	Elucidating the role of the oculomotor circuit in free viewing visual search	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY033035-04	Cellular Mechanisms of Photoreceptor Disk Morphogenesis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY033064-04	Mechanisms of persistent neural activity	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01EY034004-03	Visual signaling from retina to superior colliculus	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K99EY034576-02	In-depth molecular studies of dynein transport in the RPE	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21EY035064-02	Cortical adaptation in neural populations	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01EY036104-01A1	Outer Segment tip ingestion by the RPE	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K99EY036123-02	Molecular determinants of synaptic specificity underlying a visuomotor transformation	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01EY036572-01A1	Defining Ocular Monkey Pox Pathogenic Mechanisms	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R13EY036717-01	UCLA/American Uveitis Society 2nd International Workshop on Objective Measures for Use in Clinical Trials	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01EY036811-01	Physiology of Retinal Degeneration	UNIVERSITY OF CALIFORNIA LOS ANGELES
1K99EY036889-01	Neuronal mechanisms of selective visual attention	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM061721-20	BIOGENESIS OF THE MITOCHONDRIAL INNER MEMBRANE	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM071779-16	Phosphine-Catalyzed Annulations and their Applications	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM071940-16	High-Resolution CryoEM Reconstruction of Large Complexes	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R01GM071940-16S1	High-Resolution CryoEM Reconstruction of Large Complexes	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM074701-20	Interplay Between Chromatin and Co-Activator Complexes	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM096133-13	Collaboration between actin nucleators - Spire and Cappuccino	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM102308-11	High-throughput experimental determination and computational prediction of variant effects in yeast	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K12GM106996-09	IRACDA at UCLA	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM118056-10	MIRA: Enzymology and Self-Resistance of Natural Product Biosynthesis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM119856-10	Population genomics of the selective effects of new mutations	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM124746-08	Inorganic Chemistry Tools for Bioconjugation, Recognition and Imaging	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM126986-09	New Directions in Nickel and Photoredox Catalysis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM128761-08	Ultrafast bioimaging	UNIVERSITY OF CALIFORNIA LOS ANGELES
7R35GM128852-06	Metallobiochemistry of Mn/Fe protein cofactors	UNIVERSITY OF CALIFORNIA LOS ANGELES
2R35GM128867-06	Micro Electron Diffraction of Toxic and/or Infectious Macromolecular Nanoassemblies	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM130370-07	The control of gene expression by eukaryotic ribonucleases	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM131901-07	Structural biology of telomerase and telomeres	UNIVERSITY OF CALIFORNIA LOS ANGELES
2R35GM133481-06	Evolution on epidemiologically-relevant timescales	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R25GM135043-05	Computational Genomics Summer Institute and Mentoring Network	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM135380-04	Robust microdroplet-based mechanical probes for wide-ranging mechanobiology applications	UNIVERSITY OF CALIFORNIA LOS ANGELES
2R35GM136426-06	Mechanisms of Post-transcriptional Gene Regulation by RNA Binding Proteins	UNIVERSITY OF CALIFORNIA LOS ANGELES

5P41GM136508-05	MEDIC - MicroED Imaging Center at UCLA	UNIVERSITY OF CALIFORNIA LOS ANGELES
2R35GM138003-06	Understanding How Metabolic Cofactors Control Cell Function and Fate	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM139539-05	Investigating the Cell Division Machinery	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM139593-05	Exploiting Unconventional Building Blocks in Chemical Synthesis	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R35GM139593-05S1	Exploiting Unconventional Building Blocks in Chemical Synthesis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM140106-04	Understanding the function of histone H3 as an oxidoreductase enzyme	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R00GM140209-04	Dynamic interplay of eukaryotic translation and mRNA decay	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM140888-05	Statistical methods for elucidating regulatory mechanisms and functional impacts of transcriptome variation at population and single-cell scales	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM141798-05	Modeling, Inference, and Optimization for Genomic and Biomedical Big Data	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM142511-05	Understanding spontaneous mitotic crossover by single-cell multi-omics	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM142799-05	Steroid hormone dependent gene expression and neuroplasticity in the brain	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM143097-05	Mechanisms of regulation of mitochondrial H+ leak and thermogenesis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM143127-05	Elucidating the mechanism behind oscillation between glycolysis and gluconeogenesis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM143378-04	Developing tools for the unbiased analysis and visualization of scRNA-seq data	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM143485-04	Regulation of cell reprogramming by matrix stiffness	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM144108-04	Mechanisms of microridge protrusion morphogenesis on mucosal epithelial cells	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM145286-04	Advancing Mass Spectrometry Analyses of Proteins, Assemblies, and Proteoforms	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32GM145388-04	Research Training in Cell and Molecular Biology	UNIVERSITY OF CALIFORNIA LOS ANGELES
4DP2GM146246-02	A systems-level approach to decipher the protein interactome.	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM147114-03	Understanding cascading cellular protein responses following multi-protein stimuli using network modeling and real-world evidence	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM147391-04	Nanoscale Temperature Mapping and Thermal Regulation of Intracellular Dynamics	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM148249-02	Phage-inspired engineering and evolution	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01GM148761-03	Bayesian Modeling and Inference for High-Dimensional Disease Mapping and Boundary Detection	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F32GM149135-02	Causal mechanisms of anesthetic induction and emergence in human cortical organoids	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F31GM149161-03	Enantioselective Reactions with Amide Electrophiles Utilizing Transition-Metal Catalysis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM149290-03	Mechanisms of messenger RNA splicing and RNA processing regulation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM151023-03	Evolutionary Dynamics of the Human Gut Microbiome During Colonization	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM151199-02	Lineage-Specific Mechanisms of Cell Cycle Timing Control	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K99GM151453-02	Data to Design: An Integrated Approach to Developing New Synthetic Methods	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32GM152342-02	UCLA-Caltech Medical Scientist Training Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F32GM153130-03	Neural and molecular control of subordinate social status in a cichlid fish	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM153406-02	Expressive and scalable statistical models for genomic and biomedical data	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35GM153408-02	Understanding Ubiquitin-dependent Regulation of Iron Metabolism using Mass Spectrometry	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T34GM153514-02	MARC at the University of California, Los Angeles	UNIVERSITY OF CALIFORNIA LOS ANGELES
1DP2GM154012-01	Imaging Spatiotemporal Regulation of Acetyl-CoA	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F31GM154466-02	Defining the role of DUSP12 in the regulation of cell division and apoptosis.	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R35GM155833-01	Developing synthetic RNA organelles for spatiotemporal separation, control, and monitoring in living cells	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R35GM156610-01	Harnessing the orthogonality of fluorine for advanced biomaterials and biotechnologies	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R35GM156893-01	Exploring the fundamental cellular mechanisms driving cellular senescence in macrophages	UNIVERSITY OF CALIFORNIA LOS ANGELES
1K99GM157504-01	Understanding eukaryotic proteasome assembly regulation	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R35GM158109-01	Understanding the function and impact of histone H3 as a copper reductase enzyme	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HD099924-05	Epitranscriptomic regulation of spermatogenesis and male fertility	LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER
5R61HD114186-02	IND-enabling studies to develop triptonide into the first nonhormonal male pill	LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER
5R01HD054453-17	Circuit Defects Underlying Deficits in Social Touch in Fragile X Syndrome	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HD079546-10	Cellular and Molecular Basis of Human Primordial Germ Cell Specification	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32HD091059-07	Doctoral Training in Brain and Behavioral Development During Adolescence (UCLA BBDA)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HD098284-05	Modulation of sex steroid-induced female social behaviors in an animal model	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HD100298-05	Coupling neuroimaging with CLARITY and single cell genomics to dissect sex differences in the developing brain	UNIVERSITY OF CALIFORNIA LOS ANGELES
4R00HD105001-03	Functional analysis of histone modifier Autism Spectrum Disorders risk genes in vertebrate development	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R25HD108136-03	Modelers and Storytellers: Transdisciplinary Training to Advance Community Health Intervention Research	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HD108370-04	Cortical Interneuron Dysfunction in Fragile X Syndrome	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R25HD109116-03	UCLA Pediatric Research Education Program in Bioinformatics, Computational Biology, and Omics	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K00HD109205-05	The neural control of thermoregulatory changes accompanying pregnancy	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K12HD111040-03	UCLA Child Health Research Career Development Award	UNIVERSITY OF CALIFORNIA LOS ANGELES
1DP2HD111538-01	Compliant Limb Reconstruction: Co-engineering Body and Machine to Revolutionize Limb Salvage	UNIVERSITY OF CALIFORNIA LOS ANGELES
3DP2HD111538-01S1	Compliant Limb Reconstruction: Co-engineering Body and Machine to Revolutionize Limb Salvage	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HD114495-02	Drug repurposing of a novel synthetic progestin for the prevention of preterm labor and fetal inflammation	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21HD115071-01	Structure-based antisense therapeutics targeting dystrophin exons 44 and 45 for Duchenne Muscular Dystrophy	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HD115349-02	X chromosome dosage compensation and the regulation of the feto-maternal interface	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F30HD117619-01	Role of Intracortical Mechanisms Vs. Bottom-Up Influences in Developmental Desynchronization of Cortical Network Activity	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R13HD118736-01	American Pediatric Society: Building the Evidence Base to Improve Pediatric Care for Youth in Custody Conference	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U54HG012517-04	Building BRIDGES: Coordinating the Dissemination and Training for Biomedical Artificial Intelligence	UNIVERSITY OF CALIFORNIA LOS ANGELES
3U54HG012517-04S1	Building BRIDGES: Coordinating the Dissemination and Training for Biomedical Artificial Intelligence	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HG012925-02	Whole organ transcriptome reconstruction by dimensionality reduced fluorescent in situ hybridization	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F31HG013462-02	Identifying sources of variable penetrance and expressivity in monogenic diseases at population scale	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F31HG013890-01	Hierarchical modeling and simulation to optimize cell village experimental design and the analysis of scRNA-seq data	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL087228-18	Refining Physiologic Mechanisms for Intravascular Triglyceride Metabolism	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL105699-13	Dynamics of cardiac nuclei in heart disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL129727-08	Shear stress and light-field to elucidate the initiation of cardiac outflow tract	UNIVERSITY OF CALIFORNIA LOS ANGELES
2R01HL139549-06	RNA binding proteins in atherosclerosis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL142951-04	Netrin-1 and Netrin-1 Preconditioned EPCs in Vascular Protection	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K24HL143055-07	Sleep health in special populations	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL146821-05	Trek-1 Potassium Channels Protect from Hyperoxia-Induced Acute Lung Injury	UNIVERSITY OF CALIFORNIA LOS ANGELES
7R01HL148781-05	Therapeutic Use of High Molecular Weight Hyaluronic Acid in Acute Lung Injury Following Severe Bacterial Pneumonia or Sepsis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL149658-04	Targeting cardiac fibroblast-myocyte cross talk to enhance heart function after cardiac injury	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL149808-06	Intravascular Deployment of a Wirelessly Powered Micro-Pacer	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL151391-04	Role of intermittent activation of parathyroid hormone receptor in exercise-induced vascular calcification	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL152176-04	Role of GPNMB in cardiac remodeling	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL152296-04	Sodium Dependent Inactivation of the Na+-Ca2+ exchange: Relevance to Cardiac Function	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U01HL153000-04	Validation of an in vitro model of progressive fibrosis that mimics Idiopathic Pulmonary Fibrosis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL154754-04	Endothelium-driven signaling network in the development of pulmonary hypertension	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL155905-04	Impacts of transcription elongation on cardiac gene regulation during homeostasis and regeneration	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R03HL157012-02	Investigating the Role of MYH14 in Tension-Dependent Cardiomyocyte Hypertrophy	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL157710-04	Investigating the impact of a fatty acid-cRel inflammatory circuit in atherosclerosis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL158053-04	Endothelial Regulation of Vascular Calcification	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL159001-04	Mechanisms of Cardiac TRPV1 Afferent Remodeling in Ventricular Arrhythmias	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL159507-04	ZIP8: A Metal Transporter with Pathophysiologic Roles in the Lung, Spleen, and Placenta	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL159970-04	Integrating Volumetric Light-Field with Computational Fluid Dynamics to Study Myocardial Trabeculation and Function	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL160554-03	Investigating pulmonary complications due to abnormal collagen/ER stress in Osteogenesis Imperfecta	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL160730-04	Regulation of Cardiac Collagen Content by SLIT3	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL160850-04	Identifying Cardiotoxic Manifestations of Posttraumatic Psychopathology: A Population-based Longitudinal Investigation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R25HL161609-04	Cultivating Interest in Research Careers (CIRC)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL162124-04	Role of intestinal inflammation in oxidized lipid induced pulmonary hypertension	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL162407-04	Targeting NOX4-dependent mitochondrial dysfunction, autophagy and defective calcium handling in AF	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL162408-03	MYCT1 as a moderator for signaling between human HSC and their niche	UNIVERSITY OF CALIFORNIA LOS ANGELES

5R01HL162643-04	Erasing ill features of arterial endothelial cells in hereditary hemorrhagic telangiectasia	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL162921-03	Bioelectric monitoring and neuromodulation of the heart	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL163025-03	Novel Signaling Mechanism in Chamber-Specific Postnatal Heart Growth	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL163908-03	Targeting the gut-liver axis in cardiovascular disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
7R01HL166449-03	Lung-derived complement in pneumonia	UNIVERSITY OF CALIFORNIA LOS ANGELES
7R01HL168493-02	Genetic Predisposition to Myocardial Infarction in Patients with Coronary Artery Disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R56HL169862-01A1	Structure and Biology of Tissue Factor Pathway Inhibitor-2	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL170626-02	Sex differences in cardiac autonomic remodeling after myocardial infarction	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL171307-02	Adenine metabolism in cardiac repair	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35HL171451-02	Neural Control of Breathing	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL171737-02	Solving longstanding mysteries in plasma triglyceride metabolism	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01HL172852-01A1	Regulation of angiogenesis by cardiac fibroblasts	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL174008-02	Post-transcriptional regulation of LDLR	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL174472-02	ZFP36, an RNA Binding Protein that Regulates DNA Repair and Cell Proliferation in PAH	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01HL174996-01A1	Epigenetic Regulation of Heart Failure with Preserved Ejection Fraction	UNIVERSITY OF CALIFORNIA LOS ANGELES
1K38HL175027-01	The Lipofibroblast to Myofibroblast Transition in Systemic Sclerosis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL175074-02	A population-based computational approach for arrhythmia prediction and therapy	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01HL175240-01A1	Membrane cholesterol and vascular inflammation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01HL175773-02	Mechanisms of nonvesicular cholesterol transport	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01HL176691-01	Role of macrophages in regulating cardiac muscle metabolism	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MD013913-05	The Impact of Surgeon Factors and Education/Training on Disparities in Surgical Care.	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F31MD019213-01	Early Childhood Housing Condition, Education, and Criminal Behavior	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R25MH087222-15	South American Program in HIV Prevention Research (SAPHIR)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH115676-08	Integrating case-control transcriptomic and genetic data in admixed individuals to identify disease genes for schizophrenia and bipolar disorder	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH122428-05	Functional Data Analysis for High-Dimensional Biobehavioral Data	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH123177-05	Systematic approaches to decipherng regulation and function of RNA editing in brain	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH124018-05	Defining gene regulatory networks driving cortical evolution and brain development	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH125252-05	SINGLE-CELL MULTI-OMIC APPROACHES TO MECHANISTICALLY CHARACTERIZE PSYCHIATRIC DISORDER RISK LOCI IN THE HUMAN BRAIN	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH127214-04	Prefrontal circuits underlying the maturation of learned avoidance	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R34MH128397-03	Serious mental illness and incarceration: piloting the use of a multi sector linked administrative dataset	UNIVERSITY OF CALIFORNIA LOS ANGELES
1RF1MH128888-01	Next-generation MORF Mice for Scalable Brainwide Morphological Mapping and Genetic Perturbation of Single Neurons	UNIVERSITY OF CALIFORNIA LOS ANGELES
4DP2MH129986-02	Developing long-term neuro-behavioral recording and real-time processing platforms for naturally behaving animals	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH130061-04	Elucidating the molecular mechanisms behind human neurodevelopmental disorders using brain organoids	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30MH130075-04	Regulation of Alternative Splicing in the Brain by a Large Assembly of Splicing Regulators	UNIVERSITY OF CALIFORNIA LOS ANGELES
1RF1MH130461-01	In situ Single-Cell Multi-Omic and Morphological Profiling in Mammalian Brains	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH130941-04	Neural Circuit Mechanisms of Allogrooming Behavior	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH131858-03	Role of prefrontostriatal circuits in effort-based, cost-benefit decision making	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH132689-02	Elucidating Regulation of Cell Fate Specification in Human Cortical Development to Understand Etiology of Neurodevelopment Disorders	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH132736-03	Unstable nucleus accumbens social representations in models of social behavioral dysfunction.	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21MH133212-02	Prefrontal circuit mechanisms of repetitive transcranial magnetic stimulation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F32MH133387-02	Reorganization of cortical memory ensembles across time	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21MH134158-01	Mechanisms of enhanced synaptic drive in basolateral amygdala following stress	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F31MH134521-02	Neural Basis of Inter-brain Synchrony during Social Interaction in Health and Disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30MH134633-02	Investigating circuit-specific effects of high-frequency repetitive transcranial magnetic stimulation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH134926-02	Functions and mechanisms of a subpopulation of striatal astrocytes	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30MH135660-02	Functional Genomic Interrogation of Autism Spectrum Disorder Genetic Risk on Microglia-Neuronal Interactions	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F31MH135698-02	Frontocortical representations of amygdala-mediated learning under uncertainty	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F30MH135712-02	Mapping cell type specific isoform diversity in the human brain: dissecting mechanisms of alternative splicing in ASD	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH137080-02	An Outcome-Focused Measure of Mental Health Care Quality based on Standardized Patient-Reported Symptoms	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH137276-02	Understanding spatial representations in rat orbitofrontal cortex	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01MH137461-02	Role of prefrontal dopamine circuits in threat avoidance learning	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F31MH138093-01	Exploring the Contribution of Distinct mPFC Cell-Types to the Encoding of Decision-Making Outcome	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F31MH138135-02	Investigating the effects of early life adversity on the developmental trajectory of avoidance circuitry	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS131646-02	Defining cerebellar pathophysiology in Ataxia Telangiectasia	LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER
5T32NS048004-20	Training Grant in Neurobehavioral Genetics	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS054814-17	Developmental and functional analysis of neural circuits controlling navigation in Drosophila	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R01NS054814-17S1	Developmental and functional analysis of neural circuits controlling navigation in Drosophila	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS078410-11	Sex differences in the ability to recover from sleep loss: the roles of development and sex chromosome dosage	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U24NS100685-08	Southwest Strategies to Innovate Emergency Care Clinical Trials Network (SW SIREN)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5UH3NS106945-05	Predictive accuracy of acute astroglial compromise biomarkers after traumatic brain injury	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U24NS107321-07	Los Angeles - Southern California (LASC) NIH StrokeNet Regional Coordinating Center	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS110783-05	Cerebral Mechanisms of Vulnerability Following Female Traumatic Brain Injury	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS111378-05	Precision Medicine Approach: Using genomic information to guide TBI treatment	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35NS111583-07	Fundamental astrocyte biology in intact neural circuits	UNIVERSITY OF CALIFORNIA LOS ANGELES
2R01NS112799-06	Shear Stress and Endothelial Pathophysiology in Intracranial Atherosclerosis	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS113124-05	Functional Dissection of Neural Circuitry Underlying Parenting Behavior	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08NS114165-05	Mechanisms of Somatosensory Circuit Remapping After Cortical Injury in Mice	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R25NS115554-05	Undergraduate Research Experiences in Neurogenetics and Neurogenomics	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS116383-05	Strategy to Potentiate Rehabilitation after TBI	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS116471-03	Population codes and sensory discrimination	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS117148-05	Spatiotemporal Molecular Substrates of TBI at Single Cell Resolution	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS117912-05	Optimizing and validation of gene therapy vectors to treat limb girdle muscular dystophy	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08NS119747-05	Utilizing Human Brain Organoids to Model the Differential Effects of SCN8A Mutation on Cortex and Hippocampus	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS119905-04	Investigating the role of sleep in synaptic reorganization after neural injury	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS120690-05	Control of calcium flux and mitochondrial fission by the Charcot Marie Tooth disease protein Mfn2.	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS120984-05	Olfactory neuromodulation of visual circuits and behavior	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS121319-05	CDKN2A couples lipid metabolism to ferroptosis in glioblastoma	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS121617-04	Radiation-induced vascular reprogramming in glioblastoma	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS121761-04	A Toolkit for Analysis and Visualization of Preclinical Rodent Neuroimaging Experiments	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS123187-04	Assessing the mechanisms directing cell fate in the dorsal spinal cord	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS123376-04	Patterned, Stimulus-Independent Neuronal Activity in the Developing Drosophila Visual System: Origin and Contribution to Synaptic Maturation	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K08NS123509-04	Cell Type-Specific Transcriptional Changes Underlying Memory Impairment in Temporal Lobe Epilepsy	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS125877-04	CRCNS: Multiple clocks for the encoding of time in corticostriatal circuits	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U01NS126050-03	Closed-Loop Systems for Large Scale Spatiotemporal Imaging and Actuation of Neural Activity in Freely Behaving Animals	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21NS126163-02	Converting human butyrylcholinesterase into a metalloenzyme for catalytic hydrolysis of organophosphates	UNIVERSITY OF CALIFORNIA LOS ANGELES
5K01NS127944-02	Adenosine Modulation of the Bi-Directional Relationship between Sleep and Migraine	UNIVERSITY OF CALIFORNIA LOS ANGELES
1UG3NS128148-01A1	Peripherally-restricted non-addictive cannabinoids for cancer pain treatment	UNIVERSITY OF CALIFORNIA LOS ANGELES
1RF1NS128488-01	Kilohertz volumetric imaging of neuronal action potentials in awake behaving mice	UNIVERSITY OF CALIFORNIA LOS ANGELES
5U01NS128664-03	Open-source miniaturized two-photon microscopes for large field-of-view and volumetric imaging	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS128964-04	Regulation of Pathological Tau Transmission by Soluble Tau Post-Translational Modifications	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS129517-03	Reciprocal interactions between cortical circuit dysfunction and a-synuclein pathology	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R00NS129758-03	Molecular and circuit mechanisms of nausea-associated behaviors	UNIVERSITY OF CALIFORNIA LOS ANGELES
3R00NS129758-03S1	Molecular and circuit mechanisms of nausea-associated behaviors	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21NS130326-01	Can diagnostic biomarkers for parkinsonian syndromes be measured in postmortem blood samples?	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS130677-03	Mechanopriming for cell engineering	UNIVERSITY OF CALIFORNIA LOS ANGELES

1R21NS131767-01A1	Glioblastoma-secreted GABA contributes to the immunosuppressive environment	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R35NS132150-03	Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach	UNIVERSITY OF CALIFORNIA LOS ANGELES
1RF1NS132912-01	Neural circuits for social modulation of a persistent negative emotional state	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R61NS133274-01A1	A novel platform for the discovery and characterization of migraine therapies	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01NS133744-03	A three dimensional multimodal cellular connectivity atlas of the mouse hypothalamus	UNIVERSITY OF CALIFORNIA LOS ANGELES
1K01NS134780-01A1	WNT Mediated Induction of Schwann Cell Plasticity	UNIVERSITY OF CALIFORNIA LOS ANGELES
5F31NS135993-02	Post-Stroke Neurovascular Function and Repair within a Porous Hydrogel	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01NS136137-01A1	Neurophysiology of impaired gait in mouse models of Parkinson's disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01NS137919-01A1	Improved delivery of bNAbs for targeting CNS infection in infants	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R56NS138435-01A1	The molecular basis of synaptic specificity	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21NS139078-01	Engineered GABA oxidase for GABA sensing in vivo	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R13NS139602-01	Western Neurotrauma Symposium 2024	UNIVERSITY OF CALIFORNIA LOS ANGELES
1F31NS139660-01	Identifying the cells and circuits driving stimulus-independent activity throughout the developing Drosophila brain	UNIVERSITY OF CALIFORNIA LOS ANGELES
1RF1NS139972-01	Defining the molecular spectrum of white matter vascular lesions	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R61NS140733-01	High-throughput small molecule screen to reduce endogenous level of Msh3 for disease-modifying HD therapy	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R21NS140948-01	Alternative Splicing Directed Epigenetic Regulation in Brain Development	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R01NS142690-01	Kilohertz 3D voltage imaging using near-infrared confocal squeezed light field microscopy	UNIVERSITY OF CALIFORNIA LOS ANGELES
1DP2NS142715-01	Electrified cryo-EM: a new tool to capture metastable neuron structures during an action potential	UNIVERSITY OF CALIFORNIA LOS ANGELES
1R24OD037736-01	BRC Modernization of Sterilizing Equipment	LUNDQUIST INSTITUTE FOR BIOMEDICAL INNOVATION AT HARBOR-UCLA MEDICAL CENTER
5DP5OD028181-05	Nanoscience-Inspired Acoustofluidic Assembly Lines for Gene and Cellular Therapies	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R01OD030496-05	Transformative rat models to study sex differences in disease	UNIVERSITY OF CALIFORNIA LOS ANGELES
5R21OD035421-02	Dissecting out differential molecular phenotypes across Lysine(K) AcetylTransferase mutations in mouse development	UNIVERSITY OF CALIFORNIA LOS ANGELES
1S10OD038149-01	High-Resolution Tandem Mass Spectrometer to Support Large Molecule Structural Characterization	UNIVERSITY OF CALIFORNIA LOS ANGELES
1S10OD038259-01	Automated Cell Culture System	UNIVERSITY OF CALIFORNIA LOS ANGELES
5UH3TR003148-04	Multi-organ-on-chip device for modeling opioid reinforcement and withdrawal, and the negative affective component of pain: a therapeutic screening tool.	UNIVERSITY OF CALIFORNIA LOS ANGELES
5D43TW012029-04	Sustainable Academic Capacity Building of Excellence through Research and Training Program (SACERT)	UNIVERSITY OF CALIFORNIA LOS ANGELES
3D43TW012029-04S1	Refining and Expanding the SACERT-Learning Collaborative and Integrated Measures Bank-South Africa	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32AI177290-03	Addressing Evolving Infectious Threats	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32AR059033-14	Regenerative Musculoskeletal Medicine Training Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32AR065972-10	Muscle Cell Biology, Pathophysiology, and Therapeutics	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32CA009056-47	Tumor Cell Biology Training Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32CA009120-47	UCLA Tumor Immunology Institutional Training Grant	UNIVERSITY OF CALIFORNIA LOS ANGELES
1T32CA302559-01	UCLA Surgeon-Scientist Basic Cancer Research Training Program (UCLA Surgeon-Scientist BCRTP)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32DA024635-17	UCLA Training Program in the Translational Neuroscience of Drug Addiction (TNDA)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32EB002101-48	Physics and Biology in Medicine Research Training	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32EB016640-12	Medical Imaging Informatics Training Grant	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32EY007026-48	Vision Science Training Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32GM008243-38	UCLA Medical Genetics Training Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32GM148369-03	Multidisciplinary Anesthesiology and Perioperative Medicine Research Training Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32HD007545-24	California Center for Population Research Training Program	UNIVERSITY OF CALIFORNIA LOS ANGELES
2T32HL072752-21A1	The UCLA Pulmonary and Critical Care Medicine Scientist Training Program (PCCM-STP)	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32MH015750-45	Biobehavioral Issues in Physical and Mental Health	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32MH073517-18	Training the Science of Child Mental Health Treatment	UNIVERSITY OF CALIFORNIA LOS ANGELES
5T32MH080634-18	Postdoctoral Training in Global AIDS Prevention Research	UNIVERSITY OF CALIFORNIA LOS ANGELES
5TL1TR001883-09	J. NRSA Training Core	UNIVERSITY OF CALIFORNIA LOS ANGELES

EXHIBIT G

Contact Detail Close

Date 01-Aug-2025

From Reports, ORA

To Voskuhl, Rhonda

CC (maribel.gomez@research.ucla.edu), Maribel
Johnson, Robert
Records, ORA

BCC

Contact Type Email

Subject Grant Suspension Notice - Stop Work Order [PATS 20225713]

Message

Stop Work Notice

Award #: R35NS132150
Title: Neurodegeneration Underlying Distinct Disabilities in Multiple Sclerosis Using a Cell-Specific, Region-Specific, and Sex-Specific Approach
PATS #: 20225713
Fund #(s): 29470

Professor Voskuhl,

UCLA has received a suspension notice from NIH-NINDS National Institute of Neurological Disorders and Stroke for the above referenced project.

This email is to notify you to ***immediately stop incurring costs/expenditures on the grant(s) referenced above effective July 31, 2025***.

If your grant includes active subawards, OCGA will be writing to the subawardee's administrative contact with formal notice of the subaward suspension and the requirement to stop immediately all expenditures against the subaward. You may also want to separately reach out to your collaborator to provide additional context.

UCLA is required to submit to the sponsor, within 30 days of this suspension, a financial report of expenditures through July 31, 2025. OCGA will request that the subawardee submit to you, within 15 days of the notice, an invoice for expenses incurred to date so that we can include those expenses in our report to the sponsor. Extramural Fund Management (EFM) will seek the support of your fund manager to prepare a complete and accurate financial report of expenses incurred through July 31, 2025.

We are saddened that this has happened and echo the sentiments expressed in the recent communications from Chancellor Frenk and Vice Chancellor for Research Wakimoto. Campus leadership is actively engaged in working to resolve these issues. Updates will be shared as they become available. For questions regarding the suspension, please contact awards@research.ucla.edu or reach out to me directly. For financial or reimbursement-related inquiries, reach out to your EFM contact.

ACTION REQUIRED

Please:

1. Forward any communications you may receive from the federal sponsor related to this suspension to OCGA at awards@research.ucla.edu.
2. Work with your fund manager or financial staff to ensure all expenditures are

reported and subaward invoices are approved.

We understand this is a stressful time, and we appreciate your dedication to research excellence at UCLA.

Tracey Fraser
Senior Director
UCLA Office of Contract & Grant Administration
10889 Wilshire Boulevard, Suite 700
Los Angeles, CA 90095-1406
T: (310) 825-0671 | **E:** tracey.fraser@research.ucla.edu
https://ocga.research.ucla.edu/

Posted by

Attachments

EXHIBIT H

[redacted]

From: "Tran, Alexandra N." <AlexandraTran@mednet.ucla.edu>
Subject: Grant Suspension
Date: August 4, 2025 at 3:38:04 PM PDT
To: "Voskuhl, Rhonda R." <RVoskuhl@mednet.ucla.edu>
Cc: "Carmichael, Stanley T." <SCarmichael@mednet.ucla.edu>, "White, Geoffrey A." <GAWhite@mednet.ucla.edu>

Sent on behalf of Dr. S. Thomas Carmichael

Dear Dr. Voskuhl,

With the NIH grant suspensions to DGSOM, several Neurology faculty have lost grants that support their salary and trainee and staff salaries. There is also the loss of supplies and other support for research. This is a substantial negative effect for faculty and their research programs, and we understand that it will cause a great deal of uncertainty. We are meeting with the 24 faculty affected in the department. This email initiates this process, and to calendar a meeting with myself, Geoff White (CAO), Emilie Lucas (Director of Grants Administration) and Sonya Neely (Manager of Budget and Financial Planning). In anticipation of this meeting, please consider three areas or aspects:

1. Consider additional sources of funding or projects.
2. Consider having conversations with your Program Director regarding funding that might support you and your research program
3. Consider adding clinical work to support your salary deficit.

Thank you,

Tom

S. Thomas Carmichael, M.D., Ph.D.

Professor and Chair
Frances Stark Chair
Department of Neurology
Geffen School of Medicine at UCLA
