NEUROSCIENCES CONNECT:

HUMAN RESEARCH NEWSLETTER

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Department of Neurosciences
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Vice Chair of Human Clinical Research

Vice Chair of Human Clinical Research
Dr. Jennifer Graves

Department Chair
Dr. James Brewer

WELCOME from the Vice Chair of Human Clinical Research

I am excited to introduce the inaugural issue of the Department of Neurosciences Human Research Newsletter.

This quarterly publication is designed to keep you informed about the latest milestones, achievements, and developments in human clinical research within our department. We will spotlight key projects and discoveries from our Clinical Research Units and celebrate the accomplishments of our dedicated faculty and staff.

A primary goal of this newsletter is to promote ongoing research studies, aiding in participant recruitment and fostering engagement. To ensure this platform fully represents the depth and diversity of our department's work, I encourage you to share your publications, grant awards, clinical trials, upcoming conferences and any other notable achievements you wish to highlight.

We hope this newsletter becomes a valuable resource that fosters collaboration, enhances our collective knowledge, and supports the professional growth of our great community. Your contributions will be essential in making this initiative a success.

Sincerely,

Jennifer Graves, MD, PhD, MAS
Vice Chair of Human Clinical Research

In This Issue

Scan ME

Or email me at irubio@health.ucsd.edu to submit your valuable content for the next Newsletter

Event Spotlight

1st Neurosciences Human Research Day

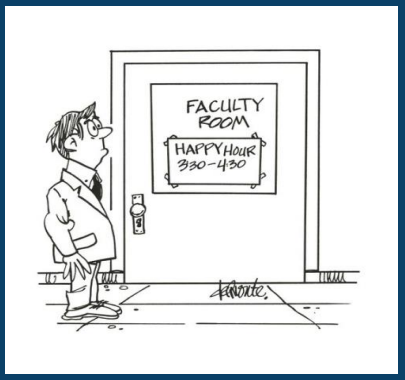
We are thrilled to invite you to the 1st Neurosciences Human Research Day, a significant milestone for the Department of Neuroscience. This event marks an exciting opportunity to celebrate our collective achievements, share groundbreaking research, and foster collaboration within our department.

Date: 06 September 2024
Time: 9:00 am – 2:00 pm
Location: ACTRI Auditorium

Register by emailing at Ileana Rubio at irubio@health.ucsd.edu or

Scant the QR code located at the bottom of this newsletter on page 12.

Welcome New Faculty!



We are thrilled to welcome several outstanding faculty members who have recently joined or will soon be joining our department. Each brings unique expertise that will greatly enhance our team and further our mission.

Ryan Cho – ADCS/Biostatistician
Megan Fitzhugh – Alzheimer's/Research
Ali Mahta – Neurocritical Care Specialist
Brittany Passiak – Child Neurology Specialist
Johannes Schlachetzki – Research/Neurodegenerative Diseases
Chelsea Zale – Neuromuscular Specialist
Hoameng Ung – Epilepsy/Research/Neurohospitalist
Victoria Wu – Neurohospitalist

We look forward to the valuable contributions each of these talented individuals will bring to our department.

Research Highlights: Publications

2024 Publications from PubMed Search Featuring Faculty and Staff from our Department

Scan ME

Characterizing Cognitive Profiles in Diverse Middle-Aged and Older Hispanics/Latinos: Study of Latinos-Investigation of Neurocognitive Aging (HCHS/SOL)

Lisa V Graves[1], Wassim Tarraf[2], **Kevin Gonzalez**[3], Mark W Bondi[4,5], Linda C Gallo[6], Carmen R Isasi[7], Martha Daviglus[8], Melissa Lamar[8,9], Donglin Zeng[10], Jianwen Cai[10], **Hector M González**[3]

A study in the SOL-INCA cohort identified five cognitive profiles among Hispanic/Latino adults, ranging from high cognitive performance to specific deficits in memory or executive function. These findings may help in understanding early cognitive changes related to Alzheimer's and other dementias in this population.

Pharmacokinetic and Pharmacodynamic Data from NEOLEV1 and NEOLEV2 Studies

Cynthia Sharpe[1,2], Derek Z Yang[3], **Richard H Haas**[2,4], **Gail E Reiner**[2], Lilly Lee[2], Edmund V Capparelli[3]; NEOLEV2 Investigators

A study on neonates with seizures showed that levetiracetam (LEV) has predictable pharmacokinetics at higher doses and significantly reduces seizure burden within 30 minutes. 28% of patients became seizure-free, and 25% had a 50% reduction in seizures, supporting further research on high-dose LEV in neonates.

Phase 2A-phase 2B randomized double-blind placebo-controlled trial to evaluate the safety and efficacy of benfotiamine in patients with early Alzheimer's disease (BenfoTeam).

Howard H Feldman 1 2 3, José A Luchsinger 4, **Gabriel C Léger** 1 2, Curtis Taylor 1 2, **Diane M Jacobs** 1 2 3, **David P Salmon** 1 2 3, Steven D Edland 1 2 3, **Karen Messer 1 2, Carolyn Revta** 1 2, Sarah A Flowers 5, Kerry S Jones 6, Albert Koulman 6, Kevin E Yarasheski 7, Philip B Verghese 7, Venky Venkatesh 7, Henrik Zetterberg 8 9 10 11 12 13, **January Durant** 1 2, **Jody-Lynn Lupo** 1 2, Gary E Gibson 14; ADCS BenfoTeam Study Group

The BenfoTeam trial investigates benfotiamine as a potential oral treatment for early Alzheimer's disease, assessing its safety, tolerability, and efficacy in a 406-participant, phase 2A-2B trial over 72 weeks. The trial aims to determine the optimal dose and long-term safety using adaptive design methods, including an adaptive dose decision rule, to optimize the treatment for early-stage AD.

Senescence marker p16INK4a expression in patients with multiple sclerosis

Jennifer H Yang[1], Annalise E Miner[2], Ashley Fair[3], Revere Kinkel[3], Jennifer S Graves[4]

A recent pilot study investigated the cellular senescence marker p16INK4a in multiple sclerosis (MS) patients compared to healthy controls. While higher p16INK4a levels were observed in MS patients over 50 compared to controls, the expression levels did not correlate with chronological age or MS disability outcomes. The study suggests caution in using p16INK4a as an aging biomarker in MS, highlighting the need for further research to understand its role in the disease.

Research Highlights: Publications

Scan ME

2024 Publications from PubMed Search Featuring Faculty and Staff from Our Department

Analysis of Evusheld Safety and Efficacy in Multiple Sclerosis Patients

Emilie N Liu[1], Marcos Real[2], **Jennifer H Yang**[3], **Ashley Fair**[2], Natalie Whitmire[2], Allyssa Perez[2], Carolyn Wilder[2], Shauna Rosengren[2], **Revere P Kinkel**[2], **Jennifer S Graves**[3]

A study at the UCSD MS Center evaluated Evusheld for COVID-19 prevention in MS patients on B-cell depleting therapies. It was well-tolerated among 48 patients receiving Evusheld and it showed a trend towards reduced infection rates, though not statistically significant. The study highlights the potential of Evusheld as a preventive tool, but also underscores the need for further research in this area to confirm its efficacy in MS patients.

Clinical Value of Alzheimer's Disease Biomarker Testing – IMPACT-AD BC

Khushbu J Patel[1], David Yang[1], John R Best[2], Colleen Chambers[1], Philip E Lee[3,4,5], Alexandre Henri-Bhargava[3,6], Clark R Funnell[3,4,5], Dean J Foti[3,4,5], Jacqueline A Pettersen[3,7], **Howard H Feldman**[8,9,10], Haakon B Nygaard[3,4,5], Ging-Yuek R Hsiung[3,4,5], Mari L DeMarco[1,11]

The IMPACT-AD BC study found that Alzheimer's biomarker testing influenced clinical management in 89.4% of cases, leading to reduced diagnostic procedures, optimized prescriptions, and increased referrals and counseling, ultimately improving care and reducing healthcare resource use. The study highlights the significant impact of AD biomarker testing on improving clinical care and reducing healthcare resource use, benefiting both patients and the healthcare system.

Effects of intensive lifestyle changes on the progression of mild cognitive impairment or early dementia due to Alzheimer's disease: a randomized, controlled clinical trial (HCHS/SOL)

Dean Ornish[1,2], Catherine Madison[3,4], Miia Kivipelto[5,6,7,8], Colleen Kemp[9], Charles E McCulloch[10], **Douglas Galasko**[11], Jon Artz[12,13], Dorene Rentz[14,15,16], Jue Lin[17], Kim Norman[18], Anne Ornish[3], Sarah Tranter[9], Nancy DeLamarter[3], Noel Wingers[3], Carra Richling[3], Rima Kaddurah-Daouk[19], Rob Knight[20], Daniel McDonald[21], Lucas Patel[22], Eric Verdin[23,24], Rudolph E Tanzi[14,25,26,27], Steven E Arnold[14,28]

A trial found that intensive lifestyle changes over 20 weeks significantly improved cognitive function and brain health in individuals with mild cognitive impairment or early Alzheimer's, compared to usual care. The intervention group showed better outcomes on key cognitive measures and positive changes in biomarkers and microbiome health.

Safety, Tolerability, and Pharmacokinetics of Antisense Oligonucleotide BIIB078 in

Leonard H van den Berg[1], Jeffrey D Rothstein[2], Pamela J Shaw[3], Suma Babu[4], Michael Benatar[5], Robert C Bucelli[6], Angela Genge[7], Jonathan D Glass[8], Orla Hardiman[9], Vincenzo Libri[10], Theodore Mobach[11], Björn Oskarsson[12], Gary L Pattee[13], **John Ravits**[14], Christopher E Shaw[15], Markus Weber[16], Lorne Zinman[17], Paymaan Jafar-Nejad[18], Frank Rigo[18], Luan Lin[19], Toby A Ferguson[19], Anthony L Gotter[19], Danielle Graham[19], Michael Monine[19], Jennifer Inra[19], Susie Sinks[19], Satish Eraly[19], Steve Garafalo[19], Stephanie Fradette[19]

This phase 1 study of BIIB078, targeting C9orf72 in ALS patients, showed target engagement, but led to increased neurofilament levels and faster clinical decline in high-dose groups, resulting in the drug's development being discontinued. The findings highlight important questions about the role of C9orf72 antisense transcripts and the potential risks of antisense oligonucleotide therapies in C9orf72-associated ALS.

Research Highlights: Other News

Approved treatment for SOD1-ALS and Abstract Presentation on Smith-Magenis Syndrome

Treatment Targeting SOD1-ALS

Biogen recently announced that the FDA has granted accelerated approval for QALSODY™ (tofersen), a treatment targeting SOD1-ALS, a rare form of amyotrophic lateral sclerosis (ALS). This approval is based on the drug's ability to reduce levels of neurofilament, a marker of neural injury, in these patients.

Dr. John Ravits, who served as the lead principal investigator, was instrumental in the early-stage clinical trials of QALSODY™ (tofersen), contributing significantly to the research that led to this important regulatory milestone.

The accelerated approval allows continued investigation of the drug's clinical benefits while making it accessible to patients with this specific genetic mutation.

Abstract Presentation

Diagnosing and Correcting Tethered Cord in Smith-Magenis Syndrome Significantly Improves Quality of Life

Gail Reiner, NP recently presented at the Research Symposium for Smith-Magenis Syndrome, held in Dallas, Texas, in July 2024. The event was sponsored by Baylor College of Medicine and PRISMS. Her presentation, titled "Diagnosing and Correcting Tethered Cord in Smith-Magenis Syndrome: Significant Improvements in Quality of Life," highlighted crucial advancements in treatment approaches for this condition.

Additionally, in August 2024, Gail was sponsored by the SMS Foundation, UK, to provide specialized consultations for patients affected by Smith-Magenis Syndrome in Matlock, England. Gail's contributions continue to make a meaningful impact in the field.

Clinical Research Studies: Open Clinical Trials

Now enrolling, referrals welcome!

- Dr. Aliya Frederick is seeking referrals for the **BHV3000-311**: Phase 3, multicenter, randomized, double-blind, group sequential, placebo-controlled study to assess efficacy and safety of rimegepant for the treatment of migraine in participants ages ≥ 6 to <18 years.
- For more information please contact Sophie Zacharek at szacharek@health.ucsd.edu

Inclusion Criteria

· Children and adolescents ages 12-17.
· Participant has been experiencing migraines for at least six months.
· Participant who experiences one-eight migraines a month.
· Children and adolescents weighing > 40 kg.

Exclusion Criteria

· Participant has a history of cluster headache or hemiplegic migraine headache.
· Participant has a continuous migraine (defined as an unrelenting headache) during within 1 month prior to Screening Visit.
· Participant has a confounding and clinically significant pain syndrome that may interfere with the participant's ability to participate in this study

- Congratulations to Dr. Taha Gholipour and the rest of the Epilepsy team for the activation of a new Phase III, **Biohaven 7000-302 RISE**, trial with a potential new anti-seizure drug. This trial provides another option for some drug-resistant patients.
- For more information please contact Natalia Menendez at nmenendez@health.ucsd.edu

Inclusion Criteria

· Age 18-75 and can provide accurate seizure diary (self/caretaker).
· BMI< 35, weight > 40Kg.
· Focal Epilepsy diagnosis > 1year.
· Focal Seizures with clinically observable signs and/or symptoms, impaired awareness and/or Focal to bilateral tonic-clonic seizures.
· Average of 4 or more observable focal seizures per month ASM.
· Current treatment with at least 1, up to 3 ASMs.
· Diet, device; prior surgery (>4 months prior) are considered epilepsy treatments in this trial, and are acceptable as 4th ASM. · ASMs must have a stable dose for 1 month .
· Past or present Felbamate, Vigabatrin, Ezogabin: additional criteria, but can be included.
· Medical marijuana and/or derivatives are allowed.

Clinical Research Studies: Open Clinical Trials (cont.)

Now enrolling, referrals welcome!

Exclusion Criteria

- Participation in any other investigational clinical trial at the same time.
- Non-focal seizures defined by ILAE criteria (e.g. Lennox-Gastaut, uncertain focal).

- Dr. Jennifer Graves is seeking referrals for the **CIELO** study - A Phase 3, randomized, double-blind, placebo-controlled, multicenter basket study to evaluate the efficacy of satralizumab in patients with NMDAR or LGI1 encephalitis. For more information or to refer study participants please contact:

- Adult subjects: Giselle Paez at g1paez@health.ucsd.edu
- Pediatric subjects: Sophie Zacharek at szacharek@health.ucsd.edu

Inclusion Criteria

- Reasonable exclusion of tumor or malignancy before baseline visit (randomization).
- Onset of autoimmune encephalitis (AIE) ≤ 9 months before randomization.
- Meet the definition of "new onset" or "incomplete responder" AIE.
- For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use adequate contraception during the treatment period and for at least 3 months after the final dose of satralizumab or Placebo.

Exclusion Criteria

- Any untreated teratoma or thymoma at baseline visit (randomization).
- Any previous treatment with anti-CD19 antibody, complement inhibitors, neonatal Fc receptor antagonists, anti-B-lymphocyte stimulator monoclonal antibody.
- Treatment with oral cyclopsphosphamide within 1 year prior to baseline treatment with any investigational drug (including bortezomib) within 24 weeks prior to screening.

AAVS-BDNF Phase 1 Study

- We are pleased to highlight a Phase I clinical trial lead by Dr. Gabriel Leger as Principal Investigator and sponsored by Dr. Mark Tuszynski. This is a Phase I study to assess the tolerability and preliminary efficacy of AAV2-BDNF in participants with mild Alzheimer's Disease Dementia (AD) and Mild Cognitive Impairment (MCI) due to Alzheimer's Disease.

- The study will attempt to determine whether BDNF administration reduces neuronal loss and rebuilds synapses in the brain of these participants.

- The first subject had surgery on August 20, 2024.

- Please contact Laura Linares lrlinares@health.ucsd.edu for more information or to refer study participants.

Upcoming Conferences:

Stay informed about neurology related conferences and other programs that may be of interest.

Gene Therapy Initiative - 1st Annual Symposium Association
September 19, 2024
Sanford Consortium, Duane Roth Auditorium
Registration is now open: UC San Diego Continuing Professional Development Continuing Education (cloud-cme.com)

149th Annual Meeting of the American Neurological Association
September 14-17, 2024
Orlando, Florida
myana.org

Glia and Neuroinflammation Research Rounds
September 26, 2024
Daneman Lab – UCSD

Presentation Schedule:
https://rb.gy/buptfy

Conferences (cont.):

Stay informed about neurology related conferences and other programs that may be of interest.

Child Neurology Society (CNS) Annual Meeting
November 11-14, 2024
San Diego, California
www.childneurologysociety.org

77th Annual Meeting of the American Academy of Neurology
April 5-9, 2025
San Diego, CA and Online
Registration for the 2025 Annual Meeting in San Diego and online will be available in the fall of 2024

Research Contacts:

Office of the Vice Chair of Human Clinical Research

General Inquiries: irubio@health.ucsd.edu
Tuesdays 9:00 am to 11:00 am - Zoom Meeting Link
Fridays 9:00 am to 11:00 am – in person/4w-217

UCSD Office of IRB Administration (OIA)

General Inquiries: IRB@ucsd.edu | 858-246-4777
Reliance Inquiries: IRBRely@ucsd.edu

Office of IRB Administration – Office Hours
https://ucsd.zoom.us/j/98732263319#success

Office for Human Research Protections (HHS)

OHRP offers this comprehensive training on human research protections based on the requirements of the revised Common Rule (or 2018 Requirements) HHS Human Research Training. A printable completion certificate is available at the conclusion of each lesson.