Quarterly news and updates from the
Stanford Alzheimer's Disease Research Center
and the Healthy Brain Aging Study

MIND MATTERS

2020 Winter Issue

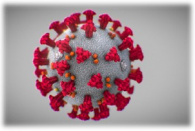
adrcstanford@stanford.edu

A·D·R·C for healthy brain aging

We hope this newsletter finds you and your loved ones safe and well as we approach the holiday season. As the end of the year approaches, everyone at the Alzheimer's Disease Research Center (ADRC) would like to express our deepest thanks and gratitude for your continued support, dedication, and participation in our research during this difficult time. We appreciate your willingness to accommodate our virtual and telephone visits.

Despite the constraints of COVID-19, we were delighted to have had the opportunity to virtually host our third annual Patient and Research Participant Appreciation Day on November 7th, 2020. We heard from our physicians, research scientists, and supportive care staff who highlighted foundational topics related to the understanding of the changes that the brain undergoes in aging, the latest developments in potential treatments and early detection techniques, learned practical exercise strategies, and about the various community and support groups that are offered free of cost here at Stanford through the Neuroscience Supportive Care Program. If you were unable to make the event, a link of the recording can be found below, along with links to the exercises and the supportive care programs. Please feel free to reach out to us at adrcstanford@stanford.edu for any questions regarding the event or the links attached. On behalf of everyone at the ADRC, we wish you all a safe and healthy holiday season and New Year! We look forward to seeing you again in 2021.

COVID-19 Survey and Resources



COVID-19 presents very new challenges for us all, and as a part of a national effort, we would like to learn about your experience and learn how COVID-19 affects memory and health. We will be contacting you either by phone or email to complete a brief COVID-19 survey for both you and your study partner.

As a research participant, you may decline to answer any or all of the questions. Please try your best to answer as many of the questions as you feel comfortable with. If you have any questions, please contact Christina Wyss-Coray, CWyssCoray@stanfordhealthcare.org or at (650) 721-2409.

For more information on our third annual Patient and Research Participant Appreciation Day please visit the following sites:

Link to recording of third annual Appreciation Day

Link to Neuroscience Supportive Care Program and slides

Link to Practical Exercise slides

Link to other exercises from NIH

Additional COVID-19 resources are listed here:

Stanford Medicine COVID-19 Updates

COVID-19 and Dementia: Imagining a Future with a Vaccine

Flu Vaccines a Link to Lower Risk of Dementia, Researchers Find

ADRC CORES

Clinical Core

Dr. Victor Henderson MD, MS
Core Leader

Dr. Kathleen Poston MD, MS
Associate Core Leader

Dr. Sharon Sha, MD, MS
Associate Core Leader

Dr. Maya Yutsis, PhD, ABPP-CN
Associate Core leader

The ADRC is composed of 7 different cores (Clinical, Biomarker, Biostatistics, Bioinformatics & Data Management; Imaging, Neuropathology, Outreach & Engagement) and one component (Research & Education) that work together to translate our research into further understanding the causes of neurodegenerative diseases and enabling early identification, effective treatment, and prevention. Each issue of our newsletter will highlight one core. This issue features the 'Clinical Core.' More details about each core can be found on our website: med.stanford.edu/adrc.html

The clinical core of the ADRC recruits and follows patients with early stage Alzheimer's disease, Parkinson's disease, and Lewy body disease; older volunteers with mild cognitive impairment; and healthy older controls without neurological disease or cognitive impairment. Composed of clinical research coordinators, neuropsychologists, and behavioral neurologists, the team coordinates and collects data from neurological and neuropsychological assessments, bran imaging, and genetic and molecular markers derived from blood, spinal fluid, skin fibroblasts, and stool which provide crucial information to the other cores of the ADRC. The clinical core is led by Dr. Victor Henderson and co-led by Dr. Kathleen Poston, Dr. Sharon Sha and Dr. Maya Yutsis. Other faculty and staff in the clinical core include: Dr. John Barry, neuropsychiatrist, Department of Psychiatry and Behavioral Sciences, Dr. Ami Bhatt, Assistant Professor of Medicine and Genetics, Department of Medicine-Hematology, Jennie Clark, gerontologist, Aging Adult Services, Dr. Allyson Rosen, neuropsychologist, Department of Psychiatry and Behavioral Sciences, Dr. Laurice Yang neurologist, Stanford ADRC and Department of Neurology, Dr. Veronica Santini, neurologist, Stanford ADRC and Department of Neurology, and Professor Hank Greely, Professor of Law.

Dr. Laurice Yang MD, MHA

Dr. Veronica Santini, MD

Dr. Allyson Rosen, PhD, ABPP-CN

Dr. Irina Skylar-Scott, MD

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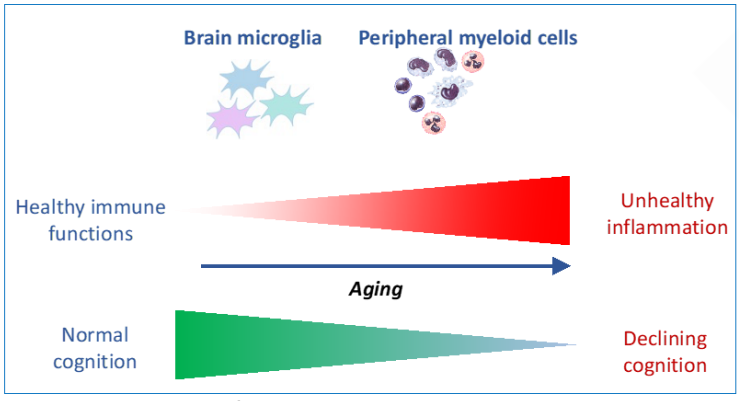
for healthy brain aging

ADRC FACULTY HIGHLIGHTS

Katrin Andreasson, MD
Professor of Neurology and Neurological Sciences
ADRC Associate Director

Dr. Andreasson is Professor in the Department of Neurology and Neurological Sciences and is a neurologist who treats patients with dementia and who is also engaged in basic research in neurodegenerative disorders. Dr. Andreasson received her M.D. degree at Columbia University College of Physicians & Surgeons, completed her residency in Neurology at Johns Hopkins School of Medicine, and carried out her postdoctoral training in the Johns Hopkins Department of Neuroscience, where she began her research studies on the function of brain inflammation in development of neurodegenerative disease.

The objectives of Dr. Andreasson's laboratory research are to identify specific inflammatory pathways that could be targeted therapeutically to prevent and treat neurodegenerative disorders such as Parkinson's disease and Alzheimer's disease. This conceptually new approach arises from increasing evidence that inflammation contributes to the development of many diseases of aging, in particular Alzheimer's disease. In addition, studies of human subjects at risk for Alzheimer's disease have identified a critical role for the myeloid branch of the immune system in increasing the risk of developing Alzheimer's disease. The myeloid branch of the immune system encompasses "first responder" cell types, like the peripheral monocytes and macrophages in the blood and the microglia that reside in the brain. Dr. Andreasson's research laboratory is seeking to understand how and why the myeloid branch of the immune system changes with age and is working to identify critical cellular pathways that drive these changes. Her laboratory is currently homing in on several key immune pathways that promote changes in immune health and function with aging that are linked to cognitive decline, and her laboratory is currently investigating ways to target these pathways to reduce inflammation and restore healthy cognition.



Additional Opportunities to Participate in Research

Studies directly supported by the ADRC

Healthy Brain Aging Study

Sponsor: National Institute of Health **Study status:** Open, enrollment ongoing
Research Coordinator: Christina Wyss-Coray CWyssCoray@stanfordhealthcare.org or 650-721-2409

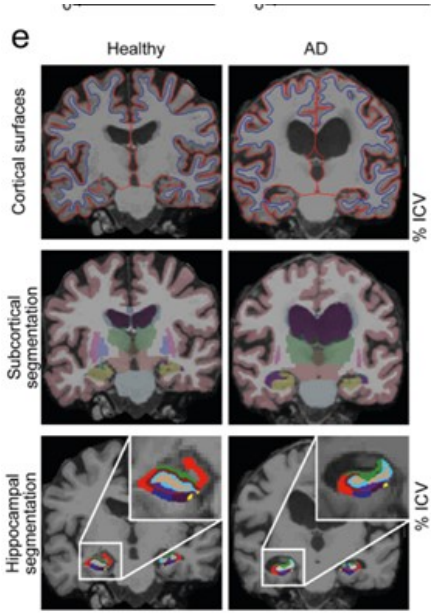
Pacific Udall Center

Sponsor: NIH/NINDS Morris K. Udall Center of Excellence for Parkinson's Disease Research **Study status:** Open, enrollment ongoing
Research coordinator: Maria-Lucia Campos udallcenter@stanford.edu or 650-721-5274

The ADRC supports internal research in the form of large research projects conducted over a five-year period and two-year developmental projects, with new developmental projects selected each year. The ADRC also supports research by other qualified investigators at Stanford and from other institutions. Center support takes various forms, including de-identified data (clinical, neuropsychological, neuroimaging, genetic, biospecimen, or neuropathological data), tissues and biospecimens, access to well-characterized ADRC participants who have agreed to be contacted, imaging expertise, and biostatistical expertise. Below are highlights from two studies recently published.

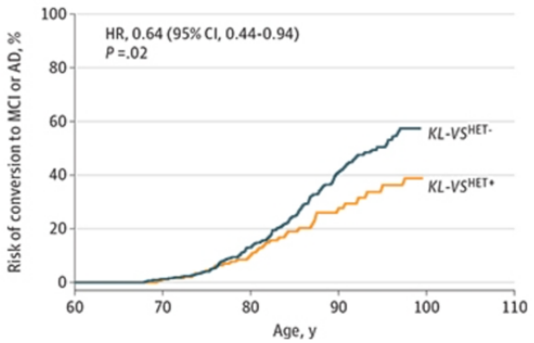
Research Highlights

Recent work by the Wyss-Coray Lab, an affiliate of the ADRC Biomarker Core, conducted a series of analyses on blood and spinal fluid collected through the ADRC to assess how the brain's adaptive immune response contributes to Alzheimer's disease. The results demonstrate antigen-specific clonal expansion of $CD8^+$ T cells in Alzheimer's disease and signify the need for greater understanding of the role of adaptive immunity in Alzheimer's disease.



Gate D, Saligrama N, Leventhal O, Yang AC, Unger MS, Middeldorp J, Chen K, Lehallier B, Channappa D, De Los Santos MB, McBride A, Pluvinage J, Elahi F, Tam GK, Kim Y, Greicius M, Wagner AD, Aigner L, Galasko DR, Davis MM, Wyss-Coray T. Clonally expanded CD8 T cells patrol the cerebrospinal fluid in Alzheimer's disease. *Nature.* 2020;577(7790):399-404. PubMed PMID: 31915375; PubMed Central PMCID PMC7445078.

Recent work from the Functional Imaging in Neuropsychiatric Disorders Lab, an affiliate of the ADRC Imaging Core, conducted a series of analyses with the aim of identifying genetic factors that interact with apolipoprotein e4 (APOE 4) allele. They found that the genotype KL is associated with decreased Alzheimer's disease risk and amyloid-beta burden, a protein in the brain associated with the development of Alzheimer's disease, in cognitively normal individuals aged 60-80 who are APOE 4 carriers. Their results suggest that this genotype should be considered with APOE 4 to refine Alzheimer's disease prediction models used in clinical trials and genetic counseling.



Klotho Protects. *Among older APOE4 carriers, klotho VS heterozygotes were 36 percent less likely to develop MCI or AD over three years. Protection seems to kick in around age 77.*

Belloy ME, Napolioni V, Han SS, Le Guen Y, Greicius MD. Association of Klotho-VS heterozygosity with risk of Alzheimer disease in individuals who carry ApoE4. *JAMA neurology*. 2020; 77(7):849-862. PubMed PMID: 32282020; PubMed Central PMCID: PMC7154955.