A large, vibrant green leaf is the central focus of the image, positioned in the foreground. In the background, a group of people is gathered outdoors, some standing and some sitting, in what appears to be a park or garden setting. The scene is brightly lit, suggesting a sunny day.

• FALL 2018

DIMENSIONS

The Magazine of the UW Alzheimer's Disease Research Center | UWADRC.ORG

- **Bringing a New Vision of Social Citizenship to the Cascadia Region**
- **Inventing a Blood Test for Alzheimer's & Parkinson's Diseases**
- **The Gut Microbiome and Brain Health**
- **"Ooh La La!" In the Garden with Ciscoe Morris**

Hello readers!

The UW ADRC and its associated clinical and educational programming at the UW Memory and Brain Wellness Center are pleased to bring you Dimensions for Fall 2018!

In these pages, you will learn about the surprising role of the gut microbiome in brain health, our center's brand new collaboration with social work researchers in Canada, efforts to invent a blood test for early detection of Alzheimer's disease, and some of the new people on our clinic and research teams. Our researchers provide dispatches from the summer's scientific conferences, including the 2018 Alzheimer's Association International Conference. Don't miss the reminder from Seattle celebrity Ciscoe Morris about the therapeutic potential of gardening, as well as the essays and poems by community members! Most importantly, we hope you hear an encouraging message about Alzheimer's disease and related conditions: persons living with memory loss and dementia have much to offer, strengths to work from, and wisdom to share.

We continue to be grateful for your interest and support of our work. The Ellison Foundation, the Richard M. and Maude Ferry Charitable Foundation, Paul V. Martinis Estate, the Anderson Foundation, and the Sky Valley Whirlwinds and other generous groups, make it possible for us to move faster in research and reach out further into the community than ever before. We're all in with you. Happy reading!



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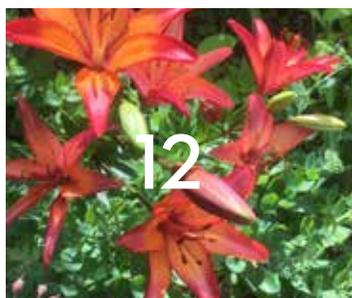
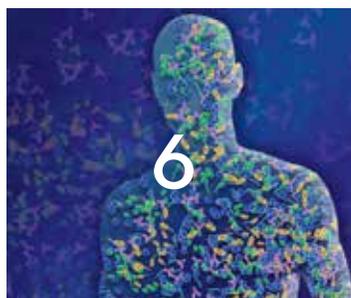
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DIMENSIONS The University of Washington Alzheimer’s Disease Research Center (UW ADRC) is affiliated with the UW Medicine Memory and Brain Wellness Center (MBWC) and the Veterans Affairs Puget Sound Health Care System (VA). The UW ADRC has been funded by the National Institute on Aging since 1985 to facilitate cutting-edge research on Alzheimer’s disease and other neurodegenerative conditions that cause dementia. The UW ADRC focuses on Alzheimer’s disease biomarker research and advancing prevention methods and clinical treatment for dementia, particularly through precision medicine. The UW ADRC is also supported by the Friends of Alzheimer’s Research, the Ellison Foundation, and members of the public.

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ADRC: uwadrc.org

MBWC: depts.washington.edu/mbwc

Facebook: facebook.com/UWMBWC

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RECENT PUBLICATIONS

Dementia Care and Resources

Involving People with Memory Loss in the Development of a Patient Handbook: A Strengths-Based Approach *Social Work, August 2018* // **Andy McCormick (retired), Marigrace Becker, Thomas J. Grabowski**

Over the past year, the MBWC clinic team developed a handbook, *Living With Memory Loss: A Basic Guide*, with guidance and contributions from people living with memory loss and their care partners, alongside university faculty and community partners. People with memory loss provided input in five areas: response to a new diagnosis, coping with memory loss and other symptoms of dementia, messages to other newly diagnosed people and health care professionals, available resources, and recommendations for the handbook design. Upon reflection, the team agreed that this unique development process reinforced a key message of the handbook: People with memory loss retain many personal strengths, which help them participate in life with a sense of belonging and purpose. The process also ensured that the handbook content and design would be relevant and valuable to its users. The handbook is now distributed as an education resource in the memory clinic and community programs. Download the full version and content in multiple languages at: depts.washington.edu/mbwc/resources/living-with-memory-loss

Genetics

Glia-Specific APOE Epigenetic Changes in the Alzheimer's Brain *Brain Research, August 2018* // **Jessica Tulloch, Lesley Leong, Zachary Thomson, Sunny Chen, Eun-Gyung Lee, C. Dirk Keene, Steven Millard, Chang En-Yu**

The gene APOE, also called apolipoprotein E, comes in three variants known as 2, 3, and 4. People who carry APOE4 have a higher risk of developing Alzheimer's disease after age 65: APOE4 is three times more common among people with later onset Alzheimer's patients than it is among the general population. However, a large portion of APOE4 carriers never develop Alzheimer's disease and therein lies the mystery that fascinates ADRC researchers: They think that additional 'epigenetic' factors must contribute to the power of APOE4 to increase risk of Alzheimer's disease in specific people.

Epigenetics refers to the mechanisms that switch our genes on and off, thus affecting their function in the body. Specifically, chemical changes, called methylation, control or modify how our genes work. In recent studies using post-mortem brain tissue samples, ADRC researchers found evidence of an epigenetic difference in methylation of the APOE gene in people with Alzheimer's, compared to people without these diseases. The teams specifically studied people who carried the 3 and 4 alleles of APOE. The work supports the overall idea that epigenetics plays an important pathological role in

APOE-related neurodegenerative disease risk. The researchers are interested in how a person's lifestyle or environmental exposures may lead to epigenetic changes in the APOE risk gene.

Neuronal Susceptibility to Beta-Amyloid Toxicity and Ischemic injury Involves Histone Deacetylase-2 Regulation of Endophilin-B1 *Brain Pathology, July 2018* // **David Wang, Chizuru Kinoshita, Yoshito Kinoshita, Bryce L. Sopher, Takuma Uo, Rona J. Lee, Joon Kyu Kim, Sean P. Murphy, C. Dirk Keene, Gwenn Garden, Rick Morrison**

At the ADRC, researchers use donated brain tissue and stem cell technology to study the biological processes contributing to Alzheimer's disease. This study focused on histone deacetylase 2 (HDAC2), an enzyme that plays an important role in the aging process. Recent studies in mouse models and human cases of Alzheimer's disease have shown that HDAC2 is abnormally elevated and harms epigenetic regulation in brain cells. ADRC researchers used patient tissue and stem cell technology to determine if high levels of HDAC2 may represent an age-related risk factor for the onset and progression of Alzheimer's disease. Their findings suggest that HDAC2 represses an important protein in the brain called Endo-B1, rendering neurons vulnerable to Alzheimer's disease. This project will provide new insights into the contribution of HDAC2-mediated epigenetic processes to Alzheimer's disease, with the ultimate aim of developing HDAC2 therapies that will delay the onset of Alzheimer's disease.

Precision Medicine Biomarkers

Cerebrospinal fluid a-synuclein contributes to the differential diagnosis of Alzheimer's disease *Alzheimer's and Dementia, August 2018* // **Min Shi, Lu Tang, Jon B. Toledo, Carmen Gingham, Hua Wang, Patrick Aro, Poul H. Jensen, Daniel Weintraub, David A. Wolk, Edward B. Lee, Leslie M. Shaw, John Q. Trojanowski, Jing Zhang**

Biomarkers are measures of what is happening inside the living body, shown by the results of laboratory and imaging tests. Biomarkers can help doctors and scientists diagnose diseases and health conditions, find health risks in a person, and see how a person's disease or health condition changes over time. In Alzheimer's disease research, reliable biomarkers are needed to characterize participants based on their underlying biology, enroll them in appropriate studies and trials, and monitor their response to a treatment over time. In general, the best biomarkers for Alzheimer's disease in living people are PET brain scans and cerebrospinal fluid (CSF) analysis for amyloid and tau proteins, which show 90% diagnostic accuracy.

However, cases of clinically diagnosed dementia often involve a mix of pathologies and vascular injury. This heterogeneity

limits researchers' ability to distinguish pure Alzheimer's disease from related disorders, using only CSF biomarkers for classic Alzheimer's proteins. In this study, a team of ADRC collaborators found the solution by using a CSF biomarker for the alpha synuclein protein, in combination for biomarkers for amyloid and tau proteins. Doing so, they were better able to tell the difference between people with pure Alzheimer's disease and those with other forms of neurodegenerative diseases, such as Lewy Body disease, frontotemporal lobe dementia, and mixed or vascular dementia. The researchers suggest that a panel of biomarkers for different pathologies will improve diagnosis and the success of clinical trials.

Neurology

Associations between recent and established ophthalmic conditions and risk of Alzheimer's disease *Alzheimer's and Dementia, August 2018* // **Cecilia S. Lee, Eric B. Larson, Laura E. Gibbons, Aaron Y. Lee, Susan M. McCurry, James D. Bowen, Wayne McCormick, Paul K. Crane**

ADRC researchers and collaborators in UW Medicine Department of Ophthalmology found that three eye diseases, including glaucoma, age-related macular degeneration, and diabetic retinopathy, are associated with an increased risk for Alzheimer's disease. In the large, longitudinal, population-based Adult Changes in Thought Study, people over 65 diagnosed with these eye conditions faced a 40 to 50 percent higher risk for Alzheimer's disease. Those with recent glaucoma had a 46 percent higher risk, and people with recent age-related macular degeneration or diabetic retinopathy had a 50 percent increased risk compared to those without these conditions. The researchers emphasize that not all people with those eye conditions will go on to develop Alzheimer's disease. Furthermore, the participants were all male and 90 percent self-identified as white, which can make the findings less relevant to other populations. The research team is planning further studies to better understand neurodegeneration in the eye and the brain and how it can lead to early diagnosis of Alzheimer's disease and better treatments.

New Grants

Reclaiming and Revitalizing ACT Study Neuroimaging Records (NIA) // **Christine Mac Donald, Paul K. Crane, Eric B. Larson**

The Adult Changes in Thought Study (ACT) is a long-running study of the aging brain and dementia risk in the general population. Since 1986, the UW/Kaiser Permanente Washington Health Research Institute study has followed over 5,000 people from the community age 65 and older, to identify the environmental, medical, lifestyle, and genetic factors that affect one's risk of brain disease and find ways to help communities delay or avoid dementia. Now, the team will retrieve over 2,000 clinical brain scans from ACT participants taken during life for medical reasons and process them for research. The investigators will also collect new research quality scans on people who already have a clinical scan,

economically obtaining a longitudinal imaging data set. The investigators will use this imaging resource to further scientific understanding of mechanisms underlying associations between anticholinergic medication use, high blood glucose levels, and Alzheimer's disease and will make clinical and research scans and data derived from them available to the research community.

A Systems Biology Approach in Drosophila to Identify Novel Factors that Influence Alzheimer's Disease Pathology (NIA RO1) // **Daniel Promislow, Leo Pallanck, John Tuthill**

The risk that a person develops late-onset Alzheimer's disease is influenced by a large number of genes, interacting in large, complex networks. To identify new pathways that cause Alzheimer's, and to better understand how and why these pathways affect AD risk, this study uses a naturally genetically variable population of fruit flies to study Alzheimer's. This project will identify genetic strains that are unusually resistant or sensitive to the toxic effects of proteins associated with Alzheimer's, and the researchers will use cutting edge technology to examine how molecular networks vary among these lines of flies. They will also study the biochemical, cellular, physiological, and behavioral consequences. Together, results from this study should lead to the discovery of novel causes and mechanisms of Alzheimer's risk.

Molecular Mechanisms of Alzheimer's Disease Neuropathological Endophenotypes (NIH K25 Career Development Award) // **Shubhabrata (Joey) Mukherjee**

Genome-wide association studies (GWAS) have so far identified about 20 genetic variants that seem to raise the risk of Alzheimer's disease dementia after age 65. Researchers are now working to go beyond that first step of gene discovery to understand of how a gene variant contributes to disease risk, and then use these variants as potential targets for therapeutics. This new grant will allow researchers to use a systems biology computational approach to identify—not individual genes—but a network of genes involved in Alzheimer's risk. His project will search for genes that have a lot of other connections, hinting that it serves a hub of a network. He will build on recent work showing that the DNA repair gene UBC is an organizing member of a network of genes involved in Alzheimer's risk, which may show decreased activity in people who eventually develop Alzheimer's disease. The hope is that a therapeutic could tweak the upstream or downstream action of the ubiquitin pathway.

Funding Opportunity!

Call for ADRC 2019-2020 Pilot Project Award Proposals: depts.washington.edu/mbwc/adrc/page/pilot-project-awards

The UW ADRC seeks proposals for one-year pilot projects that use its resources to advance the understanding, diagnosis, and/or treatment of Alzheimer's disease. The UW ADRC will fund at least two awards for junior researchers of up to \$30,000 each, and one award of up to \$75,000, which is also open to established researchers new to the ADRC. Deadlines are approaching.

The Gut Microbiome and Brain Health

Can we invite the right microbes into our gut to prevent Alzheimer's disease?

By Genevieve Wanucha

Bacteroides, *Bifidobacterium*, *Faecalibacterium*, *Ruminococcus* – these are the names of some of the 100 trillion bacteria who are living and working in your gut. These microscopic critters, collectively known as the microbiome, help our body to digest food, process nutrients, make vitamins B and K, and produce immune molecules that fight inflammation and heal wounds. The most impressive role of this busy workforce may be, surprisingly, in the brain.

While the digestive tract and the brain feel far apart in your body, they are actually connected via a 24/7 direct line of biochemical communication, set up by special nerve cells and immune pathways. It's called the gut-brain axis. Down in the gut, bacteria make neuroactive compounds, including 90% of our neurotransmitter serotonin, which regulate our emotions. In turn, the brain can send signals to the gastrointestinal system, for example, to stimulate or suppress digestion.

A healthy microbiome is a diverse microbiome. A rich community of varied species protects against one dominating and causing trouble in our gut and beyond. Shifts in the composition or function of the microbiome have been implicated in inflammatory bowel disease, autism, and blood cancers. Researchers are now discovering that a disrupted microbiome, in certain contexts, may contribute to Alzheimer's disease and related conditions that cause dementia.

"The role of the microbiome in health and disease is an exciting area at the forefront of science, but the field is in its infancy," says Dr. William Depaolo, a UW Medicine gastroenterologist and director of the UW Center for Microbiome Sciences & Therapeutics. "I think about the microbiome like a biologist thinks about the deep sea. We know there's something down there, and we finally have the technology to help us see who's actually there and how they are influencing our bodies and brains."

Advanced tools of 'multi-omics' technology allow researchers to identify species in the human gut and analyze the

bacterial genes and protein products that affect our brain health. Recently, NIH-funded research conducted at the Wisconsin Alzheimer's Disease Research Center examined the microbiomes of people with Alzheimer's disease. The team, led by Barbara Bendlin, PhD, and Frederico Rey, PhD, collected stool samples from participants and used genetic sequencing technology to identify the bacterial species present, and assess the microbial richness and diversity.

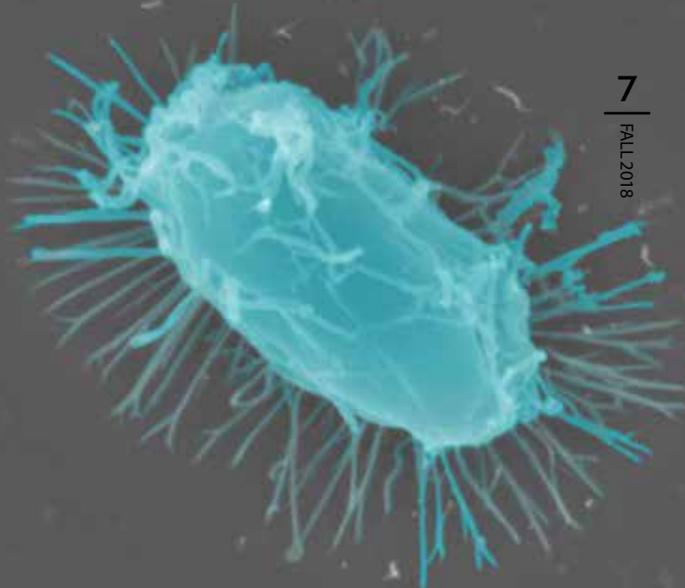
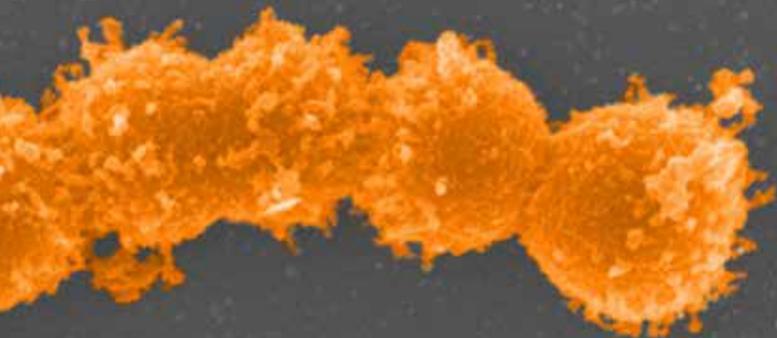
They found that people living with Alzheimer's disease have a unique, and less diverse, community of gut microorganisms than their healthy counterparts. Specifically, the microbiomes of people with Alzheimer's disease showed specific increases and decreases in common gut bacteria, especially decreases in *Bifidobacterium*, an important inhabitant of the healthy human gut. They also linked the abnormal levels of these microbe families to the amount of Alzheimer's disease proteins in the participants' spinal fluid.

The authors suggest that the unique microbiome of people with Alzheimer's disease could be contributing to the progression of their disease, through the gut-brain axis. Such findings in human and mouse models point to the tantalizing prospect that restoring healthy gut bacterial composition could prevent or slow the development of Alzheimer's in at-risk populations.

The microbiome field is optimistic about this therapeutic approach. "We know that diet can profoundly affect the microbiome," says Dr. Depaolo, whose UW lab studies the influence of the microbiome on health and many diseases.

"We know that bacterial cells are more sensitive to drugs than human cells, so we can target them without hitting human cells. So, there is a lot of excitement here in using multi-omics technology to identify microorganisms that we could promote in specific people or find strategies to manipulate the microbiome."

But, as with all quests to create precise, targeted therapeutics for Alzheimer's disease, it all comes down to genetics.



It's in the Genes

The composition of every person's microbiome is unique as a fingerprint, shaped by early life, diet, and environmental exposures over time. But it is our genetic background that influences how bacteria actually function in the human gut. What's more, bacteria themselves express different genes and make proteins that may predispose certain individuals to gut inflammation or other conditions.

In one striking example, recent NIH-funded research conducted by researchers in the NeuroGenetics Research Consortium suggested that *Corynebacterium* helps cause Parkinson's disease, but only in people with a specific genotype.

The study focused on the gene SNCA rs356219, a known genetic risk factor for Parkinson's disease. However, it's not strong enough to cause the disease by itself. Scientists have long suspected a trigger. In the study led by Zachary Wallen, PhD, and Haydeh Payami, PhD, of the University of Alabama, researchers took blood samples from 197 middle-aged patients with Parkinson's disease and 115 age-matched controls and determined the "genotype," or version, of SNCA rs356219. (Human beings have one of three genotypes of SNCA rs356219: AA, GA, or GG.)

They also extracted DNA from stool samples to see what bacteria were in their guts and then looked for interactions between the SNCA rs356219 genotype, gut microbiome, and Parkinson's disease risk.

The team found that *Corynebacterium* was most abundant in people with the GG genotype. Every person who had the GG genotype and *Corynebacterium* in the gut also had Parkinson's disease. Could there be something about the GG genotype that affects or jumpstarts this bacterium's production of disease proteins in the gut?, the researchers ask.

“ I think about the microbiome like a biologist thinks about the deep sea: We know there's something down there, and we finally have the technology to help us see who's actually there and how they are influencing our bodies and brains. ”

Corynebacterium is a common bacterium on human skin, and researchers don't know how it enters the gut, why some people have more than others, or if it could be a target for an antibiotic. The findings were presented at the 142nd Annual Meeting of the American Neurological Association.

While this study needs to be replicated in a larger population, the findings show how important it will be to consider a patient's genetic factors in microbiome research. "The issue of genetic influence cannot be ignored in this field," says Dr. Depaolo. "We don't yet know how genetics influence the microbiome, or how genes in bacteria are regulated. Before we start giving bacteria, antibiotics, or fecal transplants to people, we need to address the very basic question of how

different genetic backgrounds affect the microbiome."

CONTINUED ON PAGE 15:

What about Probiotics?



New Faces at the UW Memory and Brain Wellness Center/ADRC



Lee Burnside, MD, MBA, a geriatrician at UW Medicine, has joined the clinic team at the UW Memory and Brain Wellness Center. Lee has a research interest in evaluating the value of art for people living with dementia, such as *Here: Now*, an art museum engagement program at Seattle’s Frye Art Museum. He is now involved in a collaboration with researchers at the University of British Columbia to promote the social citizenship of people living with memory loss and dementia, and their care partners, by improving community support and social opportunities (Pg. 16). In his free time, Lee enjoys building ukuleles and playing ukulele and guitar and spending time with his dogs.



Robin Stillwell, MS, has joined the ADRC Outreach, Recruitment, and Education Core for a 6-month program consultation position. She will help to develop a metrics and tracking system to improve the effectiveness of the ADRC’s efforts in community outreach and engagement, and research education. She previously completed an internship at the ADRC as a UW graduate student in Health Informatics and Health Information Management. Robin, born and raised in Seattle, has a passion for urban adventures, such as city bike rides with her friends.



Alisa Tirado Strayer is the new Master’s of Social Work Practicum Student for the UW Memory and Brain Wellness Center. She comes with a passion and commitment to reducing stigma toward persons with dementia, and will be spearheading a pilot of the Dementia Friends public awareness and stigma reduction campaign on behalf of the WA State Dementia Action Collaborative (Pg. 9). She has worked in many roles in community mental health organization, ranging from intake coordinator at a children’s mental health clinic to leading an afterschool program for children with autism. This past year, she worked as a MSW Practicum Student with Generations Aging with Pride and researcher Karen Fredriksen-Goldsen to improve the services provided to LGBTQ elders. Alisa has since returned to school at the UW to earn a master’s degree in Social Work and Public Health with a focus on aging. She enjoys painting children’s book illustrations and playing with her nephew.

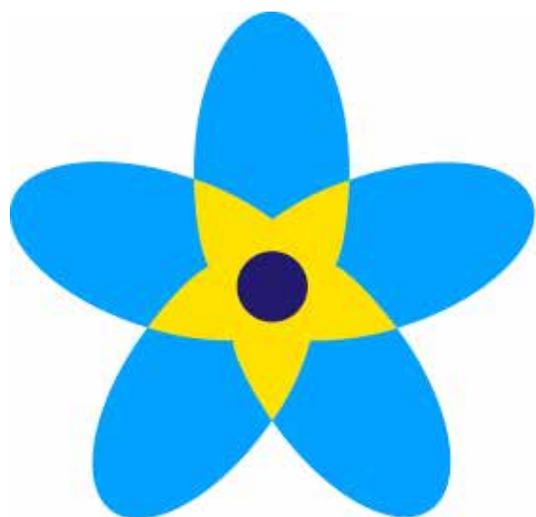


Deepa Subramaniyan is a new research coordinator at the UW Alzheimer’s Disease Research Center. In the Clinical Core, she is mainly responsible for quality control of data generated through the longitudinal study and processing of biological study samples. Deepa will learn the nuances of neuropsychological testing by observing sessions. She recently worked as study coordinator with Dr. Angela Hanson on the Meal and Memory study on the relationship between diet and cognition, screening and consenting volunteers, and seeing them through entire visits. In the long run, she hopes to take on a more regulatory oriented role in IRB communication, study start up, and consent drafting. In her free time, Deepa enjoys drawing with charcoal and creating amateur Tanjore paintings, a form of wood panel painting from India that involves stone work and inlaid gold leaves. She likes to read travel journals and hear peoples’ stories of adventures in less traveled countries.

The Dementia Friends Initiative Comes to Washington State!

By Alisa Tirado Strayer

The UW Memory & Brain Wellness Center is working with its partners in the Washington State Dementia Action Collaborative to implement a public awareness program called Dementia Friends. Dementia Friends is an anti-stigma campaign focusing on dementia and working to remove the stigma that people and their care partners face as they receive a diagnosis and symptoms progress. This program originated in Japan, moved to the UK, and about five years ago came to the U.S. Dementia Friends trains individuals on how to give a 90-minute educational talk to their community about what is dementia and how to help their neighbors, friends, and family members with dementia. The people who attend those talks become Dementia Friends. Those Dementia Friends commit to a self-selected action that they believe will make their community more inclusive for people with dementia, whether through visiting a neighbor with dementia or through having more patience when talking to a family member with dementia.



Dementia Friends

An Alzheimer's Society initiative

As a first step to implement this program in Washington State, we are performing a program evaluation to make sure this program is useful to people here. While a few trainings will take place in King County, we plan to especially focus on the Yakima region. We would like to discover how effective the program is in more rural areas, and among populations disproportionately impacted by dementia such as people of color. This evaluation will take about a year, and if the program appears to be effective at reducing stigma around dementia, we are then hoping to spread the program more broadly across Washington State. Can't wait that long? You can become a Dementia Friend now by going to dementiafriendsusa.org and taking a short online training!

Launching Dementia Friends is one strategy for accomplishing Recommendation 1.B.1 of the Washington State Plan to Address Alzheimer's and Other Dementias, to be implemented by the Dementia Action Collaborative: "Promote positive images and messages of persons with dementia and their caregivers to combat stigma and increase societal acceptance and integration." We believe that by countering stigma, we'll enable people to freely seek a diagnosis and reach out for support. We're excited to explore the impact of Dementia Friends in our state!

If you would like to learn more about Dementia Friends in Washington State, or if you are interested in becoming a Dementia Friends trainer, please contact Alisa Tirado Strayer at straya2@uw.edu.

About the Dementia Action Collaborative

The Dementia Action Collaborative is a voluntary public-private partnership working to implement the Washington State Plan to Address Alzheimer's and Other Dementias. Approved by the state legislature in 2016, the plan includes over 100 recommendations that will better prepare Washington State to serve the growing number of individuals living with dementia and their loved ones. Goals include raising awareness, ensuring early and accurate diagnosis and treatment, and improving supports and services for families.

The Freshest Data on Diet and Cognition

Dispatches from a Summer of Scientific Conferences

By Angela Hanson, MD



I'm a research scientist who studies the effects of different diets on brain metabolism and brain health, and I was lucky enough to attend three science conferences this year. It was thrilling to be surrounded by people from all over the world who come together to share their findings and their passion for science and for understanding – and treating – many of our toughest diseases. Here are a few of my favorite findings related to diet and cognition:

1) Watch out for alligators and lower that blood pressure!

At the American Geriatrics Society meeting in Orlando, Florida in May, I learned from experts in the field about blood pressure and aging. Everyone agrees that high blood pressure, or hypertension, increases the risk of stroke and Alzheimer's disease, but not all the experts agree about what the ideal blood pressure is in older adults who are at higher risk of falling and dehydration. Dr. Jeff Williamson, MD, MHS, of Wake Forest University reported that even in older adults, targeting a systolic blood pressure to <130 is a good idea to lower the risk of heart disease, stroke, and even dementia. He is one of the authors of the SPRINT MIND trial, which recently showed that decreasing blood pressure to an even lower goal of 120 mmHg, as compared to a target of less than 140 mmHg, may reduce the risk of mild cognitive impairment and dementia.

During the same lecture, Dr. Daniel Forman, MD, of University of Pittsburg cautioned us to be careful with high blood pressure medications because they all have side effects. One sure way to lower your blood pressure safely is through diet. The MIND diet is a combination of the DASH diet (Dietary Approaches to Stop Hypertension) and the Mediterranean diet developed by doctors at Rush University. This diet emphasizes ten specific food groups: chicken, fish, green leafy vegetables, other vegetables, berries, nuts, olive oil, wine (in moderation), beans, and whole grains. To benefit from the Mediterranean diet, the researchers recommend avoiding foods such as cheese, butter, and margarine, pastries and sugary foods, red meat, and fried food. Of course, I saw that last list of foods frequently at the Magic Kingdom – including cupcakes that were decorated like Mickey and Minnie Mouse. But, I did find some healthy and super tasty fish dishes at the Polynesian Village. Bottom line: if you have high blood pressure, which is defined as a systolic blood pressure 130 or greater, or a diastolic at 80 or greater, talk to your health care provider about all of the ways you can lower it, including diet and exercise.



“Don't eat too many of these.” - Dr. Angela Hanson

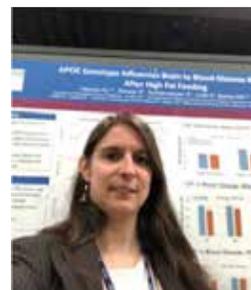
2) Measure all the things!

My next conference was the International Conference of the Metabolomics Society right here in Seattle in June. These types of -omics studies seek to measure hundreds or even thousands of molecules in a biological sample, instead of just one or two at a time. Metabolomics involves measuring all of the 'metabolites' in a sample – like sugars or amino acids. These strategies allow us to understand what pathways are affected by a disease – and might suggest therapeutic strategies. At this meeting, Dr. Rima Kaddurah-Daouk, PhD, of Duke University presented some interesting work titled “Gut- Liver-Brain Axis in Alzheimer Disease.”

Bile acids are breakdown products of cholesterol produced by the liver and are further broken down by the bacteria in our gut, called the microbiome. These bile acids can transport into the brain and may play important signaling roles. The researchers found different types of bile acids in the blood and brain tissue of patients who had died of Alzheimer disease, compared to non-Alzheimer controls. This suggests that gut bacteria may play a role in Alzheimer's disease pathogenesis, and many people are trying to identify the optimal types of gut bacteria for our microbiome. Until we have specific answers from these studies, it seems reasonable to make sure we get enough fiber in our diet, consider eating yogurt with active cultures, and talk to our doctor about probiotics if we need to be on antibiotics for an infection (See Pg. 15).

3) Eat More Salad!

Chicago might have the best pizza but we should probably avoid it and eat the leafy green vegetables! The last meeting I attended this year was the Alzheimer's Association International Conference (AAIC) in July. Scientists from Rush University in Chicago presented a lot of fascinating work related to Alzheimer's disease. One example was a longitudinal study that showed people who ate more leafy green vegetables had better cognitive performance over time. The group who ate a least 1.3 servings a day (9 servings a week) of these vegetables scored better on cognitive tests, and "the rate of cognitive decline among those who consumed the most to those who consumed the least was equivalent to being 11 years younger cognitively." Leafy green vegetables included spinach, lettuce salad, kale, collards and other greens. These data only prove a correlation, but the researchers controlled for a lot of other factors and still found the effect. When I explained these findings to my mother and told her that I still really wanted to try a Chicago style pizza, she replied with a text, "order a salad as an appetizer." Moms know best!



Dr. Angela Hanson, MD

ADRC OUTREACH SPOTLIGHT

The ADRC Outreach Recruitment & Education Core team has joined our collaborator, WSU's Partnerships for Native Health (P4NH), to support a new community partnership with the Yakima Nation Area Agency on Aging. During the annual Elder's Luncheon in May, we conducted a community-based assessment of the health needs of Native elders, mostly residing in eastern Washington. Community guidance is a key feature of this partnership, and our assessment of community needs will give agency leaders a snapshot of cognitive health in their service area. The results will enable them to plan strategies for health services and outreach for their elderly patients. We will organize the results of this work to inform a community action plan for tribal leaders. Our team also distributed informational materials about memory loss and Alzheimer's research, and we enjoyed hearing stories and having conversations with many of the elders. For more information about this needs assessment, or to find out how your community can participate in similar efforts, please contact Meghan Jernigan, MPH, at meghan.jernigan@wsu.edu. Meghan is a staff scientist at Partnerships for Native Health and project leader in the UW ADRC Satellite Core.



Meghan Jernigan, MPH

The P4NH group also attended the National Indian Council on Aging (NICOA) Conference, where Meghan Jernigan gave the keynote address about Alzheimer's disease in front of hundreds of American Indian/Alaska Native elders.

Read more about Meghan Jernigan's ADRC project at: depts.washington.edu/mbwc/news/article/Opening-Dialogues



“Ooh La La!” Momentia in the Garden with Seattle Legend, Ciscoe Morris

The **Garden Discovery Walks**, a dementia-friendly program offered in a partnership between Seattle Parks and Recreation and the UW Memory and Brain Wellness Center, had an exciting summer of garden experiences. Without a doubt, the highlight was the visit to the home garden of Ciscoe and Mary Morris, horticultural experts in Seattle! Ciscoe is a TV personality and Seattle Times garden columnist and podcaster who has long delighted the entire country with his sense of enthusiasm and passion for plants. It was time to bring an example of Momentia -the local grassroots movement to promote inclusion of people living with memory loss into his orbit.

Ciscoe and Mary’s garden includes a backyard collection of rare and unusual plants (including the world’s largest Azara tree), a colorful veggie patch, and sidewalk botanical display of pollinator plants. Even in the driest of Seattle summer days, the Morris’ garden encircles a velvety emerald cushion of grass, blemished only by a small mound of dirt, thanks to their new puppy.

“Having Ciscoe with his humor, positive energy, and warmth is a nourishing addition to our program,” says Laura Rumpf, a certified horticultural therapist and co-facilitator of the Garden Discovery Walks. “Participants experienced joy in the moment, despite their ongoing challenges. This shared camaraderie and lively conversation produced an air of social inclusion, mitigating the isolation and loneliness that one living with dementia might experience.”

Ciscoe embraced the objectives of the dementia-friendly Garden Walks. He resonates with the therapeutic potential of being in a garden that asks nothing in return except our attention to the present moment. He shared that being in the garden helped enhance the life and spirit of a family member experiencing memory loss.

“Being in the garden, all the weight just lifts off of you, no matter what else is happening,” Ciscoe said.

Ciscoe fascinated the group by sharing some gardening secrets. For example, they use hand watering as a means of interaction with the garden, regular maintenance, and testing species for adaptability to our climate. They plant all usable space, understanding microclimates and sunlight levels around their corner property, and include tender tropical and drought-tolerant cactus in their driveway.

We thank Ciscoe and Mary for welcoming us into their home garden, and for becoming champions of the grassroots dementia-friendly movement growing in Washington State!

“What a treat!” said one participant. “Can we come back next time?” •

Garden Discovery Walks

Spring 2019

Savor the season and explore nature with others living with memory loss and family and friends

First Fridays

**3/1, 4/5, 5/3,
10 a.m.-12 p.m.**



Enjoy a walk through a Seattle public garden, followed by a creative, nature-inspired project led by registered horticulture therapist Laura Rumpf. Light refreshments provided, bring a bag lunch (optional). Our short walks are at an easy strolling pace, usually with places to rest along the way.

Walks limited to 15 participants. Locations vary by month

Pre-registration required:

Cayce Cheairs, (206) 615-0100, cayce.cheairs@seattle.gov

*Offered in
partnership:*



**Seattle
Parks & Recreation**

healthy people healthy environment strong communities

UW Medicine
MEMORY & BRAIN
WELLNESS CENTER

How About Probiotics?

While we can't change our genes, we can modify our exposures and diet to nurture our microbiome as we age. General consensus holds that consuming fermented foods has some benefit to gut health, especially for those on anti-biotic medications. These are foods full of healthy 'probiotic' bacteria, such as yogurt, kefir, kombucha, sauerkraut, and kimchi. Common foods that feed and support our healthy gut bacteria include garlic, onions, Jerusalem artichoke, leeks, asparagus, bananas, barley, oats, apples, cocoa, wheat bran, burdock root, and flaxseeds, to name a few.

"To get your microbiome into the best composition you can, I think it's reasonable to make sure to get enough fiber in your diet," says Dr. Angela Hanson, MD, research scientist and geriatrician at UW Medicine Memory and Brain Wellness Center. "Consider eating yogurt with active cultures and talking to your doctor about probiotic supplements if you need to be on antibiotics for an infection."

There's a whole list of questions to answer before diet advice can get more specific than yogurt and kale: How does diet impact the microbiome long-term? How long does it take to permanently alter the gut microbiome? Can friendly bacteria in fermented foods actually establish long-lasting colonies in the gut? There has been a lack of human studies on the long-term health effects of fermented foods or probiotic supplements, which do not have FDA approval.

That said, consuming healthy bacteria has real health effects. "Probiotics do stimulate immune and epithelial cells and produce anti-inflammatory short-chain fatty acids in the intestines, which can help keep gut inflammation from getting out of control," says Dr. Depaolo. "But, taking just any probiotic won't replace a community of *Lactobacillus* after you've lost it. You would have to take a probiotic suited to you."

Individualized probiotics for brain health don't yet exist, but the microbiome is beginning to enter into Alzheimer's disease research, mainly through the NIH Alzheimer Disease Metabolomics Consortium. Additionally, NIH Alzheimer's Disease Research Centers around the country are collecting microbiome samples of study participants, in support of efforts to finally map the microbiome-brain communication axis in people with Alzheimer's disease.

For now, let's keep in mind that our microbiome has kept us alive all of these years – and that team of 100 trillion will need a little more help as it gets older. •

Bringing a New Vision of Social Citizenship to the Cascadia Region

Eyeing the day that a high-speed bullet train connects Seattle to Vancouver, a group of researchers are seizing the opportunity to foster more collaboration in the Cascadia region. Citizens Across Borders, a newly launched partnership between the University of British Columbia, Vancouver (UBC) and the UW Memory and Brain Wellness Center, aims to support the social citizenship of people living with memory loss and dementia.

Social citizenship, a concept defined by researchers in the UBC Centre for Research on Personhood in Dementia, means a relationship, practice, or status in which the person with dementia is entitled to experience freedom from discrimination, and to have opportunities to grow and participate in life to the fullest extent possible, with a sense of purpose and belonging.

The UW-UBC collaboration will bring people together to learn from each other about creating sustainable dementia-friendly communities, which are perhaps the fullest expression of social citizenship.

A major goal is for the Vancouver team to learn more about Momentia (momentiaseattle.org), a local grassroots movement spreading from Seattle across Washington State to foster dementia-friendly communities and opportunities, such as walking groups, Alzheimer's cafes, drum circles, painting classes, improv theatre, and nature engagement programs, made possible by a coalition of community partners and residents.

"The team at the Memory and Brain Wellness Center is excited to dive into this work with our new partners in Vancouver to bring a wider vision of social citizenship for people living with dementia to the Cascadia region," says Lee Burnside, MD, clinician and palliative care expert at the MBWC.

The first seeds of this collaboration were planted at the 2017 International Research Conference on Arts and Dementia in London, when Dr. Burnside met UBC researchers Alison Phinney and Gloria Puurveen. They all had deep research interests in arts-based methods to improve quality of experience for people living with dementia. "I remember us laughing about how you have to go halfway around the world to meet your neighbor who is working on the same thing!" says Alison Phinney, PhD, RN, Professor in the UBC School of Nursing.

Now funded by grants from the UBC and Canadian Institutes of Health Research, the team is currently traveling between cities to hold meetings and presentations. The topics include

innovations that will enhance social citizenship, such as the engagement of people with dementia in planning community initiatives; and the use of art as a way for someone to express their desires and leave a legacy at the end of life. Drs. Phinney, Puurveen, and Burnside bring insights gained from their research focused in these spaces. They will guide the kinds of questions asked, for example, on how best to learn from people with memory loss about what 'dementia-friendly' means to them.

"We will leverage off of each other in understanding what works and what doesn't in the context of community-based programs and experiences for people living with dementia and their care partners," says Gloria Puurveen, PhD, post-doctoral research and teaching fellow at the UBC School of Nursing and School of Social Work. "We are working on the ground level, trying to understand, in the context of this proliferation of dementia-friendly communities, what do those look like? How are they realized and lived?"

The researchers have heard from several community groups in Canada who are keen on hearing from different communities about how they can keep these kinds of memory loss programs afloat and create more.

"The power of grassroots initiatives looks different in the U.S. than in Canada," says Dr. Phinney. "There are pockets dementia-friendly initiatives here in Canada, but it's not as developed as what's happening in Seattle. I think we can learn about how American communities organize themselves to get these things going, especially in a sustainable way."

Citizens Across Borders will compare the cities of Seattle and Vancouver, especially in terms of the governmental and non-governmental resources and support for dementia and community projects, to better inform future work.

In a separate project, Carolyn Parsey, PhD, UW MBWC neuropsychologist is also working with the UBC researchers to explore the use of virtual reality (VR) technology to aid people living with dementia. Anecdotal evidence suggests the potential of VR for reducing depression and anxiety and increasing in social interaction and a sense of control in their environment. They will first conduct focus groups of people in the community and care homes to understand the feelings and interest around this technology.

This team many not be totally sure of where their paths will lead, but they certainly aren't waiting for the train to get started! • -Genevieve Wanucha



Starting Your Own Dementia-Friendly Social Engagement Program: Walking Groups and Alzheimer's Cafés

"It's the best thing I do each week. It has been interesting to watch how some of the walkers develop new friendships and come together to help one another. I think it is the fresh air, seeing different animals, being together where they are safe and the laughter we always seem to find."
-Sandy, a Memory Loss Zoo Walk volunteer.

By Marigrace Becker

We're pleased to be working with our colleagues in the Washington State Dementia Action Collaborative to help people with dementia and their families stay connected to their communities. Earlier this year, the DAC offered free webinars and written guides on how to start two popular dementia-friendly social engagement programs: Alzheimer's Cafés and Dementia-Friendly Walking Groups. And another round of these webinars are slated for the Fall!

Alzheimer's Cafés, or Memory Cafés, are monthly social gatherings for people with dementia and their loved ones that take place in welcoming public settings like coffee shops, libraries or senior centers. Developed in the Netherlands in 1997, this model came to Washington State in 2010 when Greenwood Senior Center launched the second Alzheimer's Café in the nation. Now, over 20 Alzheimer's Cafés meet monthly throughout the state. The growing list of locations can be found at: alzcafes.org and memory-cafedirectory.com

Dementia-Friendly Walking Groups are a newer program model that offers relationship-building, fresh air and light exercise through the pleasure of walking together. Seattle Parks and Recreation's Dementia-Friendly Recreation programs include an "Out & About" walk every other Friday, and a monthly Garden Discovery Walk in partnership with the UW Memory & Brain Wellness Center. Meanwhile, the Alzheimer's Association spearheads weekly walks at Woodland Park Zoo and Point Defiance Zoo. Snohomish Senior Center and Lacey Senior Center have also recently debuted dementia-friendly walking groups.

While fairly easy to implement, the impact of social engagement programs like these can be enormous for those living with dementia and their loved ones. An Alzheimer's Café attendee quoted in the how-to guide states: "Real friendship has resulted from these dinner table conversations." A walking group participant agrees: "This is where we find our support for this journey, with our new tribe."



Want to learn more about bringing these models to your community?

How-To Guides: Download from the Dementia Action Collaborative

Website: dshs.wa.gov/altsa/dementia-action-collaborative



Webinar: "The Alzheimer's Café Model: A Guide to Getting Started in Your Community"

10 – 11:30 a.m. Tuesday, October 23. This webinar, for anyone interested in starting an Alzheimer's Café, covers the basic steps including assessing interest, establishing partners, locating a venue, marketing your program and more.

Register: tinyurl.com/AlzCafeWebinar



Webinar: "Organizing Dementia-Friendly Programs: Overcoming Obstacles."

10 – 11 a.m. Thursday, November 8. This webinar, geared toward people or organizations who have already attempted to start an Alzheimer's Café or Dementia-Friendly Walking Group, provides solutions to common challenges including finding funding and getting the word out.

Register: tinyurl.com/DFProgramsWebinar

Hot off the Press: Highlights of the Alzheimer's Association International Conference AAIC 2018

By Briana Lee

Last month, the Alzheimer's Association International Conference (AAIC) took place in Chicago, Illinois, being the largest AAIC in history! As senior undergraduate working under the mentorship of Dr. Tara Madhyastha, PhD, at the UW Integrated Brain Imaging Center, I found this week-long conference to be an intense and inspiring experience. It seems the field is both growing and focusing on many emerging topics, such as the immune system, as well as classic Alzheimer's research topics like cognition and amyloid pathology. I presented my own project on the use of neuroimaging for early Alzheimer's disease detection. It's truly an exciting time to be a part of this effort and while the Alzheimer's disease research field has had many challenges and failures, the collective efforts of all these dedicated researchers makes me optimistic for the future.

Increasing Opportunity

Alzheimer's disease is currently the 6th leading cause of death in America and this number is expected to increase with our aging population. For this reason, research to understand and treat the condition has only increased as well. To support these efforts, the National Institute of Aging (NIA) at the National Institute of Health (NIH) plans to increase funding to Alzheimer's disease research and related projects three-fold, funding up to 25% of new/early-stage projects for the next fiscal year. According to Dr. Richard Hodes, director of the NIA, the field of Alzheimer's research is moving toward a more collaborative and "open science" environment. As a major force in promoting this movement, the NIA plans to continue its support of a more open-source/open-data research community so that with the collection and analysis of vast amounts of data, research progress will continue to accelerate.

Early Effects of Amyloid

Amyloid, a hallmark protein of Alzheimer's disease, can build up in the brain for 10 to 20 years before reaching disease-state levels. A major question in the Alzheimer's field surrounds the point at which individuals begin to manifest clinical symptoms. This issue is the focus of the Dallas Lifespan Brain Study, led by Dr. Denise Park at the University of Texas. Started in 2008, the longitudinal study follows 500 healthy and cognitively normal adults ages 20 to 89, who did not show significant amyloid build up at the start of the study, indicated by normal (negative) PET scan results. This database is one of the only studies following middle-aged healthy adults as they age, and scientists plan to use this resource to track the relationship between of amyloid deposition and cognitive decline before the onset of dementia.

At 4 years into this study on cognitively normal adults, Dr. Park and her team have found that the amount of amyloid in the brain correlates with rate of cognitive decline in older adults with a positive amyloid scan (a high burden of amyloid) over a 4-year time span. Strikingly, this relationship was detectable even in the middle-age cohort - however, only in scores on vocabulary tests. Early intervention will likely be key component to treating Alzheimer's disease, and this work provides a potential window for early detection and intervention by showing that early increases in brain amyloid can indeed be correlated with subtle cognitive changes.



Network Changes in the Alzheimer's Brain

In our brains, information is communicated through electrical signals between neurons. When we perform a particular mental task, certain groups of neurons become active in synchrony. We call this a "functional network." AAIC plenary speaker Dr. Lennart Mucke of the Gladstone Institute of Neurological Disease discussed his work on abnormal network activity in Alzheimer's disease. He has found that electrical activity becomes imbalanced even before clinical symptoms appear. Dr. Mucke and his group observed that this imbalanced electrical activity results in remodeling in the brain's hippocampus and overall changes in brain network activity. Because the hippocampus is a major site involved in learning and memory function, he believes these network changes may contribute to the cognitive abnormalities in Alzheimer's disease. In the future, Dr. Mucke says we need to better differentiate the network dysfunction relative to the normal function in order to understand and potentially use network measures to aid in diagnosis.

Blood-Brain Barrier and the Immune System

As a highly specialized and critical organ in the body, the brain is protected from the blood by a protective structure, called the blood-brain barrier. The blood-brain barrier is highly selective in what it allows to the brain, exchanging mostly small nutrients and gas molecules and excluding large immune cells. Research over the last decade however has demonstrated immune system involvement in many neurological conditions including Alzheimer's disease. Dr. Michal Schwartz at the Weizmann Institute of Science, Rehovot, Israel, a world pioneer in neuroimmunology, focused much of her career on this question: what is the immune system doing and how is it entering the brain despite blockage by the blood-brain barrier? From her work, Dr. Schwartz and her lab found that immune cells enter the central nervous system through a structure in the brain called the choroid plexus, an area that functions like a gateway between cerebral spinal fluid and blood. In addition, they discovered that in the healthy brain, an immune signaling factor, IFN- γ , acts on this gateway site to prepare it for important exchanges, but in the Alzheimer's brain, this activation may be reduced. Dr. Schwartz was a major player in initially promoting the notion that the immune system may play a protective role in the brain and moving forward, she and her team are focusing on ways to harness the immune system to fight against Alzheimer's disease. •

Upcoming Alzheimer's Association WA Chapter Conferences & Events

Central Washington Alzheimer's & Dementia Conference

Tuesday, October 23, 2018
Yakima Convention Center

alzheimer's association

The Central Washington Alzheimer's & Dementia Conference provides tools and encouragement to family caregivers and health care professionals caring for people with dementia. Continuing Education credits available. Dr. Barak Gaster, MD, Primary Care Liaison at the UW Memory and Brain Wellness Center, will deliver a presentation in the closing session: Advanced Care Planning for Dementia.

REGISTER: alz.org/alzwa

Central Washington Medical Provider Event

Tuesday, October 23, 2018
Yakima Convention Center

alzheimer's association

The Medical Provider Event is designed for medical providers: M.D., D.O., PA-C, ARNP, RNs, PTs, OTs, Pharmacists, Medical Social Workers, Medical Students, Diabetes Educators and front line Medical Staff working with patients with dementia and their families. Learn to identify dementia in its earliest stages in a primary care setting and effectively manage complex issues such as retirement from driving, protection from fraud, and difficult behavioral issues which patients with dementia often face. Resource tables available for local and statewide resources for dementia diagnosis, treatment and care for providers, persons with dementia and their family. Continuing Medical Education credits available. Dr. Barak Gaster, MD, Primary Care Liaison at the UW Memory and Brain Wellness Center, will deliver a presentation: Dementia in Primary Care: Evaluation, Management, and Practical Pearls.

REGISTER: alz.org/alzwa



**HUNTINGTON'S DISEASE SYMPOSIUM
IN PARTNERSHIP WITH OREGON HEALTH SCIENCES
UNIVERSITY**

SATURDAY, OCTOBER 27, 2018

KEYNOTE PRESENTATIONS BY:

**JEFF CARROLL, PHD, WESTERN WASHINGTON UNIVERSITY
&**

**JIMMY POLLARD - HD HEALTH EDUCATOR AND ADVOCATE, CHDI
FOUNDATION**

8:45AM - 9:30AM REGISTRATION

9:00AM - 4:00PM - SYMPOSIUM

LOCATION:

***UW TACOMA CAMPUS
1918 PACIFIC AVENUE
WILLIAM W. PHILIP HALL
TACOMA, WA 98042***

SESSIONS:

RESEARCH UPDATES

MEET THE DOCS

FAMILY PLANNING

NUTRITION & EXERCISE

CAREGIVING

ADVOCACY

**PLEASE REGISTER FOR THE
SYMPOSIUM AT:**

[HTTPS://BIT.LY/2VQXGWD](https://bit.ly/2vqxgwd)

This event is funded by the
Huntington's Disease Society of
America through an unrestricted
educational grant from TEVA



Students: Could a Neuroscience Major be Right for You?

by Anna Marie Yanny, BS'18, Behavioral Neuroscience, Western Washington University, Seattle

Neuroscience is a field of researchers working to solve the puzzle of the human brain, piece by piece. My neuroscience undergraduate degree taught me how the brain helps us perform extraordinary feats such as playing music, forming memories, and falling in love. In this field, I am able to contribute to neuroscience discoveries through research on how musicians process language. Chemistry, biology and psychology have become tools that I use to learn how the brain works, and what happens when it malfunctions.

When I think of brain diseases, the phrase “everyone knows someone” comes to mind. A neuroscience degree can help one understand the inner-workings of mental conditions that may be ailing herself, a family member, or friend. This personal element can compel students to study neuroscience with the hope of learning more about a brain condition that is relevant to their life.

In my case, my brother was recently diagnosed with epilepsy. When he had his first seizure, he suffered a traumatic brain injury. This experience gave me a personal drive to learn more about the brain, specifically how seizures occur and how the brain heals after sustaining a traumatic brain injury. I learned how to interpret the electrical patterns in the brains of seizure prone patients, and I came to understand why they occurred. By learning what was going on in his brain, I was better able to support my brother.

Like many, I also have family members who live with dementia. My neuroscience degree gave me the tools to better understand this brain condition. I could interpret the most recent dementia research and communicate it to my family without using scientific jargon. A personal connection to the neuroscience puzzles one studies can be a powerful motivator to find a solution. Many choose neuroscience with the goal of improving their neurological health of their loved ones or future generations.

The Career Possibilities Opened Up by a Neuroscience Major

Research

A neuroscience degree can lead to careers where you continue to learn and contribute to a growing body of research. One can work as a research assistant, lab coordinator or primary investigator. Neuroscience research can range from investigating how a single brain cell functions to measuring electrical patterns in the human brain as a whole. Someone who is more interested in chemistry may prefer sampling fluids from brain cells to learn how their chemicals interact. Someone who is more interested in clinical research may study the electrical changes in the brain over time as one develops Alzheimer’s disease. Participating in neuroscience studies as a researcher can lead to new treatments, medicines and therapies to improve the livelihoods of those with brain diseases.

Health Care

A neuroscience degree can be the first step to many health care careers. With additional schooling, one can become trained as a physician’s assistant, neurodiagnostic technician nurse, neurosurgeon, pharmacist or psychiatrist. These are only a few of many positions that allow neuroscience graduates to use their knowledge of the brain to improve the health of others.

Education

With a graduate degree (Masters or PhD) in Neuroscience, one can become a community college or university professor. They can excite the next generation about scientific exploration through clever analogies, compelling lectures and personal anecdotes from their own research.

Science Communications

A future in scientific research or clinical work isn’t for everyone who studies neuroscience in college. A neuroscience degree gives one the tools to understand complicated scientific topics and to communicate these topics to others via presentations, blog posts, and Thanksgiving dinner conversations. These tools can lead aspiring writers to careers in science communications. Science communicators work for newspapers, universities and research institutes to convey up-and-coming scientific findings to a general audience. This position allows one to stay up-to-date on science discoveries and aid the community in understanding the impact and value of research.

Research Scholarship Information for UW Undergraduates

Mary Gates Research Scholarships are one of the best sources of undergraduate research funding available on the UW campus. Approximately 160 Mary Gates Research Scholarships are awarded to UW undergraduates annually. The scholarship provides \$5000 disbursed in two installments of \$2500 over two quarters. Learn More: www.washington.edu/undergradresearch/students/funding/marygates-research/

Inventing a Blood Test for Early Detection of Alzheimer's and Parkinson's Diseases

By Genevieve Wanucha

“Imagine a world where diagnosing Alzheimer’s disease is as simple as getting your blood tested during your annual physical,” writes philanthropist Bill Gates. He’s started a venture to fund development of novel biomarkers, which are measurable signs in the brain and body of the presence of disease proteins: amyloid, tau, and a-synuclein, among others. His dream is one shared by all Alzheimer’s and Parkinson’s researchers—to bring these brain conditions into the realm of common diseases such as heart disease and cancer that are routinely caught in the earliest stages and treated before full blown symptoms arise.

Early detection of Alzheimer’s and related diseases poses a uniquely high hurdle. Obviously, it is logistically difficult to obtain, in a living brain, information about abnormal proteins. Instead, researchers must use proxy measures called biomarkers. Ideally, these proxies should be an accurate reflection of the degree of pathology in the brain, reproducible, low cost, and tolerable for most people. No biomarker currently meets these standards. The two most common methods of collecting biomarkers are cerebrospinal fluid (CSF) tests and special PET scans. However, obtaining CSF requires a spinal tap; PET scans are less invasive, but they are costly and not widely available. Compared to these tools, blood biomarker tests could be the key to early detection of Alzheimer’s because they can be scaled up for regular use in clinical settings.

Before this future of routine early detection, blood tests would immediately revolutionize clinical trials and research in general. For instance, better biomarkers are needed to bring down the cost and time of using PET scans to determine the eligibility of participants for trials of targeted therapeutic interventions. Currently, to get 100 people with preclinical Alzheimer’s disease enrolled in a prevention trial, study staff would likely need to screen nearly 700 people with a PET scan—which costs 2 million dollars.

What’s more, because of the importance of biomarkers in understanding the earliest signs of disease and determining

“There is a tremendous need to develop some form of neuropathological characterization that does not require the vast expense and difficulties that are currently needed,” said Dr. Paul Crane, MD, Professor of General Internal Medicine at UW Medicine. “Blood biomarkers would facilitate important research outside of the few urban academic centers that have the capacity to collect CSF and PET biomarkers now, for example, in home visits.”



In the face of this pressing need, researchers have their hopes set on developing effective biomarkers in the blood, as well as the urine, saliva, or eye. Now, the Zhang Lab, led by Dr. Jing Zhang, MD, PhD, Professor of Pathology at UW Medicine, is aiming to be the first group to develop reliable, accurate, and reproducible blood biomarkers in the field for Alzheimer’s and Parkinson’s diseases. Their work shows what it takes to develop the kind of tools up to the task of early detection and precise diagnosis, on a massive scale.

How Do Blood Biomarkers Work?

Blood biomarkers work on the same principle as spinal fluid CSF biomarkers, the current “gold standard”. It’s all about patterns. For example, in people with Alzheimer’s disease, amyloid levels in the CSF are low (reflecting low clearance of amyloid in the brain by the spinal fluid), but tau protein levels are high, compared to levels in people without Alzheimer’s. As such, an increased ratio of tau : amyloid is a CSF biomarker for AD. These kinds of meaningful ratios also exist in the bloodstream.

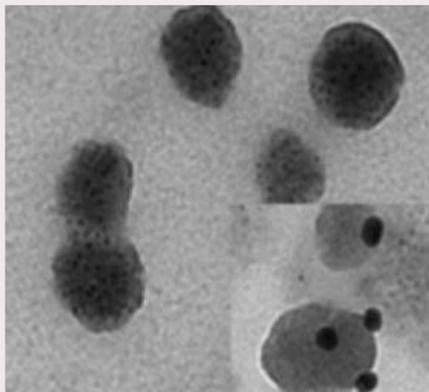
“Researchers have long known the patterns of CSF biomarkers that characterize Alzheimer’s and Parkinson’s diseases,” says Dr. Zhang, who has worked on CSF biomarkers extensively. “If we can define these patterns in the blood, it would be so powerful because we could simply make diagnoses based on blood tests. People wouldn’t need to donate spinal fluid.”

Even though the field has become invested in blood biomarkers, there has been little successful replication of promising results. “The number one reason for this difficulty is that the proteins of interest in the blood don’t uniquely originate from the brain,” says Dr. Zhang. “Amyloid and tau proteins, for example, also come from organs besides the brain.” To use these blood based-measurements of pathology as useful biomarkers, researchers need to verify that the proteins in the blood actually came from the brain.

The Zhang Lab has found that exosomes may provide the solution to probing brain disease via blood. Exosomes are lipid vesicles that normally transport proteins, genetic information, or waste between cells in our body, and out of the brain. Researchers think that these biological parcels may help the aging brain get rid of toxic proteins. The Zhang Lab has confirmed that exosomes loaded with disease proteins can cross the blood brain barrier and be detected in the blood. Conveniently, exosomes have a biological postal code.

If an exosome comes from the brain, it carries a specific molecule, called L1CAM. This marker acts like a shipping label on the surface of the exosomes, representing its point of origin in the central nervous system. Dr. Zhang’s group realized that exosomes offer a powerful way to assess pathology in blood samples and link it directly to brain disease.

The team soon developed technology to pull out the L1CAM-labeled exosomes from human blood samples. With this uncontaminated source of exosomes, they can quantify the protein content using a method called immunoassay. Other research groups around the world now use and adapt this L1CAM technology for blood biomarker research and development.



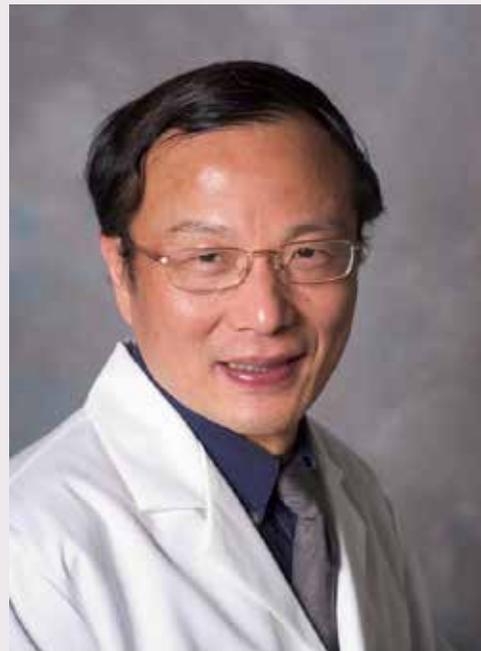
Electron micrograph of exosomes extracted from blood plasma by using the L1CAM capture technology (right-hand corner: L1CAM markers on surface of exosomes, as visualized by a staining technique used in electron microscopy.) Courtesy: J. Zhang

These blood-based exosomes have yielded valuable insight into human brain conditions. In a 2014 study, the Zhang Lab and UW collaborators analyzed blood samples from 267 people with Parkinson’s disease and 215 people without the condition, drawing on a cohort from the UW ADRC and Udall Centers. They observed that the blood-based exosome measures of a-synuclein protein were significantly higher in patients with Parkinson’s than in controls. Later, they found different patterns in the levels of tau protein in exosome samples from Parkinson’s and Alzheimer’s patients. These are the kind of data needed for measurements to become biomarkers.

Since then, the UW team has linked measures from blood-based exosomes to clinical disease manifestations. In 2018, they reported in the *Neurobiology of Disease* that changes in the blood biomarkers of a-synuclein were associated with the progression of cognitive impairment in people with early-stage Parkinson’s disease. A way to track a person’s rate of decline with a blood test would be helpful, for example, in quickly assessing the effect of an experimental treatment over time.

“I think Dr. Zhang is definitely on the right track,” says Dr. Colin Masters, MD, Professor of Dementia Research at the Florey Institute, University of Melbourne, who was not involved in this work. “Further work is needed to refine the assay and see if its performance can be enhanced. This is an area where there is a great need for a useful plasma [blood] assay.”

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Jing Zhang, MD, PhD, UW Medicine Pathology

All-In-One Biomarking

Blood biomarkers allow researchers to address the biological heterogeneity of Alzheimer's and related diseases. More often than not, cases of clinically diagnosed "Alzheimer's disease" involve amyloid and tau proteins but also show some mix of other pathologies, such as a-synuclein or TDP-43, vascular injury, and inflammation. The implication is that for precise diagnosis and appropriate treatment, people will need to be screened for a combination of biomarkers that reflect the different mechanisms driving the disease progression.

"Our hope is that with a whole panel of blood-based exosome biomarkers for multiple pathologies, we can differentiate between sub-groups of people in research studies," says Dr. Zhang. "And eventually, we will track disease progression and treatment effects in clinical trials, the goal of precision medicine."

The next step is validation. The Zhang Lab is now verifying that the blood-based exosome biomarkers for amyloid, tau, and -synuclein proteins perform just as well as the CSF biomarkers. The new tests need to be equivalent in diagnostic accuracy if they are to replace the field's gold standard. To do so, the team is working to repeat their successful biomarker results in a new cohort of people in China. As for the ultimate goal, the routine use of blood biomarkers in the doctor's office will require further replication studies and FDA approval.

The future availability of blood biomarkers will raise unanswered questions, such as what the knowledge of being biomarker-positive for Alzheimer's or Parkinson's will mean for healthy adults, considering existing stigma about dementia. Nonetheless, researchers, pharma executives, and now philanthropists see the approach as possibly the best way to prevent Alzheimer's disease and lower health care costs. This awareness could encourage people to engage in lifestyle interventions known to lower risk, enroll in research, help plan for the future, or take advantage of emerging pharmaceuticals as soon as possible. It's a world worth imagining. •

ADRC Contacts and Donation Information

- UW Alzheimer's Disease Research Center: 206.744.0588
- Visit the UW ADRC website: uwadrc.org
- Visit the UW Memory and Brain Wellness Center website: depts.washington.edu/mbwc

Support the Alzheimer's Disease Research Fund

Donations help support patient- and family-centered care, research breakthroughs in Alzheimer's-type dementia and related disorders, and the training of tomorrow's physicians. And by giving — perhaps in gratitude for care, or in memory of a loved one — you can help improve the lives of your friends, your family, and others in your region.

If you would like to be our partner in enhancing health and changing lives, please contact the UW Medicine Advancement Office at 206.543.5686. To donate online, please visit www.supportuwmedicine.org/adrc.

To ask questions or give feedback about *Dimensions*, please contact Genevieve Wanucha at gwanucha@uw.edu or 206.685.1304



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It's All Good

Nature has provided me with
Her own celebratory plaque.
It is white and, I believe, quite pure.
It fills my mind,
In a manner of speaking.

I had not previously heard
The mysterious and alliterative term,
"Pre-senile dementia."

I must admit, it has a certain authoritative ring.
Medical titles usually do,
And this one is quite official sounding.

It tells the story of a slow, crustaceous process,
Sort of like the accretion of silt
At the bend of a river
Where movement is diminished
And small bits of detritus,
No longer carried forward with enough motion,
Begin to drift downward
Until they settle, softly,
At the bottom.
Memory, like the drifting silt,
Becomes inert.

But, it is a slow process.
And I am not yet entirely transformed
From flowing river to fen.

Sometimes I feel frightened
By the future I imagine.
But, really, my fears of what may come
Are quite likely to be forgotten
Once the process is complete.

And, as I write this
I hold tightly to my secret weapon,
My willingness to live now, in this moment,
With its ever-changing kaleidoscope
Of texture, temperature, sound
And every other sense that brings me
The wonderful awareness of living.

David Leek, February 2018

The Feast of Life

Come to the table
Pull up a chair
The feast of life is here.

So many dishes to sample
Some hot, Some cold,
Sour, sweet, and picante' too.

Don't be picky.
Try them all.
It's cheap to dither,
To sniff and poke.
Sit down and begin,
Take a bite!
Don't nibble!

Fill your mouth.
Enjoy the flavors and textures.
Don't rush!
Give each moment the
Interest and curiosity
It deserves.

Those moments never recur.
They rise and dispel
Like bubbles in champagne.

David Leek, July 2017

About the Poet David Leek, a local community member, lives in Seattle, Washington with his beloved wife, Ania.

Personal Experiences with Lewy Body Dementia

by Jean Rough, July 2018

Knowing that I have both Alzheimer's and Lewy Body disease, I found myself interested in what I could learn. In my search, I discovered Dave Itzkoff who wrote a book *Inside the Final Days of Robin Williams*. Robin Williams, the actor, had Lewy body dementia (LBD) but it was not discovered until an autopsy after his death. Itzkoff learned about Robin's symptoms mostly from Robin's wife Susan. I learned from Dave. Itzkoff's book was a BIG breakthrough for me. As I read about how much Robin suffered, I felt my own suffering. I no longer was alone. For instance, he and I had the frustration of not knowing if a LBD symptom is leaving, arriving, or returning. No way to prepare. And no way for caregivers to prepare. Robin's wife and others tried everything to stop a symptom but nothing would work. His body had its own time. And so does mine.

Here is the "endless parade of symptoms" that Robin went through, mostly in his last year of life. It shocked me that his symptoms were so similar to my own symptoms.

** anesthesia	** constipation	** moments of quiet; moments of crying
** severe loss of weight	** trouble seeing	** motor impairments
** loss of sense of smell	** cogwheel rigidity (limb stops itself)	** difficulty remembering
** heartburn	** stooped posture	** indigestion
** tremor in left hand	** "freeze" current motion	**Hallucinations are not mentioned in Robin's list, but they have been important for me
** less voice	** anxiety (off the chart)	
** stomach cramps	** thinner and frail	

For each symptom there is a story. I have been keeping a journal for my stories. For example, four years ago, I was changing my niece's diaper. In cleaning it up, I noticed that I was not smelling it. That night at dinner with my husband and my 90 year old father I asked them to smell with eyes closed. They could smell. I could not. At the moment Lewy body Dementia was not a part of my life. But last year I realized that it was most likely due to Lewy. And I still can't smell.

Another all time experience is that my weight was around 124 lbs in 2014 and now is about 97. No matter what and when I eat, my body is not responding. Of course there are many Lewy symptoms that appear and then disappear. This was true with my rheumatoid arthritis. It lasted for a couple of years and then disappeared. Please note that RA does not usually disappear!

How did this begin for me? Four years ago, at least, I began noticing that I was being different, such as trouble with words. I took one of those tests and did fairly well making a clock, knowing where I lived, and remembering the three animals proposed to me when I arrived. A doctor did an X-ray and said it was fine with slight mild cognitive impairment (MCI).

Two years later those small mistakes and thoughts on the tests had shifted. My husband Jim and I decided to attend an event in Seattle focused on Alzheimer's disease with Dr. Thomas Grabowski who is Director of UW Medicine Memory and Brain Wellness Center. After attending one of his private sessions and taking a MRI, we were ready to hear the news. Later Dr. Grabowski suggested that I bring someone who could be a caregiver. I decided to bring Jim my husband and our son Dan and his wife Bonnie.

As we were preparing to leave our home in Port Townsend for our session, I remembered that I had that X-ray from the years before. But where would it be in our home after all of these years? I gave it one possibility, in my husband's closet pushed way back. I went into the closet and there it was! We took the X-ray with us to Seattle. It was a good choice because it gave Tom enough to measure and see a few differences.

At the UW Memory and Brain Wellness Center, Dr. Grabowski asked lots of questions. He also shared what he saw on the MRI. It was hard for me to see what clearly was OK and what was not. It was very important to include our caregivers. They asked good questions and now I have better knowledge of what I can expect.

Another UW Memory and Brain Wellness Center event was held a month ago with the focus on Lewy body dementia: Lewy Body Education Day. I was impressed how well the organizers allowed time to share and for us to hear other stories that professionals shared. And two of my caregivers attended by taking off of work (and picking me up at the ferry!). They had the chance to learn more about Lewy. We hope that the Center will offer more events.

What It's Like to have LBD

A friend asked me what is it like to "have" LBD. The image that comes to my mind is a ferris wheel except you don't know when it will start or stop. What helps me is to be conscious about how I feel each day. If it is something a bit unusual, then see if it is in the LBD list or maybe something new for the list appears. And give yourself a moment to relax or take a walk knowing that this event will pass. In the meantime, check to see if you need to inform your caregivers in preparation for the ups and downs.

I'm Cleaning!

Recently, I cleaned our dishwasher. Then I brought my cleaning stuff to the bathroom. I noticed that there was lots of dust on the floor behind the toilet. Obviously, it had not been cleaned for a while. I got down on my knees and cleaned. Then I noticed the wall had some spots, and another wall to clean. I cleaned them. I was in the midst of the next wall when I suddenly realized something. I stopped and screamed with a huge smile: "I'm cleaning! I'm cleaning!" Something was released that had been locked up along with LBD. The "locked up" had been keeping me safe. I could only face so much at the time of my life. But the "doing the cleaning" released me. That is how great I feel!

Driving my car

Something else I notice. If I share with someone about a problem, such as forgetting where they put things or getting lost when driving their car, their response often is: "I know what you mean. That happens to me all the time." Yes, that is true as how she/he experienced it. However, there is this different kind of loss. My car loss situation shortens my thinking. For instance I might not think to call "Siri." My friend with getting lost with a car has the choice to think and perhaps check with Siri.

Recently I was driving my car and pulled out from our hospital to a larger street. My destination was to turn left to a grocery store. It looked clear. When I looked to the right, two cars were coming. Knowing the left was clear I moved out, but the left was not clear. I had to make a quick choice. In the moment, turning a bit fast to the left seemed the best choice. I gave the car a quick move and made it. But it only worked because the car to the right slowed down. As I drove away, I hoped the driver would follow me so I could apologize. He did pull in right next to me. I walked over and apologized. He happened to be someone I knew and was mayor of our town for years. We talked about the almost crash. We knew that all of us were over 72. I shared that I had Alzheimer's and Lewy. And that Dr. Grabowski had mentioned that I should consider not driving. Now I know why.

Two weeks later I was driving to pick up my great niece and take her to a friend's house. An easy task. However, I made a wrong turn and had no idea where to drive. It was like being in a swirl from street to street, with little thinking. Finally I found a way to get out of the swirl and finish my task with the car.

That night Jim and I talked about our choices. It hit us hard. How could we manage without my driving? It would be far more difficult for both of us. But as we talked, we remembered Tom's words. And we remembered two other events in Seattle that would follow in as Lewy. And we talked about our grandchildren. This is our first week with Jim driving me to someplace. I am riding my bike more often.

Hallucinations

I saw Jim walk by with morning light under the doorway while I was lying on my bed. I called out to have him join me. But he doesn't hear me. As I am watching the door, I now see these crazy looking creatures, very small, parade under the door going in a perfect line, the opposite than what Jim was doing. I smile and speak to the creatures. Soon I realize that I have been in a visual hallucination, once again.

Finding Help

We have someone who helps with cleaning, gardens, and paying bills. But there is no one who helps with our daily living. As simple as keeping our calendar up to date. It can no longer be me. Small tears come. We begin to consider our options, such as having someone who stays during the day. Or how later could sleep where. There is some laughter as to how we could sleep. But mostly we are caught in a maze that has no way out. As if we have hit ground. The reality is that we have a long way to go. Maybe it is closer than we think. The thought is scary, sometimes more so for Jim than me. •

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Alzheimer's Disease Research Center