

Hope from the Hill

2024 » NEWS FROM THE OHSU MS CENTER www.ohsu.edu/ms



The MS Center celebrates 40 years of service



The early years of the OHSU MS Center

December 2023 marks a significant milestone in MS care in the Pacific Northwest as we celebrate the 40th year of the first MS Center in the area. When the OHSU MS Center was founded in 1983 by Dr. Dennis Bourdette, the landscape of MS care was very different from what it is today. Diagnosing and treating MS was challenging, MRI scans for lesions weren't

available for diagnosis, and there were no treatments that altered the progression of the disease.

In the 40 years since the MS Center's inception, there have been remarkable strides made in MS diagnosis, treatment and management. Between 1983 and 1993, things changed dramatically with two major advances in the field. Brain

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Our first clinic in 1983 consisted of a nurse, Bernie Sanders, and I seeing four people with MS. From that modest beginning, a large, robust and nationally recognized MS Center arose. I was honored to lead the MS Center for over 35 years and personally to provide care to over 1,000 people with MS and related disorders. The future of the MS Center and our ability to treat MS is brighter than ever.

Dennis Bourdette, M.D., FAAN, FANA
Founder and former director,
OHSU MS Center

Innovative research on MS And mechanotransduction



Swetha Murthy, M.D.

Multiple sclerosis is a neurological condition caused by the loss of myelin induced by inflammation. Myelin is the protective coating around nerve fibers that promotes fast communication between nerve cells. Myelin loss in MS leads to slower communication and leaves nerve fibers vulnerable to irreversible degeneration.

Dr. Swetha Murthy studies the molecular processes that govern how cells and tissues sense and respond to

mechanical force. Hair cells in the inner ear, for example, detect sound, while other cells may regulate blood pressure or sense changes in cell shape. Work in her laboratory will demonstrate that the cells responsible for myelination (encasing nerves in protective myelin) are mechanosensitive: that they sense and respond to mechanical force.

The process of converting physical stimuli into biological signals is called mechanotransduction. Dr. Murthy's research focuses on types of proteins — called mechanically activated ion channels — that are crucial to mechanotransduction. Her laboratory aims to describe the molecular and

physiological characteristics of one form of these channels that cause hypomyelinating leukodystrophies in humans due to the presence of loss-of-function mutations. Further, her work will show how this specific channel regulates myelination.

In collaboration with the laboratories of Drs. Kelly Monk and Ben Emery, they will conclusively demonstrate, for the first time, the involvement of mechanosensation in myelination. This work will provide insights into how mechanical cues might regulate myelination. It will guide us in understanding disease progression in MS and other hypomyelinating leukodystrophies, as well as inform therapeutic interventions.

Vascular disease risk factors in MS



Growing evidence suggests that the presence of vascular disease risk factors (VDRF), such as high blood fats, high blood pressure, obesity,

diabetes and peripheral vascular disease can contribute greatly to the worsening of disability in MS. But how these factors accelerate MS progression is unknown.

Dr. Vijayshree Yadav conducted a three-year observational study looking at the progression of MS disability in relation to these risk factors. Baseline results were published in *Multiple Sclerosis and Related Disorders Journal* titled "Vascular Disease Risk Factors in Multiple Sclerosis: Effect on Metabolism and Brain Volumes."

This paper reported that there were no observed differences in normalized brain volumes between the two VDRF groups at baseline. The subjects with VDRF did show lower brain adenosine triphosphate and higher inorganic phosphate compared to those without VDRF. That could suggest that metabolic changes may be an earlier, more sensitive and potentially more responsive marker of brain tissue at risk. More information will be reported when longitudinal analysis finishes.

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and spinal MRI became available in the mid-to-late 80s, making diagnosis earlier and more accurate. In 1993, the first MS disease modifying therapy became available, altering the course of relapsing MS.



The OHSU MS Center now

It is amazing and heartening to know that the OHSU MS Center is still thriving and providing cutting edge clinical care, research and advocacy for people with MS and related disorders. I started my career at the OHSU MS Center 40 years ago at its inception, and I have seen so many advances over that time. It was such a privilege to be a part of the OHSU MS Center, and so gratifying now to see its continued success. The OHSU MS Center continues to offer hope and expertise that changes lives. Congratulations on 40 years!

Ruth Whitham, M.D.
Former faculty member,
OHSU MS Center

For more information about the OHSU MS Center, visit www.ohsu.edu/ms

MOGAD study offers clues for predicting relapse

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a neurological, autoimmune disorder that shares some symptoms with MS. It causes inflammation in the optic nerve, spinal cord and/or brain.

Dr. Kayla Martin and colleagues completed a comprehensive study describing the demographic, clinical, and radiographic features of the disease in a cohort of adults and children at OHSU. The study is the first of its kind in the Pacific Northwest.

Prior studies report that 30-80% of children and adults with MOGAD go on to have relapses though there are no reliable predictors. As well as detailing the demographic, clinical and radiographic (imaging) patterns of MOGAD, Dr. Martin's study identified possible predictors of relapsing disease.

A novel finding of the study is the effect of race and ethnicity on risk of relapsing disease in adults. Martin found that Hispanics and Non-Hispanic Non-Whites had an increased risk of relapsing disease, when accounting for age, sex, and index event phenotype. More studies on racial and ethnic differences and disease course in MOGAD are needed to confirm these findings.

Identifying those at risk for relapsing disease early on may allow for initiation of preventative immunotherapy before the second attack.

The impact of exercise on myelin repair



OHSU has a rich history of research on myelin repair in MS animal models. Dr. Lindsey Wooliscroft is expanding on this important work by studying whether aerobic exercise on a stationary bicycle over a six-month period can repair damaged myelin in the brain and spinal cord. Her clinical trial incorporates novel ways to measure myelin damage and repair, including research-based MRI techniques and blood markers.

Dr. Wooliscroft and her team hope to show that exercise can enhance the effects of myelin-repair medications and, ultimately, improve disability. The study will also help identify the optimal biomarkers to measure myelin repair in future drug trials.

Dr. Wooliscroft is grateful to the study participants and her funders, including the National Institutes of Health, charitable foundations and donations to the OHSU Foundation. If you are interested in participating, please contact Dr. Wooliscroft's research team at mscycle@ohsu.edu.

Uncovering the role of glucose in neurodegeneration

Oligodendrocytes are cells in the central nervous system that produce and repair myelin. Myelin is the protective coating that surrounds nerve fibers (axons) allowing them to transmit their messages fast and efficiently. In MS, lasting damage to white matter tracts—housing axons and myelinating oligodendrocytes—underlies disease progression. While autoimmune processes drive MS, the mechanisms behind failed myelin repair and chronic neurodegeneration remain elusive. Recent insights highlight vascular pathology and metabolic irregularities in patients with MS, particularly reduced glucose metabolism within the white matter lesions. However, the exact contributions of these factors to MS pathology remain unclear. The endothelial cells within the cerebrovascular network play a vital role in transporting glucose from the bloodstream to the brain, facilitated by a gene known as Glut1 (glucose transporter 1).

The Chavali lab has generated a mouse model in which endothelial cell-Glut1 is inactivated, resulting in reduced glucose transport to the central nervous system. Initial findings in this model have unveiled oligodendrocyte maturation defects, disrupted myelination, and central nervous system inflammation—characteristics reminiscent of those observed in MS lesions.

With funding from the Race to Erase MS foundation, Dr. Manideep Chavali and his team are poised to delve deeper into understanding how this reduced glucose transport contributes to neurodegeneration and influences disease progression in animal models of MS. This work not only uncovers the biological mechanisms involved in disease progression but also provides an opportunity for therapeutic intervention.

News from the MS Center Director

As the OHSU MS Center celebrates 40 years of serving the MS community in December, we are proud of our accomplishments. Our clinic, research and education have all expanded and evolved over the decades making us even more hopeful about the future of MS care.

We welcomed two new MS fellows to the center: Drs. Helen Wu and Jacob Perlman. Our fellows are board-certified neurologists who receive advanced training in MS and neuroimmunology under the collaborative effort of the OHSU MS Center and the Portland VA Medical Center. Our Pediatric MS and Neuroimmunology Fellowship, created in 2020, has become one of the top ten pediatric neurology programs in the country. The first pediatric fellow, Dr. Maria Xiang, returned to OHSU as a faculty member to meet the needs of children with neuroimmunological diseases. This year Helen Wu, M.D., Ph.D., joined as the second pediatric fellow.

This year saw a revolutionary shift in treatment options available for patients with refractory MS. In collaboration with the Knight Cancer Institute, the MS Center is participating in a multi-site study to compare the efficacy, safety, immunologic effects and cost-effectiveness of stem cell transplant

versus the best available therapy in participants with relapsing MS. We have successfully conducted a stem cell transplant in an MS patient. This opens the door for the possibility of doing transplants at OHSU for MS.

Our center continues to investigate comprehensive and innovative treatments for MS, including dietary and lifestyle factors. The NMSS-funded study on the effects of a low-fat dietary intervention on MS fatigue revealed significant improvement in fatigue levels in people with MS compared to the control group. We also saw improvements on cholesterol and triglyceride levels in the low-fat diet group. A study funded by the VA, evaluating the impact of vascular diseases on MS using 7T brain MRI and MR spectroscopy, showed that vascular disease risk factors in MS are associated with significantly lower brain ATP and higher inorganic phosphate in those with vascular risk disease compared to those without. Ongoing analysis from this study will evaluate the relationship of phosphate metabolites, brain atrophy and disease progression in people with MS with and without vascular disease. The clinical trial investigating oral Mitoquinone Q, a mitochondrial co-enzyme and over-the-counter supplement for improving

fatigue in MS, is anticipated to be completed by December and has potential to lead to another novel pathway for MS management.

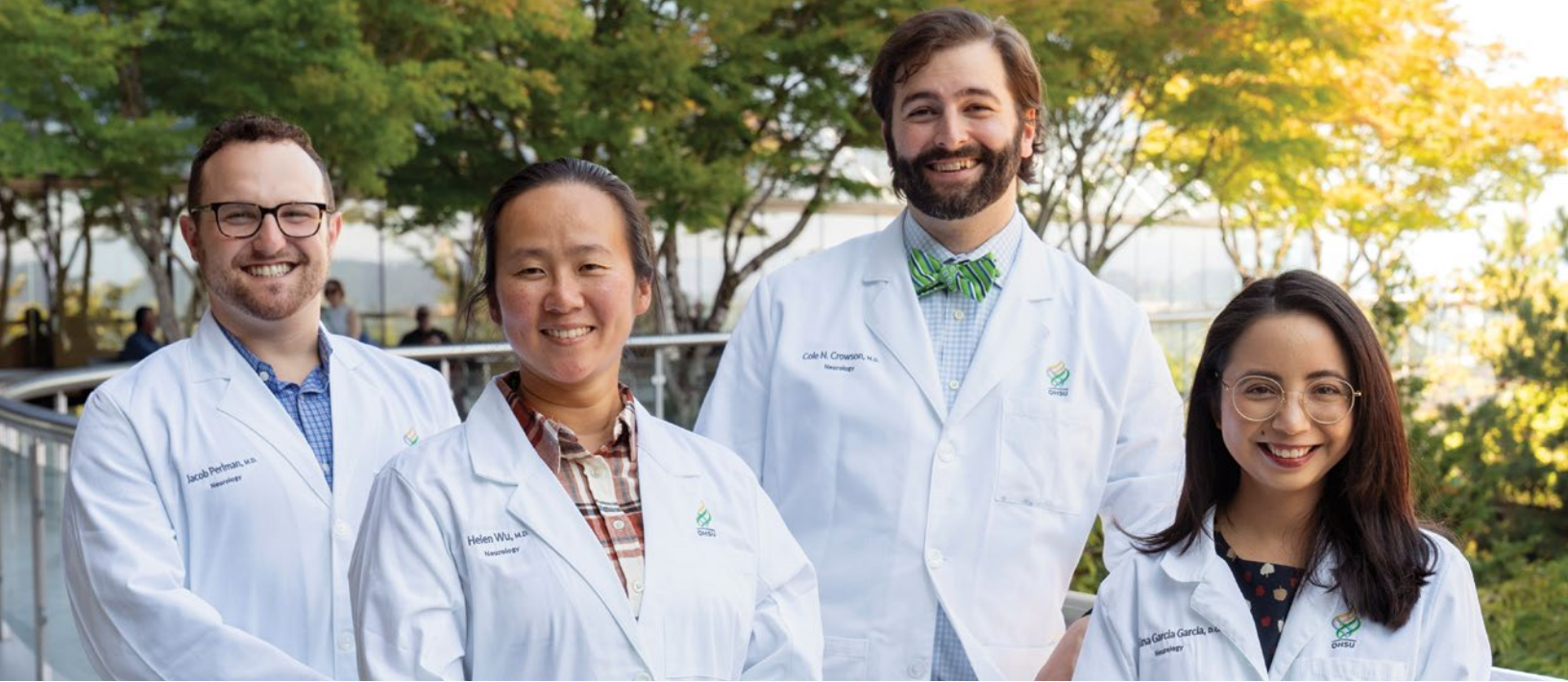
The MS Center's educational endeavors continue to expand to include participants from nearly every state and several other countries. The OHSU MS Center's longest running conference, At the Frontier and Beyond, reached over 900 people by the end of the month that it was held online. The Annual MS and CNS Neuroimmunology Symposium was held for the 6th year, bringing together multi-disciplinary medical professionals to improve the care of people living with MS and neuroimmunological disorders.

I am proud of the MS Center's accomplishments this past year as we continue our work and strive to improve the lives of people living with MS and neuroimmunological disorders.

Sincerely,
Dr. Vijayshree Yadav



Vijayshree Yadav, M.D., M.C.R.,
FAAN, FANA



Left to right: Drs. Perlman, Wu, Crowson and Garcia

Training the Next Generation of MS Clinicians and Scientists

Jacob Perlman, M.D. is from Toms River on the Jersey Shore. He went to medical school at New York Medical College, then completed his neurology residency at the University of Virginia. Dr. Perlman was drawn to neuroimmunology and MS, not only because he found autoimmune disease interesting and intellectually challenging, but because neuroimmunologists possess unique tools to help prevent disability from otherwise devastating diseases. He chose a two-year clinical research fellowship at OHSU for a few reasons. Dr. Perlman's mentor in residency trained at OHSU and highlighted the engaged faculty and rigorous curriculum. Further, Dr. Perlman was involved in MS diet research in residency

and identified OHSU as an institution that heavily supports lifestyle modifications research. Finally, he has always wanted to live in the Pacific Northwest.

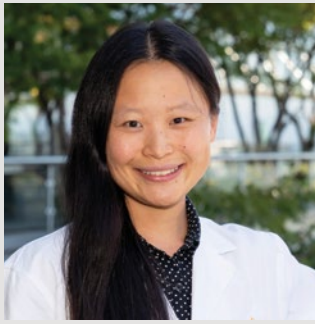
Helen Wu, M.D., Ph.D. grew up in Michigan where she completed her undergraduate education at the University of Michigan and received her medical and graduate education at Wayne State University in Detroit. She completed her Child Neurology Residency at Cincinnati Children's Hospital and Medical Center, where she became interested in neuroimmunology. OHSU offered an opportunity for her to gain knowledge and expertise in both pediatric and adult neuroimmunology.

She plans to use her one-year fellowship to develop her clinical skills and be involved in promising research to improve the outcomes of patients with neuroimmunology disorders.

Cole Crowson, M.D. is in his second year of fellowship at OHSU and the Portland VA Medical Center. Dr. Crowson was born and raised in Huntsville, Alabama and completed his undergraduate degree at Wake Forest University. He obtained his medical degree from the University of Alabama at Birmingham School of Medicine. He completed neurology residency training at the University of Virginia, where he found a passion for working with

patients with MS and other neuroimmunology-related disorders. He has enjoyed the supportive and collaborative nature of the faculty and clinical exposure at OHSU and the Portland VA Medical Center. He has completed a medical review of cannabis use in MS and is currently investigating prescription patterns and patient outcomes of anti-CD20 immunotherapy agents used for MS.

Carolina Garcia Garcia, D.O. has completed her first year of MS and neuroimmunology fellowship. Dr. Garcia was born in Mexico and raised in McAllen, Texas. Dr. Garcia completed her undergraduate education in Dallas, Texas before completing medical school at the Texas College of Osteopathic Medicine. She completed her neurology residency at Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire. Dr. Garcia sought a fellowship at OHSU and the Portland VA Medical Center to expand her knowledge and skills in neuroimmunology in an environment where she would be challenged with complex cases. Recently Dr. Garcia started research focusing on volumetric analysis of brain MRIs in patients with progressive MS.



Maria Xiang, M.D.

OHSU welcomes pediatric neuroimmunologist Dr. Xiang

Dr. Maria Xiang has joined the OHSU MS Center as a pediatric neuroimmunologist. After completing her pediatric neurology residency in New Orleans, she came to OHSU in 2020 when the university, with the support of the National MS Society, began to offer one of the only pediatric MS/neuroimmunology fellowship training programs in the country at the time. OHSU's spirit of innovation in medical training, compassionate culture, and the beauty of the Pacific Northwest drew her to Portland. Under the mentorship of Dr. Yadav and Dr. Bourdette, she completed and co-created a customized fellowship program that focuses on MS care for people of all ages with an emphasis on caring for children with neuroinflammatory disorders. Dr. Xiang is looking forward to helping grow medical education as the associate program director of the MS and Neuroimmunology Fellowship. Dr. Xiang loves to learn from her patients, who have greatly inspired her research focus in encephalitis and MOG-antibody associated disorder. She is also interested in the effects of chronic stress on the brain and body. She enjoys spending time outdoors with her family, including her young daughter, as well as writing, painting, and connecting with her family's Native American community.

The MS Center welcomes Reinabeth Phengthalangsy



Reinabeth Phengthalangsy

Reinabeth or Reina, is a medical assistant who recently joined the MS Center team as the care coordinator. She supports MS Center providers by helping with MyChart messages, patient records, phone calls, prescription refills, and a variety of other needs. Reinabeth has been a medical assistant for four and a half years. She previously worked in family medicine at the Vancouver Clinic and at OHSU's Facial Plastic and Reconstructive Surgery Clinic, part of the Department of Otolaryngology. She completed her schooling at Clark College. She wanted to join the MS team to learn more about the disease and how to help patients feel better. Her interests are reading, hiking, camping with Kato, her Shiba Inu, and trying new food spots with friends.



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Upcoming patient events

Save the date – June 8, 2024

The OHSU Multiple Sclerosis Center's annual conference, *At the Frontier & Beyond*, is scheduled to take place on Saturday, June 8, 2024. The half-day conference provides practical information about managing, treating and living with MS.

Please visit www.ohsu.edu/ms/events to check in about other scheduled events, or contact Dawn at chrisdaw@ohsu.edu to subscribe to the mailing list for MS Center events.

Upcoming professional events

Save the date – September 14, 2024

The 7th Annual MS and CNS Neuroimmunology Symposium is scheduled to take place on Saturday, September 14, 2024. This accredited symposium for health care providers will explore diagnosis, management and treatment challenges in MS and CNS neuroimmunology disorders.

For more information about the OHSU MS Center events, visit www.ohsu.edu/ms/events.

Giving to MS Research

In the last decade, researchers at OHSU have moved closer than ever to unraveling the mysteries of MS. With your help, we can combat this disabling disease. Please consider making a gift today to further MS research. Contact Maddy Abulencia at 503-552-0663 or email abulenci@ohsu.edu for more information. Thank you for your support!