UW Medicine
DEPARTMENT OF NEUROLOGY

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NEUROTRANSMISSIONS

DEPARTMENT OF NEUROLOGY
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From the Chair

Just as the blossoming trees and increasing daylight mean that Spring has come to the Pacific Northwest, so too arrives the Spring 2018 issue of *Neurotransmissions*, the UW Department of Neurology's newsletter for colleagues, alumni and friends. I am proud to share the latest exciting developments in our department, including news on research, clinical resources, and education.

In this issue we spotlight the UW Multiple Sclerosis Center Clinic, based at Northwest Hospital. The Center is co-directed by **Dr. Annette Wundes** from Neurology and Dr. Gloria Hou from Rehabilitation Medicine. The evaluation and treatment of MS has changed at breakneck speed in the past 10 years, with the introduction of many new potent biologic therapies. Dr. Wundes and her team of neurologists, physiatrists, and other allied professionals possess the expertise to assess each patient with MS and create an individualized treatment plan that best takes advantage of the improved efficacy these novel drugs offer—while skirting potential complications they may bring. Read about this tremendous group of clinicians on page two.

Bruce R. Ransom, MD, PhD

We welcome the newest member of UW Neurology leadership on page four. **Mark Wainwright, MD, PhD** has arrived in Seattle from Northwestern University in Chicago to take on the role of Head of Pediatric Neurology at Seattle Children's, a position ably filled by **Sid Gospe, MD, PhD** for many years until last June. Mark brings to the Division expertise in pediatric neurocritical care, an area that is achieving growing recognition and importance, especially with the increasing use of bedside electrophysiological monitoring in the ICU setting. Mark is a great addition to our faculty and we look forward to further growth in the pediatric division under his leadership.

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INSIDE THIS ISSUE

The UW Multiple Sclerosis Center: at the cutting edge of a rapidly changing field

The field of multiple sclerosis (MS) and other CNS demyelinating diseases is rapidly evolving. The advent of newer, more potent disease-modifying treatments (DMTs) for MS that have become available can present a dizzying array of choices for the non-specialist clinician. And with new information that has emerged on the molecular basis of demyelinating disease, MS can now be more readily differentiated from its mimics, such as neuromyelitis optica spectrum disease or myelin oligodendrocyte glycoprotein (MOG)-antibody associated entities. The UW Medicine Multiple Sclerosis Center is a multi-disciplinary clinic specialized to meet these challenges posed by patients with MS and other CNS demyelinating diseases. Since 2012, the UW MS Center, at its new location at the Northwest Hospital campus, has been providing services to patients and collaborating with local providers across the entire WWAMI region to address the needs of this complex patient cohort.

A team of providers with extensive training and experience in MS and related disorders provide a comprehensive focus on the patient, beginning with accurate diagnosis, continuing to optimal DMT choice and management, and including symptom management and rehabilitation. They see patients ranging from those at initial diagnosis to those with very advanced disease; every effort is made to address their individual needs according to their disease stage and severity. The UW MS Center's team consists of neurologists with expertise in MS, a rehabilitation physician, a nurse practitioner, a vocational counselor, a social worker, MS-trained nurses, infusion nurses, and a pharmacist. A dedicated infusion suite and pharmacy are integrated parts of the UW MS Center. A monthly patient program available on-site and by webinar is offered. Because of the breadth of clinical expertise available, the National MS Society has awarded the UW MS Center the "Partners in MS Care" designation for the highest level of comprehensive MS care.

The UW MS Center proudly supports the annual MS Walk in Seattle, and has been awarded the "Largest Team Award" for multiple years in a row

Disease modifying strategies for MS have become quite complex: newer agents offer opportunities to optimize disease control, but may pose greater risks. Here a thorough analysis of patient-specific disease trajectory in the context of patients' other health information allows our neurologists **Gloria von Geldern, MD**, Assistant Professor of Neurology, **Michael Persenaire, MD**, Acting Instructor of Neurology, **Gary Stobbe, MD**, Clinical Associate Professor of Neurology, and **Annette Wundes, MD**, Associate Professor of Neurology and co-director of the UW MS Center, to guide patients and partnering community providers towards an individualized treatment plan. **Pamela Davies, ARNP**, Teaching Associate of Neurology, with extensive experience in chronic pain and chronic disease management, has recently joined the team for optimal management and safety surveillance of patients. Our pharmacist Deborah Gallaro, RPh, supports providers and patients alike regarding complex medication regimens.

The neurology team works directly with other faculty of the interdisciplinary team, including physiatrist Gloria Hou, MD, co-director of the UW MS Center, rehabilitation psychologists **Kevin Alshuler, PhD**, Adjunct Assistant Professor of Neurology, Samantha Artherholt, PhD, Tiara Dillworth, PhD, as well as vocational counselor Joe Stuckey. Patients may be co-managed with any of these providers for optimal patient outcome. Community providers taking care of patients with MS can

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Swanson's History of Neurology
The Bronze Age of UW Neurology: Part 4, 1975- 1980s.

By Phillip D. Swanson, MD, PhD,
Professor of Neurology

In the 1970s, after one year of training in internal medicine and three years of clinical neurology, neurologists usually would opt either for private practice or for an academic career. Those planning for an academic career often applied for further research fellowship training to be prepared to do both research and clinical work. In those days, at the University of Washington, there was only one academic track towards promotion, now called the clinician/scientist track. There are now additional clinician/teacher, and clinician tracks. So in the early 1970s, most academic neurologists managed every type of neurologic disorder in the clinics or on the wards. Changes to this pattern occurred quite gradually, so that at the present time it has become the norm for a neurological resident to seek fellowship training in a clinical subspecialty, such as multiple sclerosis or clinical neurophysiology, before moving on to practicing. At the University of Washington, establishment of some of these subspecialties had to wait until the Neurology division became a department in 1996, as the need for appropriately trained faculty members had not yet been met.

Neuro-oncology. Dr. Alexander (Alex) Spence joined the Division in 1974. A graduate of the University of Chicago School of Medicine, he trained as a neurologist in the Harvard Longwood program, followed by a stint of military service. He was doing a neuropathology fellowship at Stanford, where he became interested in the pathogenesis of primary brain tumors. He became the first neuro-oncologist at the University of Washington. Alex joined the Division at about the time that Richard Nixon resigned from the U.S. presidency. Alex Spence was a superb clinician and a devoted researcher into the pathogenesis of brain tumors. He developed a model of glioma in the rat, using tumor-inducing chemicals. He studied tumor metabolism using PET scanning techniques, and then began studies in humans, measuring tumor metabolism and the effects of treatments. He gained the respect of neurosurgeons and radiation oncologists, and led the weekly tumor board meetings. His loss in 2010 was deeply felt. Several neurology residents, including Rich Peterson, Sonia Partap, and Brian Vaillant, were inspired by Alex to enter the field of neuro-oncology.

Neurogenetics. Tom Bird finished his neurology residency in 1974. He was a graduate of Cornell School of Medicine, and in 1970 started his training in Seattle as a rotating intern at the University Hospital. After his N1 year he was required to fulfill his military service obligation, having been deferred until then under the Berry Plan. After two years at the Naval Hospital in San Diego, he returned to Seattle and completed his residency. He then took the unusual (at that time) step of undergoing fellowship training in medical genetics under Arno Motulsky, one of the founders of this field. Tom then began his illustrious career with joint appointments in the Divisions of Neurology and Medical Genetics. Though he was a full-time employee of the VAMC, at the UWMC he was allowed to establish the first neurogenetics clinic in the US as a unique resource for neurological patients with genetic diseases. This clinic continues to evaluate patients with genetic disorders affecting the neuromuscular and central nervous systems. Many previously unreported conditions have been studied in the clinic, including the finding of novel mutations for Charcot-Marie-Tooth Disease, familial Alzheimer Disease, and spinocerebellar ataxias. Tom became Chief of Neurology at the Seattle VA Hospital in 1987, serving until 1997 when he was succeeded by Bill Spain. Both Sumie Jayadev and Marie Davis were mentored by Tom. (Please see page 7 for an additional tribute to Tom.)


Alexander Spence, MD

Movement disorders. The finding in the late 1960s that levodopa could remarkably improve the symptoms of patients with Parkinson's Disease led to a worldwide expansion of interest in movement disorders. Before this time, medical therapy consisted primarily of anticholinergic medications such as trihexyphenidyl, although neurosurgical procedures such as thalamotomy were often successful in improving tremor, limb rigidity, and bradykinesia. At the UW, we participated in clinical trials of other drugs acting to enhance dopaminergic activity, such as entacapone and ropinirole. We established a Parkinson's Information and Referral Center sponsored by the American Parkinson Disease Association, which allowed the hiring of Maria Linde, a Neurological Nurse Specialist who was instrumental in establishing a local Parkinson's chapter and patient support groups. With the discovery of the genetic mutation causing Huntington Disease, HD could now be diagnosed

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Update from the Division of Pediatric Neurology

WELCOMING MARK WAINWRIGHT, MD, PHD, DIVISION HEAD

Beginning in December 2017, **Mark Wainwright, MD, PhD,** Professor of Neurology, became Head of the Division of Pediatric Neurology, succeeding long-time Head Sid Gospe, MD, PhD, who retired in June 2017. He originally hails from Liverpool, England, and was motivated to emigrate to the US for love: as a college student, he met his future wife in England while she was on an exchange program from the University of Rochester. In the US, he entered an MD/PhD program at the University of Chicago and pursued doctoral research on the molecular properties of the dopamine receptor. As a medical student doing clinical rotations, he had the good fortune to be on-service with Peter Huttenlocher, one of the great figures of child neurology.
"I watched him get on the floor and play with the kids with blocks, and realized, that's the kind of neurology I wanted to do," he said.

Following his graduation from Chicago, Dr. Wainwright entered the child neurology program at Duke. During his last year in the program, he discovered he enjoyed practicing in the intensive care environment, and also developed a research interest in neuroprotection in critically ill children. Following his recruitment to Northwestern University (where he remained from 2000 until his move to the UW), he started a lab focused on neuroinflammation and traumatic brain injury. In parallel, he started a pediatric neurocritical care program at Northwestern, which grew from a one-person operation to six faculty, a busy consult service, and a training program which now trains two fellows each year. "Neurological issues impact every child in the ICU," he said, "and what was key to our success was building a partnership between neurologists and intensivists."

Dr. Wainwright came to Seattle Children's because he saw an opportunity "to build on strengths in an already excellent division." Neurocritical care is one such area where he hopes to recapitulate his success story at Northwestern. He cites other potential growth opportunities in pediatric neuromuscular disease, neuro-oncology, and demyelinating disorders. A novel clinical and research focus will be on a "big data" approach to monitoring children in the ICU using real-time streaming of multiple lines of physiologic data, so to predict those patients at risk for impending clinical deterioration.

Since moving to Seattle from Chicago—albeit just in time for the dreary Pacific Northwest winter—he does laud the climate for being appreciably milder than that of the Windy City. Another difference he noted was the fact that "people stop to let you cross the street—bizarre!" While getting a feel for the Division and setting up a home in anticipation of the move of his wife and possibly his two daughters in their 20s as well to Seattle, Dr. Wainwright does not have much free time at present. But he is harboring ambitions of taking up the bagpipes, so to import a bit of the UK to the PNW.

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definitively. Developing a movement disorders program with fellowship training had to wait until Dr. Ali Samii joined us in 1996.

Clinical neurophysiology. With the exception of Children's Hospital, where Coldevin Carlson carried out electromyography (EMG) on children, EMGs on the adult services were all performed by the Department of Physical Medicine and Rehabilitation (now Rehabilitation Medicine). Neurology residents were welcomed for EMG training by Drs. Walter Stolov and George Kraft. For full fellowship training, however, trainees usually went elsewhere to programs at UCSD or University of Utah. Not until departmental status was achieved in 1996 was Neurology allowed to carry out EMGs. The first EMGer hired by the Department was Dr. Eric Yuen. He was succeeded by Michael Weiss in 2001. Dr. Weiss has expanded the EMG services with the help of Drs. B. Jane Distad, Eric Kraus, and Leo Wang, sharing the studies with Rehabilitation Medicine.

Neurology Residency Update

We congratulate the 2018 graduating class of Neurology residents! We thought, How better to send them off into the world of fellowship or practice than to give them each a parting shot? Below, we bring you our diverse cast of uniquely talented neurologists!

Thomas Foutz, MD
EPILEPSY FELLOWSHIP, UNIVERSITY OF NORTH CAROLINA

I'm so grateful to everyone for the support and education I have received these 5 (long) years. It has been an marvelous, arduous and life-altering journey. I will not miss Q4 call, but will miss pretty much everything else. My wife, our three kids, and I will be moving to Chapel Hill, North Carolina for Epilepsy fellowship.

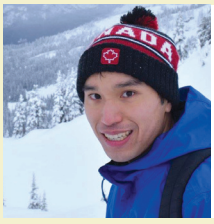
Huan Li, MD, PhD
GENERAL NEUROLOGY PRACTICE, KADLEC REGIONAL MEDICAL CENTER

We came from near and far
To form a great team
As proud neuro residents
To pursue the same dream

We have amazing attendings
Who help us take flight
Great neurologists we'll become
Rising together to show our might

Hand in hand we can laugh and cry
Still working hard in all this time
Achieving objectives
Our work is sublime

Graduation's coming soon,
Lift your hands up to the sky
We grew our wings and now we fly!



Justin Low, MD
NEURO-ONCOLOGY FELLOWSHIP, DUKE

Thanks for the memories UW, it was a blast.

Anusha Mannava, MD
HEADACHE FELLOWSHIP, UW

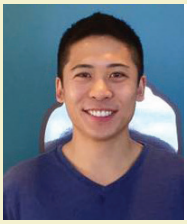
Coming to UW as an R2 as opposed to other neuro residents was scary initially, but soon realized not to be! It's been a smooth journey and was only possible through the immense support of colleagues, seniors and attendings. I am glad to stay back as a Headache fellow and cherish one more year of being with some of these awesome people!

Anisha Chandra Schwarz, MD
NEUROMUSCULAR FELLOWSHIP, UW

It turns out that pediatric neurology residency is a wonderful thing to have done. Thanks to all the patients (ages one minute to ninety years), mentors, and peers who taught me, encouraged me, and shaped the past five years. What an amazing group I trained with. You made it worthwhile to come in every day. Favorite attending remark: "It is better to round with an empty bladder than a full mind." (Dr. Kollros). I'm looking forward to neuromuscular fellowship at UW next year. Do keep in touch, and please keep sending me good papers. I have plans to read them.

Breana Taylor, MD
VASCULAR NEUROLOGY FELLOWSHIP, UW

At first it was a big adjustment moving to Seattle from Chicago, but my co-residents and incredible faculty teachers and mentors have made my experience at UW unforgettable. I am excited for the Vascular Neurology fellowship next year. I am thankful for the opportunity to continue to grow, and become the best neurologist I can!

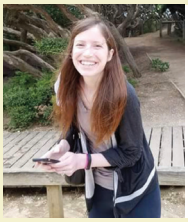


James Wang, MD
VASCULAR NEUROLOGY FELLOWSHIP, UW

Thank you to everyone in the Department of Neurology that have taught and shaped us into the neurologists that we are today. Best to all going forward. Cheers!

Yujie Wang, MD
NEURO-IMMUNOLOGY FELLOWSHIP, JOHNS HOPKINS

Residency has flown by, from the first Botox injection at the VA to the last Stroke Code at Harborview. It has been quite a rewarding and humbling experience, and I will forever be grateful to my co-residents and the faculty members for being there every step of the way. It is bittersweet to be leaving Seattle and the UW Neurology family, but I know that I have made lifelong colleagues and friends. For the next step of my career, I will be pursuing a fellowship in Neuro-immunology, and am excited to continue to learn.



Jennifer Wax, MD
HEADACHE FELLOWSHIP, UW

Thank you to my co-residents and many faculty mentors for their support during residency. And thank you to my family, without whom I'd never have made it to - much less through - these past few years. Another doctor once said, "all of time and space...where do you want to start?" I'm grateful to have received my start in neurology at UWMC, and to be continuing the journey as one of the Headache fellows next year.

Selected Recent Publications by Neurology Faculty

Compiled by Nadine Waldmann,
Budget/fiscal analyst lead

Novotny EJ Jr. Early genetic testing for neonatal epilepsy: When, why, and how? Neurology. 2017.

Berg AT, Coryell J, **Saneto RP**, Grinspan ZM, Alexander JJ, Kekis M, Sullivan JE, Wirrell EC, Shellhaas RA, Mytinger JR, Gaillard WD, Kossoff EH, Valencia I, Knupp KG, Wusthoff C, Keator C, **Dobyns WB**, Ryan N, Loddenkemper T, Chu CJ, **Novotny EJ Jr**, Koh S. Early-Life Epilepsies and the Emerging Role of Genetic Testing. *JAMA Pediatr* 2017.

Wang AC, Ibrahim GM, Poliakov AV, Wang PI, Fallah A, Mathern GW, Buckley RT, Collins K, Weil AG, Shurtleff HA, Warner MH, Perez FA, Shaw DW, Wright JN, Saneto RP, **Novotny EJ,** Lee A, Browd SR, Ojemann JG. Corticospinal tract atrophy and motor fMRI predict motor preservation after functional cerebral hemispherectomy. *J Neurosurg Pediatr* 2018.

Weaver KE, Poliakov A, **Novotny EJ,** Olson JD, **Grabowski TJ**, Ojemann JG. Electrocorticography and the early maturation of high-frequency suppression within the default mode network. *J Neurosurg Pediatr* 2018.

Grinspan ZM, Shellhaas RA, Coryell J, Sullivan JE, Wirrell EC, Mytinger JR, Gaillard WD, Kossoff EH, Valencia I, Knupp KG, Wusthoff C, Keator C, Ryan N, Loddenkemper T, Chu CJ, **Novotny EJ Jr**, Millichap J, Berg AT. Comparative effectiveness of levetiracetam vs. phenobarbital for infantile epilepsy. *JAMA Pediatr* 2018.

Chen DH, Ma M, Scavina M, Blue E, Wolff J, Karna P, Dorschner MO, Raskind WH, **Bird TD**. An 8-generation family with X-linked Charcot-Marie-Tooth: Confirmation of the pathogenicity of a 3' untranslated region mutation in *GJB1* and its clinical features. *Muscle Nerve* 2017.

Schutz REC, **Creutzfeldt CJ.** Three big things in neuropalliative care: Communication, personhood and uncertainty. *J Neurol Sci* 2018.

Granstein JH, **Creutzfeldt CJ.** A qualitative look at end-of-life care in the ICU. *Crit Care Med* 2017.

Cox CE, Jones DM, Reagan W, Key MD, Chow V, McFarlin J, Casarett D, **Creutzfeldt CJ**, Docherty SL. Palliative care planner: a pilot study to evaluate acceptability and usability of an electronic health records system-integrated, needs-targeted app platform. *Ann Am Thorac Soc* 2018.

Kirk V, Baughn J, D'Andrea L, Friedman N, Galion A, Garetz S, Hassan F, **Wrede J**, Harrod CG, Malhotra RK. American Academy of Sleep Medicine position paper for the use of a home sleep apnea test for the diagnosis of OSA in children. *J Clin Sleep Med* 2017.

Selected Recent Grant Awards to Neurology Faculty

GRANT TITLE	SPONSOR	PI
A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial in Subjects with Relapsing MS to Evaluate the Efficacy and Safety of 8115033 as an Add On therapy to Anti-inflammatory diease modifying Therapies	BIOGEN	**Wundes**
A Phase 2, Multi-center, Randomized, Double-blind, Placebo Controlled Study in Subjects With Late Prodromal and Early Manifest Huntington's Disease (HD) to Assess the Safety, Tolerability, Pharmacokinetics, and Efficacy of VX15/2503	VACCINEX	**Samii**
West Virginia Stroke Center of Biomedical Research Excellence	NIH / P20	**Weinstein**
A Phase 2, Multi-Center, Double-Blind, Randomized, Dose-Ranging, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of CK-2127107 in Patients with Amyotrophic Lateral Sclerosis	CYTOKINETICS	**Weiss**
Advancing Research and Treatment for Frontotemporal Lobar Degeneration (ARTFL) consortium	NIH / U54	**Domoto-Reilly**
A Study to Model Rates of Change on Neuropsychological Test Measures in Subjects Diagnosed with Behavioral Variant Frontotemporal Dementia and Healthy Subjects	BIOGEN	**Domoto-Reilly**
A Phase 2b/3 Randomized, Double-blind, Placebo-Controlled, Parallel Group, Multicenter Study Investigation the Efficacy and Safety of JNJ-54861911 in Subjects who are Asymptomatic at Risk for Developing Alzheimer's Dementia	JANSSEN	**Domoto-Reilly**
Dynamics of Kv channel function in identified populations of pyramidal neurons in neocortex	NIH / R01	**Spain**
Genetic Movement Disorders: Etiologies and Pathogeneses	VA MERIT	**Zabetian**

Neurology Faculty News

Joe Zunt, MD, MPH, Professor of Neurology, received a Global Innovation Fund award for his collaborative projects "Using a mobile apps and citizen science to reduce mosquito-borne disease: a pilot project in Peru" and "Global health partnerships in disaster preparedness and response." In honor of these awards, he was cited by Paul Ramsey, MD, Dean of the School of Medicine, for his "strong commitment to improving health."

Bruce Ransom, MD, PhD, Professor and Chair of Neurology, was honored with a special issue in the journal *Neurochemical Research* for his lifetime of achievement in research into the basic biology of neuroglia and the mechanisms of white matter injury during anoxia. The issue editor, Helmut Kettenmann, PhD assembled an international cast of eminent scientists, all with past links to Dr. Ransom, who contributed reviews and reminiscences in his honor. Among the contributors were Bill Catterall, PhD; George Richerson, MD, PhD and **Chris Ransom, MD, PhD, Assistant Professor of Neurology**; and Steve Waxman, MD, PhD and Joel Black, PhD, who penned an "Ode to glia" for the issue. (They write, "He was great with a tuning fork and reflex hammer / But Bruce also worked on the brain and its glamour.") Dr. Kettenmann cited the highlights of Bruce's lifetime of scientific work as being "the first studies of mammalian neurons in the dish, ionic mechanisms of white matter injury, the role of hemichannels on astrocytic glutamate release and the role of astrocytes as glycogen stores for maintaining axonal function." You'll find these articles and a heartfelt tribute to Dr. Ransom under this reference: *Neurochem Res* (2017) 42:2437–2441.

Bruce Ransom, MD, PhD and some of his research colleagues in 2009.

Tom Bird, MD, Professor of Neurology, was profiled in *Lancet Neurology* in the article "Tom Bird: one of the world's first experts in neurogenetics." The profile traces Dr. Bird's beginnings as a genetics fellow with Arno Motulsky, shortly followed by his establishment of the first adult neurogenetics clinic. Seminal achievements in the genetic basis of Charcot-Marie-Tooth disease and early onset Alzheimer's disease are described, among others. See this wonderful tribute in the February 5th, 2018 issue of the journal.

Our neurology faculty took the lion's share of awards in the *Seattle Magazine* 2018 Top Doctors list. Honored were **Will Longstreth, Jr., MD**, Professor of Neurology; **Ali Samii, MD**, Professor of Neurology; **Lynne Taylor, MD**, Professor of Neurology; and **Michael Weiss, MD**, Professor of Neurology. Note that this is Dr. Taylor's 11th year of being cited in this survey!

Neurology Faculty News

HAVE SOME NEWS TO SHARE?

A recent grant, publication, or award? Please send it along to Nadine Waldmann (dine33@uw.edu) so we may include it in the next issue of *Neurotransmissions*.

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On page 7 of this newsletter, please take a look at some of the latest kudos that constantly come the way of our faculty. **Tom Bird, MD**, was recently lionized in the pages of Lancet Neurology as "one of the world's first experts in neurogenetics," while **Lynne Taylor, MD** collected her 11th consecutive "Top Doctor" award from Seattle Magazine, an honor bestowed by her community neurology peers who vote in this annual survey. Read about these and others of our Neurology faculty being honored for their contributions to patient care and research.

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consider referring their patients to our allied practitioners for collaborative care—a valuable resource, as providers with their expertise and skill set are not often available in the community setting. **Samantha Artherholt, PhD** leads groups where patients meet for several weekly sessions focusing on improving self-care skills, cognitive skills or adjusting to a new MS diagnosis.

In addition to providing high quality clinical care, the UW MS Center is actively involved in research and training. As such, patients may opt to participate in clinical trials expanding the range of treatment options to control disease activity and possibly promote remyelination. The team is also very actively engaged in research on topics of care delivery models, adjustment to chronic disease, and rehabilitative strategies, with large scale research projects funded by the Patient-Centered Outcomes Research Institute, National MS Society and National Institutes of Health. In addition, Dr. Wundes directs the Clinical MS Fellowship program, which was awarded a competitive multiple-year training grant by the National MS Society. MS fellows participate in the care of our patients, and have gone on to successful careers serving patients with MS throughout the country.