Innovations in Neurosciences
# Table of contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>From the chairs</td>
<td>3</td>
</tr>
<tr>
<td>About OHSU</td>
<td>5</td>
</tr>
<tr>
<td>About the OHSU Brain Institute</td>
<td>7</td>
</tr>
<tr>
<td>Movement disorders</td>
<td>9</td>
</tr>
<tr>
<td>Interdisciplinary cancer care</td>
<td>15</td>
</tr>
<tr>
<td>Racial equity</td>
<td>17</td>
</tr>
<tr>
<td>Minimally invasive spinal deformity surgery</td>
<td>19</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>23</td>
</tr>
<tr>
<td>Research highlights</td>
<td>25</td>
</tr>
<tr>
<td>Educating the next generation</td>
<td>31</td>
</tr>
<tr>
<td>Recent representative publications</td>
<td>35</td>
</tr>
<tr>
<td>Faculty</td>
<td>37</td>
</tr>
</tbody>
</table>
From the chairs

Dear colleagues and friends,

Improving human health has never been more challenging. COVID-19 has devastated aging populations already subject to neurodegenerative and neurovascular disease and affected care delivery for all ages. Despite these challenges, we continue to promote the well-being of every patient through leading and innovative neuroscience care.

During the pandemic, we continue to deliver leading edge, minimally invasive and robotic procedures for epilepsy, Parkinson’s disease, brain and pituitary tumors, spinal disorders, stroke and pediatric nervous system illness. To provide improved access and keep our patients safe, we have rapidly expanded the use of virtual visits and remote care. Our scientists continue to advance knowledge of basic nervous system function, disease mechanisms and novel therapies. Our team members are improving racial and gender equity in medicine. Through all this work, we are also educating the next generation of physicians, surgeons and researchers.

With a strong tradition of diverse, interdisciplinary teams, we believe OHSU is uniquely positioned to advance human neuroscience. Our clinicians and scientists partner with experts across OHSU, the region, nation and world to further understanding and improve human health.

We are honored to share with you some annual highlights of how the OHSU Brain Institute is transforming care for people affected by nervous system disease.

Sincerely,

Helmi Lutsep, M.D., FAAN, FAHA
Interim Chair and Professor, Neurology

Nathan R. Selden, M.D., Ph.D., FACS, FAAP
Campagna Chair and Professor, Neurological Surgery
About OHSU

Based in Portland, we have more than 1 million patient visits each year, operate the top-ranked adult and children’s hospitals in Oregon, and secure competitive research funding of over $550 million. As a public corporation serving the best interests of Oregon and the region, we also provide outreach that improves health in communities across the state and provides services to the most vulnerable Oregonians.
### Research

**OHSU award dollars:** $558 million

**Amount of funding focused on clinical trials:** $121 million

In 2019, OHSU disclosed 149 new innovations and filed 172 patent applications.


According to Nature Index 2020, OHSU is No. 89 of the top 100 in life sciences, No. 258 of the top 500 academic institutions.

### Facilities and employees

**Employees:** 18,480

OHSU owns and leases space beyond its campuses. Altogether, OHSU occupies more than 8.7 million square feet on about 400 acres.

### Community service

OHSU has more than 200 community health care programs, reaching out to vulnerable groups in urban areas as well as underserved rural communities throughout the state, and in fiscal year 2020 had a community benefit contribution of $498 million.

### Education

OHSU helps educate over 5,000 students and trainees each year.
About the OHSU Brain Institute

The OHSU Brain Institute is a national leader in neuroscience patient care, research and education. Our mission is to advance and understand the diagnosis, treatment and prevention of nervous system diseases by promoting interdisciplinary research in basic and clinical neurosciences.

ACCREDITATIONS AND RECOGNITIONS

- Ranked as a top 50 hospital for adult and pediatric neurology and neurosurgery by U.S. News & World Report
- DNV GL Comprehensive Stroke Center
- Level 4 Comprehensive Epilepsy Center (Adult and Pediatric)
- One of 32 NIH Alzheimer’s Disease Centers in the country
PHYSICIANS

56 Neurology clinical faculty

16 Neurology fellows

17 Neurological surgery clinical faculty

3 Neurological surgery fellows

RESEARCH

300+ Neuroscience researchers

$124M Current neuroscience research funding

PARTNERSHIPS AND CLINICAL COLLABORATIONS

As Oregon’s only academic medical center, we work with hospitals around the state to expand exceptional care to patients in their home communities.

Pediatric neurological surgery
Legacy-Randall Children’s Hospital, Portland
Shriners Hospital for Children, Portland

Adult neurological surgery
OHSU Health Hillsboro Medical Center
Adventist Health Portland
St. Charles Medical Center, Bend
VA Portland Health Care System
OHSU Stroke Telemedicine Network

OHSU.EDU/BRAIN
Movement disorders

Joseph F. Quinn, M.D., director of the OHSU Parkinson Center and Movement Disorders Program. He is a noted Alzheimer's disease physician-scientist known for his work in animal models, biomarker studies and clinical trials in neurodegenerative disease, including Alzheimer’s disease and Parkinson’s disease.

Expanding frontiers in the science and treatment of movement disorders

The OHSU Parkinson Center and Movement Disorders Program is a world leader in delivering advanced therapies and translational research for these diseases. In addition to investigator-led development of new therapies, we also collaborate with the larger scientific community by contributing to all major multicenter trials. We are committed to improving therapies for Parkinson’s disease and all the diseases in our field through compassionate care, research opportunities and collaborations.
The research of Vivek K. Unni, M.D., Ph.D., on understanding the role of the protein alpha-synuclein in the mechanisms of Parkinson’s disease was one of the most frequently accessed papers published in Scientific Reports in 2019. It was listed No. 26 on the journal’s “Top 100 papers in Neuroscience” list.

Aggregated alpha-synuclein Lewy body pathology in the hippocampus of a mouse model of Parkinson’s disease.

Discovery of the role of alpha-synuclein in DNA repair may lead to targeted treatment

The Parkinson’s disease-linked protein alpha-synuclein plays an unexpected role in helping the cell repair DNA damage caused by double-strand breaks (DSBs), according to research presented by Vivek K. Unni, M.D., Ph.D. Conversely, the lack of healthy alpha-synuclein results in higher levels of DSBs. When the healthy protein becomes entangled in Lewy bodies found in Parkinson’s disease and related disorders, the lack of appropriate DNA repair may play a role in triggering cell death. This important finding may assist in developing new therapies targeting alpha-synuclein-mediated DNA repair mechanisms for Parkinson’s and other neurodegenerative diseases to prevent or reverse cell death.

“We with this discovery, we are taking a fundamental question in the field about the influence of alpha-synuclein aggregates in disease and proposing something very different from traditional assumptions,” Unni said. “Our work has potential significance for the field in the next decade as we to continue to test this hypothesis to develop and create new therapies.”

Vivek K. Unni, M.D., Ph.D.
Exercise program changes brain and walking skills for Parkinson’s disease patients

An Agility Boot Camp at OHSU Brain Institute’s Balance Disorders Laboratory for people with Parkinson’s disease showed improvements in participants’ balance and walking with exercise intervention. The exercise program developed by Fay B. Horak, Ph.D., P.T. and Laurie King, Ph.D., P.T., M.C.R., combined motor and cognitive challenges (attention, set switching, etc.).

Discoveries included:

- Brain network changes post-exercise on MRI images.
- Significant improvement in walking speed while dual-tasking, foot angle at heel contact with the floor, and torso range of motion.
- Improvements in patient-reported perceived functional independence, including improved balance confidence and ability to do activities of daily living.

Right SMA-PPN Connectivity
Novel use of neuroimaging leads to deeper understanding of gait disorders

Prefrontal cortex activity during continuous turning and walking is significantly greater in Parkinson’s disease patients, according to research by Martina Mancini, Ph.D. Mancini used mobile functional near-infrared spectroscopy (fNIRS) to compare younger adults, older adults and adults with Parkinson’s. The study showed that mobile fNIRS reliably collected prefrontal cortex activity data and differentiated among the three study cohorts. Prefrontal cortex activation was significantly greater in the Parkinson’s subjects compared to the other cohorts during walking, particularly when beginning to walk. By using mobile fNIRS, continuing research aims to better understand mobility deficits and help with the development of appropriate therapeutics.

The unique setup includes simultaneous data collection from movement monitors to quantify gait and turning. Martina Mancini, Ph.D., and her team measure the cortical correlates of walking and turning with and without cueing intervention and different pharmacological treatments.
Providers who participated in Project ECHO for Parkinson's disease hailed from the Portland metro area to the farthest corners of Oregon. Many participants represented rural communities (34 percent) or medically underserved communities (27 percent). Participants also represented various roles, from M.D.s and D.O.s to nurse practitioners, naturopathic doctors and physical therapists. In a follow-up survey, all participants responded that the ECHO event was effective, and that they would recommend it to a colleague.

Elevating the standard of care in rural and underserved areas

Lisa Mann, R.N., B.S.N., M.A., coordinated a Project ECHO (Extension for Community Healthcare Outcomes) medical education initiative to train other health care providers in Oregon about Parkinson’s disease. Participants could submit a case for a bimonthly video board, bringing together expertise from OHSU’s neurologists and neurologic rehabilitation team.
Deep brain stimulation (DBS) therapy has a proven track record in reducing upper extremity tremor associated with essential tremor. The OHSU Brain Institute pioneered asleep DBS in the U.S. and remains a leader in the field. In the past two years, we have adopted new, MRI-compatible electrodes that create a directional field. These have already proven to minimize side effects. This is a significant advancement compared to the previous omnidirectional electrodes that could affect the neighboring areas of the brain, causing some problems with weakness or numbness. We are continuing to work to validate the further advantages of this new approach. OHSU’s team is now the nation’s most experienced DBS provider group, attracting patients from around the world.

Using repetitive transcranial magnetic stimulation (rTMS) to treat gait disorders

In a novel approach, Marian Dale, M.D., M.C.R., used cerebellar rTMS in a study of progressive supranuclear palsy (PSP). In the subjects with PSP, there was a notable increase (32 to 50 percent) in cerebellar-brain inhibition for improved postural stability and speech. Stimulatory cerebellar rTMS is a promising tool to improve motor control in neurodegenerative disorders. Further study will evaluate the therapeutic value for the treatment of medication-refractory variants of Parkinsonism.

Dr. Marian Dale’s research seeks to understand the causes of balance dysfunction in supranuclear palsy.
Interdisciplinary cancer care

Pioneering RADIANS clinic provides multidisciplinary CNS tumor care to the community

When patients visit the RADIANS (RADIation oncology And NeuroSurgery) clinic, they meet their neurosurgeon and their radiation oncologist in the same room at the same time. Unlike most oncology clinics, RADIANS clinicians provide evaluation, planning, treatment and follow-up together rather than rotating patients through different specialties.

Neurosurgeon Jeremy N. Ciporen, M.D., co-created the novel clinic model in 2016 to optimize patient and physician experience at OHSU Health Hillsboro Medical Center, a community hospital serving a large population west of Portland. Ciporen, director of surgical neuro-oncology at OHSU Health Hillsboro Medical Center, collaborates with radiation oncology colleagues Jerry Jaboin, M.D., Ph.D., and Timur Mitin, M.D., Ph.D., the medical director of the OHSU Health Cancer Center, Hillsboro.
The clinic serves patients with primary CNS disease as well as those with metastatic disease of the brain and spine. OHSU Health Hillsboro Medical Center offers both stereotactic radiosurgery and complex neurosurgical expertise, unusual in the community setting.

“Not only do we see patients at the same time, but we can also treat them there at the clinic,” Ciporen said.

In nearly four years, the clinic has seen exponential growth in patient volume without patients returning via the emergency department with complications from tumor growth causing neurological deficits. Ciporen attributes this to the fact that the RADIANS clinic is not just procedural. Instead, the team follows patients long-term with regular in-office and virtual visits, attempting to stay ahead of emerging issues.

Through this advanced clinic model, patients can receive complex care in a community location, access clinical trials and, if needed, access the additional resources of a quaternary health center at OHSU.

Due to rapid change in virtual capabilities during the pandemic, the RADIANS clinic is hosting team meetings with patients and families in an active virtual multidisciplinary clinic. Patient feedback is overwhelmingly positive, and the clinicians have found they can accomplish all but surgical and radiation treatments online.
Racial equity

Fostering a culture of belonging

OHSU has a strong reputation for collegial, interdisciplinary collaboration, but we recognize that work remains to provide an equitable healing environment for all. OHSU has set out to dismantle structural racism and become an anti-racist institution.

“The Department of Neurological Surgery organized a #whitecoats4Blacklives gathering, observing eight minutes and 46 seconds of silence, the duration of time that a Minneapolis police officer had his knee on George Floyd’s neck before he died.

“We must hold the mirror up to ourselves and get our house in order so that we can best educate, inform and lead others on behalf of those we serve.”

OHSU President Danny Jacobs, M.D., M.P.H., FACS
Anti-racist initiatives by the departments of Neurology and Neurological Surgery

Clarifying mission statements to support inclusion.
OHSU Department of Neurology is diverse in race, ethnicity, gender, sexual orientation and gender identity, ability and disability, age and appearance. We strive to provide the highest quality care for all people, with understanding of historical racial, ethnic and gender biases that have undermined care equity.

Expanding the structure for departmental diversity, equity and inclusion committees.

Leveraging Grand Rounds to provide anti-racism education.
"The Neuroscience of Racism" by Larry Sherman, Ph.D.
"Exploring Implicit Bias in Clinical and Academic Settings" by Jeffrey Proulx, Ph.D.

Enhancing recruitment of residents underrepresented in medicine.
The Department of Neurological Surgery invested in a software program that reduces unconscious bias via blind applications for residency recruitment.

Encouraging learning and meaningful dialogue.
In one example, the Department of Neurological Surgery held small group sessions about microaggressions. In a follow-up survey, faculty and staff reported the sessions helped them individually to realize that continuing self-education is important and improved their confidence to speak up when witnessing racism and bias.

Widening the path to careers in medicine.
OHSU Neuroscience Post-baccalaureate Initiative: A pathway to Ph.D. programs for college graduates who identify with groups underrepresented in science. This competitive training opportunity provides scholars with a mentored research experience as well as tailored academic and professional development support.

BUILD EXITO: An undergraduate research training program at Portland State University that prepares students who identify with underrepresented groups to succeed as scientists. The OHSU Layton Aging and Alzheimer’s Disease Center within the Department of Neurology has served as the research learning community for these students, providing crucial support, guidance and expertise.
Minimally invasive spinal deformity surgery

Minimally invasive techniques are changing the options patients have for spine deformity surgeries. At OHSU Health Hillsboro Medical Center, neurosurgeon David Yam, M.D., corrects advanced scoliosis and advanced kyphosis — the most challenging spinal surgeries — through purely percutaneous methods. He has performed more than 150 percutaneous anterior column release (ACR) procedures over the last five years in a community hospital setting. Combining ACR with other minimally invasive techniques produces excellent correction results, but with significantly less risk to patients and faster recovery.

“Traditionally, percutaneous deformity correction couldn’t match the results of open surgery, but now we can,” Yam said. “At the same time, we are improving every aspect of the patients’ care: less bleeding, fewer takebacks, less morbidity. A T10 to pelvis open surgery comes with the anticipation of complications and long stays in the intensive care unit. Our patients who receive minimally invasive ACR for spinal deformity go directly to a floor bed, bypassing the ICU.”

Yam credits innovations in technology and technique that allow for complex preoperative planning, utilizing software to determine the exact number of levels and the amount of correction needed.
This preoperative planning results in fewer operative levels and shorter operative times than traditional methods. While the patient is still on the operating table, the surgical team uses software to measure the correction obtained to make sure the goal is achieved, avoiding secondary surgeries or failed corrections.

“In all cases, the blood loss was below 500 CCs, and we’ve had only one case of proximal junctional kyphosis (PJK) in patients treated with purely MIS techniques,” Yam said. “Comparatively, the literature says PJK occurs in around 20 to 26 percent of open deformity cases and blood loss is typically 1.5–2 liters. Using a minimally invasive method may be the solution for reducing PJK and transfusions.”

Because the patients have lower acuity postoperatively, Yam is able to perform these surgeries in a community hospital at OHSU Health Hillsboro Medical Center.

With the diversity of minimally invasive options now available, Yam said it is possible to help many more patients who would not previously have been candidates for spine surgery due to age, health issues or previous failed surgeries. About 35 percent of Yam’s patients seek him out for revision treatment. Yam uses the same minimally invasive techniques for revision surgery as he does for deformity correction, with positive outcomes.

OHSU will be contributing to the literature in coming years to move the bar for the indications of minimally invasive spine surgery for spinal deformities, sharing the latest innovations and treatments for better spine surgery options for the people of Oregon and beyond.

Dramatic advantages of percutaneous spinal deformity surgery

- Reduced blood loss (below 500 cubic centimeters)
- Shorter operative times (single-day operations)
- Low complication rate (10 percent)
- Markedly reduced risk of serious incision complications (0 percent)
- Earlier discharge (4.5 days)

“We’re proving that highly complex percutaneous spine surgery can be done without the resources of a quaternary center. If we can broaden the access, these minimally invasive or even hybrid methods potentially make spine deformity correction much less risky and easier for recovery.”

David Yam, M.D.
OHSU Health neurosurgeons are at the forefront of exploring the boundaries of possibility with minimally invasive spine surgery. We can now perform countless percutaneous spine surgeries. For example:

**Cervical**
- Cervical discectomy for selected disc protrusion
- Cervical foraminotomy for stenosis
- Cervical laminectomy for spondylotic myelopathy
- Cervical laminotomy for epidural abscess
- Cervical laminotomy for selected benign and malignant tumors
- Cervical laminotomy for synovial cyst

**Thoracic**
- Thoracic laminotomy for selected benign and malignant tumors
- Thoracic laminotomy for stenosis
- Thoracic laminotomy/facetectomy for selected thoracic disc protrusion
- Thoracic laminotomy for selected intradural pathology including dural AV fistula
- Thoracic fusion for tumor or trauma
- Thoracic fusion for degenerative disease
- Thoracic fusion for thoracic disc herniation

**Lumbar**
- Lumbar far lateral discectomy
- Lumbar laminectomy for selected benign and malignant tumors
- Lumbar laminectomy for stenosis
- Lumbar laminotomy for epidural abscess
- Lumbar laminotomy for selected intradural pathology including dural AV fistula, filum lipoma, schwannoma
- Lumbar laminotomy for synovial cyst
- Lumbar paramedian discectomy
- Lumbar fusion for tumor or trauma
- Lumbar fusion for spondylolisthesis
- Lumbar fusion for degenerative disease

**Other**
- Scoliosis surgery for complex deformities including scoliosis and kyphosis
- Revision surgery for patients needing correction of failed hardware or pseudarthrosis
- Revision surgery for adjacent segment disease
- Paraspinal access for foreign body removal (e.g., shrapnel)
Medically fragile patients have positive outcomes from minimally invasive laminectomy

Older adults with major medical comorbidities usually aren’t candidates for surgical procedures. Using the Charlson comorbidity index, Elixhauser comorbidity index, Edmonton frailty scale and NSQIP risk calculator, three patients of Donald Ross, M.D., would have been high risk for open cervical procedures for myelopathy. In fact, these patients had all been declined for surgery elsewhere due to their high medical risks. However, Ross performed minimally invasive spine decompression procedures through an 18 mm tubular retractor for these male patients, who had a mean age of 73.

All three patients left the hospital after an uncomplicated overnight stay, and no patient had any immediate or delayed postoperative complications up to 11 months later. Three months after surgery, their MRI scans showed good decompression and no need for further surgery. Ross’ pioneering study, published in 2019, shows the opportunity minimally invasive spine surgeries may offer for older adults and that the existing risk calculators may not be appropriate tools for minimally invasive procedures.
Multiple sclerosis

Stimulating myelin repair through molecule may revolutionize MS treatment

OHSU Brain Institute researchers have advanced the hope of an effective multiple sclerosis treatment by discovering a compound that stimulates myelin repair, now in clinical development.

Thomas S. Scanlan, Ph.D., professor of physiology and pharmacology in the OHSU School of Medicine, developed the synthetic molecule sobetirome 20 years ago. He was testing this novel thyroid hormone receptor beta agonist (TRβ1) for reducing cholesterol and as a treatment for the rare genetic disease adrenoleukodystrophy.

Six years ago, Dennis Bourdette, M.D., then director of the OHSU Multiple Sclerosis Center, suggested Scanlan develop sobetirome to stimulate remyelination in MS.

Using a prodrug strategy, Scanlan’s lab added a chemical tag to the sobetirome molecule, creating an inert compound called Sob-AM2. The tag allowed sobetirome to efficiently penetrate the blood-brain barrier, enabling a tenfold increase in concentration of the active parent compound in the central nervous system. When the compound reaches the brain, fatty acid amid hydrolase cleaves the tag and converts Sob-AM2 back into sobetirome. Using a genetic mouse model of demyelination/remyelination developed by OHSU neuroscientist Ben Emery, Ph.D., the research team found that sobetirome and its prodrug accelerated remyelination and reversed neurological disability in the mice.

“The treated mice showed close to a full recovery,” Scanlan said. “A drug that will stimulate remyelination of demyelinated nerve fibers would be a major advance for treating MS, and ours does that in MS animal models.”

The study also demonstrated that sobetirome promotes remyelination without the severe side effects of thyroid hormone therapy.

Bourdette and Scanlan credit the breakthrough to a collaboration among scientists and clinicians with expertise in physiology and pharmacology, neurology, advanced imaging and genetics.

OHSU has licensed the technology to Autobahn Therapeutics in California, which has already raised more than $76 million in investment finance for the clinical development of the technology for use in MS. Notably, three of the largest global pharmaceutical companies are investors, demonstrating confidence that a drug based on the OHSU technology will make it to the bedside.
“The drugs our team has developed offer a real hope of promoting myelin repair in the 2.5 million people worldwide who have MS.”
Dennis Bourdette, M.D.

OHSU Multiple Sclerosis Center

The OHSU Multiple Sclerosis Center is at the forefront of research and treatment for the care of MS and related disorders. Beyond comprehensive diagnostic and medical treatment, our MS Wellness Research Group is internationally known for managing MS through diet, exercise and stress relief. Working with the basic researchers at OHSU, we are bringing forward exciting translational opportunities.
Research highlights

The OHSU Brain Institute has nine research institutes in addition to the internationally renowned Vollum Institute, which is dedicated to the study of the molecular basis of nervous system function. At OHSU, we’re rooted in a culture that questions the status quo and pushes the boundaries of what’s possible.

Connection between photosensitivity and pain may be a biomarker

In 2017, Javits Award winner Mary M. Heinricher, Ph.D., described how brain circuitry linked to light can be activated to produce abnormal pain in animal models. Her discovery of a neural mechanism for photosensitivity in chronic pain gave fascinating insight into the brain mechanisms of pain and pain modulation.

Soon after, Heinricher, who is a faculty member in the Department of Neurological Surgery, attended OHSU’s annual interdisciplinary Pain Awareness Investigation Network (PAIN) Day event. She fell into discussion with a rheumatology clinician, who mentioned that fibromyalgia patients have multisensory hypersensitivity. This is when everything came together for Heinricher.

Over the next three years, Heinricher became the principal investigator on a Department of Defense grant to study and quantify photosensitivity and underlying neuronal responses to light in veterans with complex traumatic brain injury (TBI). Out of 400 patients (many affiliated with the Veterans Affairs Portland Health Care System), the research team found that photosensitivity was associated with chronic pain and other long-term effects of TBI. In the few functional MRI tests accomplished before the pandemic, there was evidence that light activates elements of the “pain matrix.”

In addition to Heinricher, the research team includes OHSU clinician-scientists Miranda Lim, M.D., Ph.D. (TBI and sleep specialist); Scott Mist, Ph.D., MacOM, (functional imaging and pain specialist); and Matthew Butler, Ph.D., of OHSU’s Oregon Institute of Occupational Health Sciences (behavioral neuroscience). The team is developing a box with a controlled light source that would allow remote testing, broadening the participation to veterans around Oregon.

“This project is an unbelievably exciting interface between basic and clinical science,” Heinricher said.
"As a career basic scientist, I never thought I would work on something that so directly applied to a current human condition," she said. "But the ability to interact with people with different expertise but all interested in same topic — in this case, pain — is hugely valuable, supporting the importance of having sciences embedded in clinical settings."

Mary M. Heinricher, Ph.D.

Potentially, this research may influence treatment for TBI and other chronic pain syndromes by:

- Targeting pharmacological treatments. Ones that act on brain mechanisms are more likely to be effective in individuals exhibiting abnormal photosensitivity.

- Reducing harm. Many patients receive inappropriate or even harmful treatments for pain.

- Modifying the environment. Simple changes in the light environment may improve function.
**Can sleep prevent neurodegeneration?**

In 2009, the highly cited research of Miranda M. Lim, M.D., Ph.D., described the causal role that lack of sleep plays in the acceleration of amyloid plaque formation in mice.

“However, despite our initial findings over 10 years ago, mechanisms underlying the role of sleep in preventing amyloid plaque formation are still unclear,” she said. “Now, we are continuing the study of sleep in aged mice by analyzing sleep EEG. We will use novel techniques to quantify EEG slow-wave coherence, as slow waves have been implicated in amyloid and Alzheimer’s disease.”

In parallel, Lim’s group will work with the BNFRA Center to compare sleep EEGs collected in humans.

“Our groups will also analyze sleep EEG using the same techniques via transfer learning from mouse to human, as well as apply machine learning and deep learning approaches to classify Alzheimer’s disease severity and trajectory,” Lim said.
Botanical supplement research center funded by $6 million NIH grant

The new Botanicals Enhancing Neurological and Functional Resilience in Aging (BENFRA) Center will attempt to discern how two of the most popular botanical supplements, ashwagandha and gotu kola, affect brain health and function. For generations, people have used these two botanicals to lower stress and improve sleep and cognition, which may decline in aging.

“We have a wealth of knowledge that comes from traditional use of various botanicals,” said neurologist Amala Soumyanath, B. Pharm., Ph.D., director of the center. “But, practically speaking, if you look on the shelves, you’ll find multiple products made of a given botanical and they vary a lot. The dose, how they were grown, where they were grown, how they were processed — all of these things will affect the constituents in that product and its efficacy.”

By cultivating and measuring the chemical properties of withania somnifera (ashwagandha) and centella asiatica (gotu kola) under tightly controlled conditions, researchers at the BENFRA Center hope to tease out the herbs’ underlying mechanisms and active constituents. The goal is to develop well-designed clinical trials to investigate efficacy, possibly using blood tests and/or MRI to attempt to measure specific biomarkers connected to the herbs.

OHSU received a five-year, $6 million award from the National Institutes of Health for the study of these two botanicals. OHSU is now among three NIH-supported botanical research centers across the country.
Edward Neuwelt, M.D., has spent more than 20 years researching pediatric hearing loss caused by platinum-based chemotherapies. A clinical trial based on his work has found a treatment protocol that reduces hearing loss by nearly 50 percent when treating a form of pediatric liver cancer.

Drug prevents hearing loss from chemotherapy in children

Decades of research led by neurosurgeon and neuro-oncologist Edward A. Neuwelt, M.D., is nearing the approval finish line of a new drug application. Children all over the world will have much less hearing loss from chemotherapy thanks to Neuwelt’s research.

Neuwelt and colleagues at the OHSU Brain Institute showed that cisplatin plus sodium thiosulfate (STS) significantly reduces the incidence of cisplatin-induced hearing loss. Critically, using STS did not show any evidence of tumor protection in children with localized solid tumors. In clinical trials, patients had 50 percent less hearing loss with the addition of STS than without it.

In 2018, the Food and Drug Administration granted STS Breakthrough Therapy and Fast Track designations. In 2020, the FDA granted Priority Review for a formulation of STS (Pedmark) by North Carolina-based Fennec Pharmaceuticals, which has a license agreement with OHSU. In its response, the FDA noted some facilities issues for Fennec Pharmaceuticals to address but did not note any clinical safety or efficacy issues. When Pedmark is approved, it will be the first drug for hearing protection of any kind.
Though platinum-based chemotherapy is effective in treating solid tumors, patients often experience hearing loss as an outcome. Tracking the long-term effects on these patients, the hearing loss proved to have a negative impact on school and life success. In younger children, hearing loss can affect learning to talk and, in later years, cause social isolation. Pedmark is seeking approval for use associated with cisplatin chemotherapy in pediatric patients at least 1 month of age to 18 years of age with localized, nonmetastatic solid tumors.

Structural biologist elected to prestigious National Academy of Medicine

Eric Gouaux, Ph.D., was elected to the National Academy of Medicine in 2020. Gouaux, senior scientist at the OHSU Vollum Institute, is an investigator for the distinguished Howard Hughes Medical Institute. Also, Gouaux is OHSU’s principal investigator for the Pacific Northwest Center for Cryo-EM (electron microscopy). Gouaux has an international reputation for discoveries related to molecular structure and mechanisms of chemical synapses in the brain.
The brain surgery simulator developed at OHSU includes a brain, skull and dural membrane (produced using a 3D printer) rigged to a bag containing mock blood. A computer program controls the simulation, displaying “life” signs on real patient monitors and recording the resident surgeons’ every move.
At OHSU, we challenge conventions in education and pioneer new ways of teaching. Not only are our inventive educational programs changing how neuroscience physicians receive training across the United States, but we are also responding to emerging education needs for practicing clinicians through creative continuing medical education.

**Surgical crisis simulators in neurosurgery boot camps become required training**

With blood spurting and alarms sounding, a surgeon only has seconds to respond in a catastrophic simulation developed by OHSU to be as immersive and realistic as possible. Residents practice neurosurgery skills through these realistic but inexpensive model-based simulators in boot camps that are part of the national curriculum for neurosurgery training.

"By creating this immersive environment to practice the technique under stress, we are making a whole generation of surgeons safer and more capable. This year we are reporting in the *Journal of Neurosurgery* on two decades of work that has made neurosurgery training in America radically more effective and safe, and is turning out better neurosurgeons. OHSU has been a leading center driving this."

*Nathan R. Seiden, M.D., Ph.D.*
Neuroscience nurse residency training program

In this special training program, OHSU recruits exceptional nurses for 20 hours of free education to prepare for board certification as neuroscience registered nurses. Lorin Daniels, B.S.N., R.N., CNRN said the nurse residency training program provides specialized education for work in the neurosciences ICU, ensuring that patients will be cared for by competent nurses trained in the nuances of neurological care. OHSU’s NSICU team is one of only three on the West Coast to receive a Silver Beacon Award of Excellence by the American Association of Critical Care Nurses. In one example of their expertise, a protocol devised by NSICU nurses substantially reduced catheter-associated urinary tract infections at OHSU Brain Institute.
MS and neuroimmunology fellowship graduates garner awards

The OHSU Multiple Sclerosis Center’s successful fellowship program celebrated several awards received by new graduates and faculty. Vijayshree Yadav, M.D., M.C.R., the current MS and neuroimmunology fellowship director and the MS Center’s medical director, received a prestigious five-year National MS Society Institutional Clinician Training Award in 2019.

Two recent OHSU fellow graduates received notable awards: a prestigious K23 award from the National Institutes of Health National Center for Medical Rehabilitation Research and a Department of Veterans Affairs Career Development Award (VA CDA). A current fellow also has a pending VA CDA. Also, the OHSU MS Center fellowship added a first-ever pediatric neurologist.
Recent representative publications

Neurosurgery

**Bouchet CA, Ingram SL.** Cannabinoids in the descending pain modulatory circuit: Role in inflammation. *Pharmacology & Therapeutics.* 2020;107495-107495.


Neurology


Faculty

Department of Neurology
Helmi Lutsep, M.D.
Professor and Interim Chair
Prakash Ambady, M.D.
Shannon Anderson, P.A.
Zach Beattie, Ph.D.
Jacqueline Bernard, M.D.
Elis Boudreau, M.D., Ph.D.
Hormoz Bozorgchami, M.D.
William Brewster Smith, M.D.
Matthew Brodsky, M.D.
Michelle Cameron, M.D.
Nizar Chahin, M.D.
Kathryn Chung, M.D.
Wayne Clark, M.D.
Raina Croff, Ph.D.
Marian Dale, M.D.
Walt Dawson, D.Phil.
Alexandra Dimitrova, M.D.
Hiroko Dodge, Ph.D.
Nancy Doolittle, Ph.D.
Julia Durrant, M.D.
Jonathan Elliott, Ph.D.
Ben Emery, Ph.D.
Lia Ernst, M.D.
Deniz Erten-Lyons, M.D.
Melanie Fried-Oken, Ph.D.
Nora Gray, Ph.D.
Nathan Hantke, Ph.D.
Amie Hiller, M.D.
Holly Hinson, M.D., M.C.R.
Scott Hofer, Ph.D.
Fay Horak, Ph.D., P.T.
Cinda Hugos, P.T.
Kim Hutchison, M.D.
Stefanie Kaech Petrie, Ph.D.
Jeffrey Kaye, M.D.
Marissa Kellogg, M.D., M.P.H.
Ed Kim, M.D.
Laurie King, Ph.D.
Eran Klein, M.D.
Jeff Kraakevik, M.D.
Michael Lane, M.D.
Miranda Lim, M.D.
Allison Lindauer, Ph.D., N.P.
Mary Logan, Ph.D.
Pippa Macdonald, M.D.
Martina Mancini, Ph.D.
Ian Martin, Ph.D.
Matthew McCaskill, M.D.
Anusha Mishra, Ph.D.
Paul Motika, M.D.
Leslie Muldoon, Ph.D.
Andrew Natanson, M.D.
Edward Neuwelt, M.D.
Halina Offner-Vandenbark, Ph.D.
Barry Oken, M.D., Ph.D.
Ron Pfeiffer, M.D.
Aimee Pierce, M.D.
Juliette Preston, M.D.
Joseph Quinn, M.D.
Emily Riddle, M.D.
Delaram Safarpour, M.D., M.S.C.E.
Martin Salinsky, M.D.
Sonemany Salinthon, Ph.D.
Lynne Shinto, N.D.
Elizabeth Silbermann, M.D.
Lisa Silbert, M.D.
Asha Singh, M.D.
Amala Soumyanath, Ph.D.
Rebecca Spain, M.D., M.S.P.H.
David Spencer, M.D.
Peter Spencer, Ph.D.
Lauren Talman, M.D.
Andrew Treister, M.D.
Desire Tshala-Katumbay, M.D., Ph.D.
Tarvez Tucker, M.D.
Vivek Unni, Ph.D., Ph.D.
Arthur Vandenbark, Ph.D.
Shawn Westaway, Ph.D.
Gary Westbrook, M.D.
Katherine Wild, Ph.D.
Lindsey Wooliscroft, M.D.
Kirsten Wright, N.D.
Letisha Wyatt, Ph.D.
Vijayshree Yadav, M.D., M.C.R.
Ilker Yavlali, M.D., Ph.D.

Department of Neurological Surgery
Nathan R. Selden, M.D., Ph.D., FACS, FAAP
Campagna Professor and Chair
Nabil Alkayed, M.D., Ph.D.
Prakash Ambady, M.D.
Peter Andersen, M.D.
Kim J. Burchiel, M.D., FACS
Justin S. Cetas, M.D., Ph.D.
Jeremy N. Ciporen, M.D.
Kelly L. Collins, M.D.
Aclan Dogan, M.D.
Maria Fleseriu, M.D., FACE
Mary M. Heinricher, Ph.D.
Susan L. Ingram, Ph.D.
Ines Koerner, M.D., Ph.D.
Jesse Liu, M.D.
Christopher J. Madden, Ph.D.
Shirley McCartney, Ph.D.
Shaun F. Morrison, Ph.D.
Kellie Nazemi, M.D.
Gary Nesbit, M.D.
Edward Neuwelt, M.D.
Josiah Orina, M.D.
Ahmed M.T. Raslan, M.D.
Donald A. Ross, M.D.
W.H. Andrew Ryu, M.D., M.Sc., M.T.M., FRCSC
Christina M. Sayama, M.D., M.P.H.
Domenico Tupone, Ph.D.
Kamil Vagnerova, M.D.
Elena Varlamov, M.D.
Jesse Winer, M.D., FAANS
David Yam, M.D.
Chris Yedinak, M.N., F.N.P., D.N.P.
Garrett Zoeller, M.D.