



FEATURES

Mayo Clinic advances in cancer diagnosis, treatment and prevention

- Mayo Clinic Cancer Center report
- Endometrial cancer testing breakthrough
- Pediatric Brain Tumor Clinic 10
- Colorectal cancer screening game changer 16
- Breast cancer vaccine milestone 20
- Prostate cancer imaging development 22

Connecting disparate investigators 24

Young Investigators Research Symposium

Balfour Award for Meritorious Research 26

Wisit Cheungpasitporn, M.D.

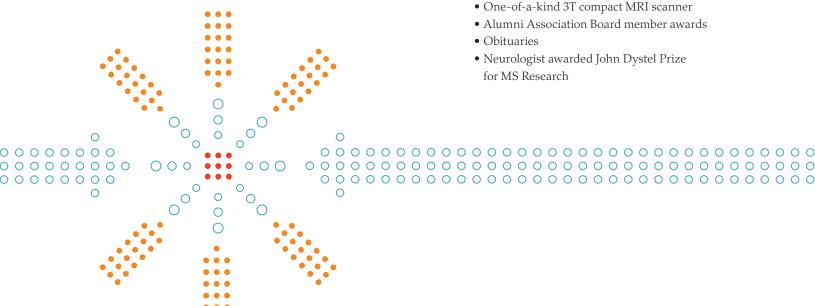
Kendall Award for Meritorious Research 28

Jacqueline Limberg, Ph.D.

Know your Board of Directors 30

MAYO UPDATE 31

- Zika virus vaccine development
- New executive dean for education
- New nanotechnology research lab in Florida
- New Department of Clinical Genomics
- Florida neurogeneticist receives Potamkin Prize for Research
- CEO honored for research advocacy
- One-of-a-kind 3T compact MRI scanner
- Alumni Association Board member awards
- Obituaries
- Neurologist awarded John Dystel Prize for MS Research



Letter from the secretary-treasurer

We've all been touched by cancer — a parent, a friend, a spouse or partner, a colleague, a child or oneself. While the diagnosis is still accompanied by fear, there are many reasons to be hopeful. This issue of *Mayo Clinic Alumni* includes stories about advances in cancer prevention, diagnosis and treatment at Mayo Clinic, affecting children, women and men. You'll see language such as on the brink, game changer and major milestone.

In 1977 Charles Moertel, M.D., then-director of Mayo Clinic Cancer Center, provided a spirited state-of-cancer-care report for the alumni magazine. We use that as the springboard for a current look at cancer care at Mayo Clinic. One key area in which we've progressed in the 39 years between these reports is in translating knowledge from our research into patient care.

Case in point, our researchers have developed a newly commercialized noninvasive colorectal cancer screening tool, and are developing the first-ever screening tool for endometrial cancer — hopefully to be commercialized within two years. We're also conducting vaccine trials for breast cancer and are estimating we'll have vaccines to prevent several cancers within 10 years. And for our youngest patients, we're on a path to have a better treatment for highgrade brain tumors in four to five years.



Peter C. Amadio, M.D.

- Secretary-Treasurer, Mayo Clinic Alumni Association
- Lloyd A. and Barbara A. Amundson Professor of Orthopedics

Indeed, research informs our patient care across the board. You'll see this focus is alive and well in the stories about the Young Investigators Research Symposium and the Balfour and Kendall awards for meritorious research.

In the next issue of this magazine, we'll report on the International Meeting in Whistler, British Columbia, Canada. Be sure to mark your calendar for the next Biennial Meeting (back cover), which is only a little more than a year away. In October 2017 we'll gather in Florida — in Jacksonville for the CME program and Ponte Vedra Beach for lodging and socializing. I hope to see you there.







ABOUT THE COVER | Jamie Bakkum-Gamez, M.D (OBG '06, GYNO '09), Division of Gynecologic Surgery at Mayo Clinic in Rochester, has developed a minimally invasive testing modality to detect endometrial cancer by sensitive molecular testing. This innovation will be the first screening or early-detection test for endometrial cancer.

Mayo Clinic Cancer Center



IS GOOD by Robert Diasio, M.D., Director, Mayo Clinic Cancer Center

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In 1977 Charles Moertel, M.D. (I '58), director of what was then called the Mayo Comprehensive Cancer Center, gave a report on the current state of the center. In conclusion, he said:

> "... I hope I have convinced you that the primary purpose of the Center is to bring the best possible cancer care to today's cancer patient and to tomorrow's cancer patient; that the Center is a mechanism for enriching the practice of a large proportion of our staff through integration of basic research, clinical research, and clinical practice; that the Center is a fiscally sound operation that provides no threat to us, today or tomorrow; and that a strong Comprehensive Cancer Center will help ensure the continued identity of Mayo Clinic as among the finest

> tertiary care centers anywhere."

To read Dr. Moertel's 1977 overview, visit alumniassociation. mayo.edu.

> Thirty-nine years later, I doubt anyone still needs to be convinced that this statement is true. The U.S. News and World Report 2015-2016 rankings list Mayo

> > Clinic at number three on its list of best hospitals for adult cancer care.

> > > The Mayo Clinic Cancer Center has grown and matured in many ways since Dr. Moertel wrote his report. In 1977 Mayo Clinic saw 21,000 cancer patients. In 2013 we saw 122,000 cancer patients at Mayo Clinic. In 1977, 196 Mayo Clinic staff had a "major or total commitment to cancer." Today more

than 1,100 Mayo Clinic physicians, care providers and researchers play a role in caring for our cancer patients.



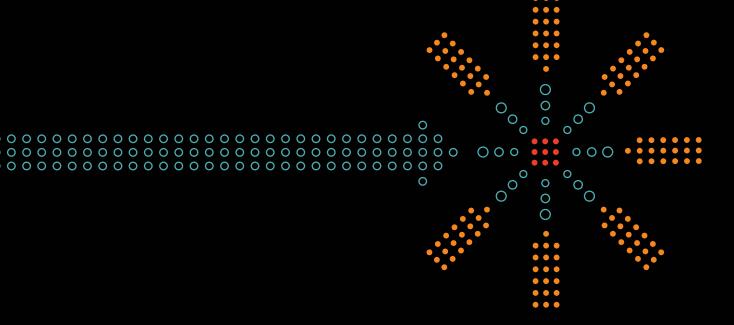
A leading-edge research center

William J. and Charles H. Mayo Professor

The Mayo Clinic Cancer Center is ranked sixth among comprehensive cancer centers in the amount of funding received from the National Cancer Institute (NCI). After the most recent NCI competitive grant renewal in 2013, the Mayo Clinic Cancer Center earned the NCI's highest ranking — exceptional and received \$28.6 million in funding over five years.

Today we also receive more than \$109.7 million in competitive peer review grants that support cancer research, including the NCI's highly sought-after Specialized Programs of Research Excellence (SPORE) grants. SPORE grants support projects intended to produce new approaches to the prevention, early detection, diagnosis and treatment of cancer. The Mayo Clinic Cancer Center has five NCI SPORE grants and one SPORE grant that is shared with another institution. These grants support research in brain cancer, breast cancer, multiple myeloma, ovarian cancer, pancreatic cancer and lymphoma.

les Moertel, M.D.



We've become a leader in translating knowledge gained from cancer research into better patient care. We have 10 major cancer research programs that translate scientific discoveries in the laboratory into leading-edge treatments and therapies for patients:

Cancer Immunology and Immunotherapy
Cancer Prevention and Control
Cell Biology
Developmental Therapeutics
Gastrointestinal Cancer
Gene and Virus Therapy
Genetic Epidemiology and Risk Assessment
Hematologic Malignancies
Neuro-oncology

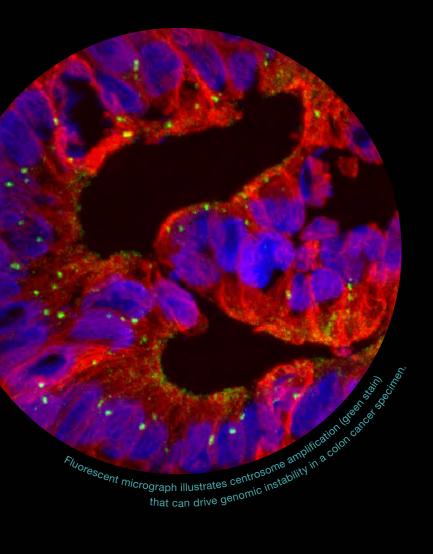
Women's Cancer

More than 330 Mayo Clinic Cancer Center member researchers and about 250 allied health staff contribute to our research initiatives. These efforts are bolstered by research support services that provide access to cutting-edge technology and methodology, scientific consultation, reliability, cost-effectiveness and quality control.

These resources help to provide our patients with access to hundreds of clinical trials led by Mayo Clinic physicians and scientists. Even more trials are available through cooperative research agreements with the NCI and clinical trial study groups.

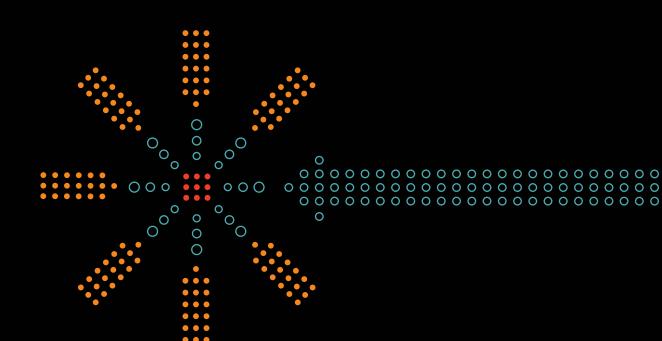


The National
Cancer Institute (NCI)
awarded the Mayo Clinic
Cancer Center its
highest ranking:
EXCEPTIONAL



We play a leadership role in the nation's clinical trial study groups and receive NCI funding to serve as one of 30 Lead Academic Participating Sites in the NCI National Clinical Trials Network, the Statistics and Data Center for the Alliance for Clinical Trials in Oncology, and the Alliance NCI Community Oncology Research Program Research. Our other national research initiatives include:

- Leading the NCI-funded Lymphoma
 Epidemiology of Outcomes Cohort Study, which
 will enroll 12,000 patients with non-Hodgkin
 lymphoma and follow them to learn more about
 their long-term prognosis and survivorship
- Serving as the administrative and research base for the Cancer Prevention Network, a clinical trial study group
- Conducting phase I clinical trials of new anticancer agents or combinations of agents as part of an NCI Experimental Therapeutics Clinical Trials Network grant
- Serving as the base for the Pancreatic Cancer Genetic Epidemiology Consortium, a group of NCI-funded individuals searching for the genetic underpinnings of pancreatic cancer
- Hosting the Research Coordinating Center for Academic and Community Cancer Research United



Research-driven, patient-centered care

Dr. Moertel called for "the wave of the future in cancer management [to] bring the fruits of the basic science laboratory to the bedside of the patient." Thirty-nine years later our cancer research transforms our cancer practice on a daily basis.

In 2014 researchers at the Mayo Clinic Cancer Center proved they had developed an effective new method of screening for colorectal cancer that uses stool DNA (page 16). Called Cologuard, the screening test was developed to provide a new choice in colorectal cancer screening. Research shows that patients who are offered alternatives are more likely to comply with screening. Cologuard is mailed to patients at home and requires only a stool sample. It is easy to use, inexpensive, and requires no bowel prep, medication or dietary restrictions. Colonoscopy, the most widely used screening method, is expensive and requires bowel prep, sedation and time off work. Cologuard may help remove some of the barriers that prevent people from getting screened.

In 2015 Mayo Clinic researchers demonstrated that it was possible to detect endometrial cancer using tumor DNA picked up by ordinary tampons (page 8). The new approach specifically examines DNA samples from vaginal secretions for the presence of chemical "off" switches — known as methylation — that can disable genes that normally keep cancer in check. The finding is a critical step toward a convenient and effective screening test for endometrial cancer, the most common gynecologic malignancy in the United States.

Mayo Clinic physicians, care providers and researchers care for our cancer patients

May 2015
Minnesota

Proton Beam
Therapy Program

March 2016
Arizona

We collaborate closely with the Mayo Clinic Center for Individualized Medicine to use genetics to more effectively and precisely diagnose, treat, predict and prevent cancer. Some highlights from our advances in targeted and precision medicine over the past year include:

- A team of Mayo Clinic researchers announced that it had succeeded in identifying the source of cancer in patients' gastrointestinal tracts by analyzing DNA markers from tumors. The results open the possibility that physicians could one day screen for cancer anywhere in the body with a noninvasive blood test or stool sample.
- Herceptin has been touted as a wonder drug for women with HER2-positive breast cancer, an aggressive form of the disease that is fueled by excess production of the HER2 protein. However, not all of these patients respond to the drug, and many who do respond eventually acquire resistance. A team of researchers led by Mayo Clinic found a promising way to circumvent this obstacle. They identified a small site in the HER2 protein that enables it to form a molecular switch that sets off a cascade of events that turn normal cells cancerous. The researchers showed that disrupting this site can stem the growth of breast cancer cells even more effectively than drugs currently used in the clinic.

• A team of researchers, including scientists from the Translational Genomics Research Institute (TGen) and Mayo Clinic, reported that analyzing circulating tumor DNA can track how a patient's cancer evolves and responds to treatment. This type of blood test, known as a liquid biopsy, is less invasive, less costly and less risky than conventional tissue biopsies, which essentially are minor surgeries. Obtaining liquid biopsies could occur more frequently too, providing physicians with up-to-date information about how a patient's cancer might be changing and helping in the selection of the best possible treatments to combat it.

We embrace new technology to provide the best possible cancer treatment for our patients. The Mayo Clinic Cancer Center launched a Proton Beam Therapy Program on our Minnesota campus in May 2015 and on our Arizona campus in March 2016. The radiation beam used in proton beam therapy targets only the tumor, better sparing surrounding healthy tissue from harm. Proton beam therapy is used to treat many kinds of cancers located deep within the body and close to critical organs and body structures, especially in children and young adults.

We're constantly looking to expand our reach in advancing the science and practice of cancer care. In 2014 the Mayo Clinic Cancer Center became a member of the National Comprehensive Cancer Network (NCCN), a not-for-profit alliance of leading cancer centers dedicated to improving the quality, effectiveness and efficiency of care for cancer patients. Forty-seven Mayo Clinic representatives now serve on 47 different NCCN Guidelines Panels. Together with other NCCN member institutions, we're working to continuously advance our national expertise in cancer care.



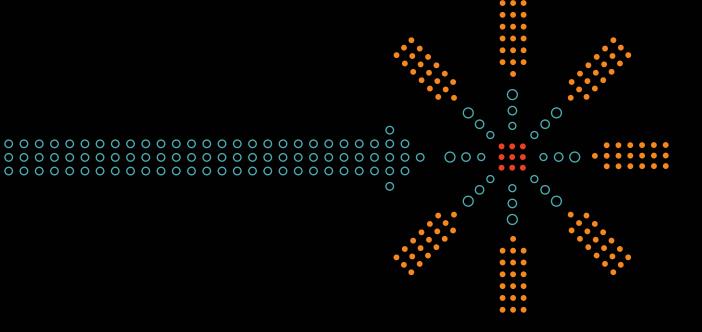
We've made incredible progress in the almost four decades since Dr. Moertel wrote his report."

- Robert Diasio, M.D.









The prognosis is good — with increased research funding

We've made incredible progress in the almost four decades since Dr. Moertel wrote his report. Since then, advances in biomedical research have helped us better understand the collection of diseases we call cancer. We now know that genetic mutations cause most cancers — knowledge that has launched the era of precision medicine. According to the American Association of Cancer Research (AACR), as of July 31, 2015, there were 52 different therapeutics targeting specific molecules involved in cancer. Precision therapy and immunotherapy have been firmly established as the future of cancer care.

More people diagnosed with cancer now survive the diagnosis. In 1975 the five-year relative survival rate for all cancers combined was 49 percent. By 2010 it had risen to 68 percent. From 2002 to 2011 overall cancer death rates declined by 1.8 percent per year for U.S. men, by 1.4 percent per year for U.S. women and by 2.1 percent per year for 0–19 year olds.

Despite such progress, cancer remains a weighty diagnosis. It is estimated that 8.9 million people will die from some form of cancer in 2015 — 589,430 of those people in the United States. Cancer still accounts for one in four deaths in the United States and one in seven deaths worldwide. Cancer is the number-one

cause of disease-related death among U.S. children. And the number of cancer diagnoses is expected to grow — from 1,658,370 U.S. cancer cases in 2015, to 2,387,304 in 2035 (AACR Cancer Progress Report 2015).

Sadly, our continued progress in understanding and treating cancer remains at risk. Budgets for the National Institutes of Health (NIH) and NCI have not kept pace with inflation. Direct cuts in 2011 and 2013 further eroded budgets. The AACR reports that since 2004 the NIH has lost approximately 25 percent of its ability to fund lifesaving biomedical research.

If we are to secure continued progress in the fight against cancer, we must urge Congress to increase funding for the NIH and the NCI.

As the Mayo Clinic Cancer Center looks to the future, our vision echoes that of Dr. Moertel — to continue to build and strengthen an integrated cancer practice across all Mayo Clinic sites, departments, service lines and care delivery platforms. A practice that provides an unparalleled health care experience to our patients.

Remembering our primary value as an institution — the needs of the patient come first — will ensure Mayo's continued status as one of the finest cancer centers in the world. •



ON THE BRINK

First-ever screening test for endometrial cancer

recently awarded her team a Transform the Practice Team Award to push the work toward a commercially available clinical test within two years.

Women from around the U.S. have contacted Mayo Clinic to participate in the ongoing clinical trial.

"We've had immense support for this project, including Mayo's Department of Research, which recognizes this aspect of women's health as important and deserving of support and research," says Dr. Bakkum-Gamez. "Our work has only been possible due to a multidisciplinary team with expertise from Laboratory Medicine and Pathology, Experimental Pathology, and OB/GYN providers across the enterprise, including nurse practitioners and physician assistants."

With baby boomers now in the age risk category for endometrial cancer, the number of women diagnosed each year is increasing, as is the mortality rate. Black women have lower incidence than Caucasian women but have a higher mortality rate, likely attributable to access to medical care.

"We're working on an epidemiologic study to validate risk predictors and determine when women should be screened," says Dr. Bakkum-Gamez. "Because our test is a first, we don't have existing guidelines to steer us."

amie Bakkum-Gamez, M.D. (OBG '06, GYNO '09), is on a course to change women's health care. Her work could yield results similar to that of Georgios Papanikolaou, M.D., inventor of the Pap test used around the world to detect and prevent cervical cancer and other diseases of the female reproductive system.

Dr. Bakkum-Gamez, Division of Gynecologic Surgery at Mayo Clinic in Rochester, is working on the development of a minimally invasive testing modality — a tampon — to detect endometrial cancer by sensitive molecular testing (DNA methylation). This will be the first screening or early-detection test for endometrial cancer.

"The Pap test changed the lives of millions of women, and a screening test for endometrial cancer could do the same," she says. "Our goal has always been to improve the outcomes for women at risk for endometrial cancer — to prevent cancer or at least detect it earlier. Ultimately we want to save lives."

Support externally, internally and from women around the country

Dr. Bakkum-Gamez's research has been funded by the National Cancer Institute and Mayo Clinic, which



This is a low-cost, easy-to-access screening test that could address racial and socioeconomic disparities in mortality from endometrial cancer."

- Jamie Bakkum-Gamez, M.D.



Learning from Cologuard experience

Dr. Bakkum-Gamez points out that the simplicity of the tampon test will be similar to Cologuard for colorectal cancer — a prescribed, self-administered mail-in test (page 16). These features may help to overcome access-to-care barriers. "A low-cost, easy-to-access screening test could address racial and socioeconomic disparities in mortality from endometrial cancer."

Her team continues to work on fine-tuning the gene panel, with help from David Ahlquist, M.D., who developed Cologuard, and his team in the Division of Gastroenterology and Hepatology.

"Dr. Ahlquist is collaborating with us to make sure we're being as comprehensive as possible and not missing a potential signature gene," says Dr. Bakkum-Gamez. "We're learning from his Cologuard experience and expertise."

Easier way to obtain specimens for analysis

In addition to early detection of endometrial cancer, the test also promises to improve the patient experience. "Women can have signs of endometrial cancer that turn out to be caused by a polyp or dysfunctional uterine bleeding," she says. "Currently, they may have to have an endometrial biopsy to rule out cancer. Our test will provide a way to obtain specimens for analysis more comfortably.

"This is an exciting time in women's health as we're on the brink of introducing a life-changing test for cancer." •

HOPE FOR YOUNG PATIENTS

Pediatric Brain Tumor Clinic

ddyson Cordes, now almost 5 years old, was diagnosed at age 13 months with an atypical teratoid/rhaboid tumor (AT/RT), a rare and aggressive malignant brain tumor. Neurosurgery, chemotherapy and proton beam therapy followed, all before she was 3. She has needed additional Mayo Clinic services including physical medicine and rehabilitation, audiology, ophthalmology and endocrinology due to side effects of her treatment. She'll continue to be monitored throughout her life.

Addyson has benefited from Mayo's Pediatric Brain Tumor Clinic, which was established right around the time she was born.

Neuro-oncology-led team

Addyson's parents, Michele Zidlicky and Nathan Cordes, of Wanamingo, Minnesota, have had a central

V_{nulsa} Nageswara Rao, M.B.B.S.

care at Mayo Clinic. Before the Pediatric Brain Tumor Clinic was created, patients' parents worked with the neuro-oncologist, neurosurgeon, radiation oncologist and other specialty services separately.

contact for and coordination of all of their daughter's

"Prior to having this integrated approach, parents received information in a less connected way, which made their decision-making more difficult," says Amulya Nageswara Rao, M.B.B.S. (PDHO '10), a neurooncologist and director of the Pediatric Brain Tumor Clinic. "Now we bring together all of the experts, led by the neuro-oncologist, who serves as the primary physician. We explain what the months and years ahead will look like and what the challenges will be. This makes the family's journey easier."

Zidlicky says everyone involved in her daughter's care has been wonderful, but Dr. Nageswara Rao has been an important point person. "When Addy was on the rehab floor, Dr. Rao came to talk to us just to learn more about us, what we do for work and fun, and what our concerns were. She understood we were scared that our most precious gift would be taken away from us. She and everyone on the team talk to us in a way we can understand — not using medical terms."

Clinic's genesis

Dr. Nageswara Rao had a vision to establish the clinic when she was a pediatric hematology/oncology fellow at Mayo Clinic in 2007.

"I'd wanted to work with kids since medical school," she says. "I chose Mayo Clinic for my fellowship because of its reputation for the team approach to medicine. >>

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Proton beam therapy — powerful advance for pediatric tumor treatment

Mayo Clinic's Proton Beam Therapy Program – Rochester campus opened a year ago. The program on the Arizona campus opened this spring. To date in Rochester, almost one-fourth of patients treated with proton beam therapy have been children.

Because of their increased sensitivity to the effects of radiation, children may particularly benefit from proton beam therapy's precision. Mayo Clinic uses intensity-modulated proton beam therapy with pencil beam scanning, closely targeting tumors and sparing healthy tissue.

"Although reducing unnecessary radiation is beneficial for many cancer patients, children with cancer stand to benefit the most from proton beam therapy," says Nadia Laack, M.D. (RADO '06), a pediatric radiation oncologist at Mayo Clinic in Rochester. "Proton radiotherapy reduces the low-dose radiation exposure that is seen with conventional radiation. Because their organs are still developing, children can have significant long-term harm from even low doses of radiation including growth problems, hearing and vision loss, radiation-induced cancers and heart disease."

I began to establish the relationships I'd need for a comprehensive clinic. As I started to work in oncology, I realized our work goes beyond cures. These young patients endure the long-term effects of cancer and its treatment. Our work must involve making sure they also have the best adulthood possible and helping with all aspects of the care they need throughout their lives."

To establish the clinic she envisioned, Dr. Nageswara Rao wanted additional training and experience. She pursued a subsequent fellowship in pediatric neuro-oncology at Children's National Medical Center in Washington, D.C., training with Roger Packer, M.D., a well-known figure in pediatric brain tumors.

"I planned to learn a good care practice model, return to Mayo to establish a pediatric brain tumor clinic, and bring together the right team to provide patients and their families with comprehensive, integrated care," she says.

Clinic realized

Dr. Nageswara Rao returned to Mayo Clinic in 2011 and outlined the comprehensive team model for the clinic.

"These types of tumors are challenging and complex, and require an integrated team approach to help with decision-making," she says. "As the new comprehensive clinic was formed, we agreed that our experts would come together and determine a course of action that we would discuss with the family to help them make decisions. Every division that would be involved in caring for these patients was immediately supportive and shared a vision to help these children."

In addition to neuro-oncology, neurosurgery, radiation oncology and neurology, patients often need care from endocrinology, neuropathology, neuroradiology, neuropsychology, audiology, and physical medicine and rehabilitation.

Today the Mayo Clinic Pediatric Brain Tumor Clinic diagnoses 60 to 70 new patients a year and treats many recurrent tumors. Treatment advances include computer-assisted brain surgery, brain-mapping techniques, intraoperative MRI, awake brain surgery, proton beam therapy, and chemotherapy ranging from a phase I clinical trial to bone marrow transplantation.

Dr. Nageswara Rao, with the support of Mayo Clinic neuropathologist Caterina Giannini, M.D., Ph.D. (N '89, APATH '94, NPATH '96), has been building a robust research component into the clinic, including establishing tumor banks and national and international





collaborations. One of these is for diffuse intrinsic pontine gliomas (DIPGs) — fatal brain tumors with no cure.

She also developed national and international partnerships for clinical trials. In 2015 Mayo Clinic started a new phase I clinical trial in pediatric cancer (page 15).

"All of these specialties have expertise in different aspects of diagnosis and treatment of kids with brain tumors," says Dr. Nageswara Rao. "We try to achieve a cure and ensure the best functional and neurocognitive outcomes for each child."

Addyson's case

Addyson Cordes was no exception. She recently marked three years since completing treatment. "She's stable but has to be watched," says Zidlicky. "We return to Mayo regularly for scans."

Zidlicky says the family's outlook is markedly different from when her daughter was diagnosed. It was predicted Addyson would not live past 2 years old, in part because of the aggressive nature of the tumor and the effects treatment would have on someone so young.

"When Addy was diagnosed, we faced having only a few months left with her," says Zidlicky. "Dr. Rao told us it wasn't an easily treatable cancer, and it had already spread to the spinal fluid and spinal cord. She said it was the fourth AT/RT case Mayo had seen, and the other children hadn't survived. She was honest with us from the start about how bad it was and what to expect."

Addyson had surgery followed by rehabilitation therapy at Mayo Clinic to regain function. Although she'd

begun walking at 9 months old, she lost that function as a result of surgery and had to start over. It took a full year of rehabilitation before she could stand by herself again.

She had seven rounds of inpatient chemotherapy as part of a clinical trial. The last three rounds included high-dose stem cell chemotherapy (autologous bone marrow transplant). One of the chemotherapy drugs affected her hearing and required her to be fitted with two hearing aids.

When she was 18 months old, Addyson had proton beam therapy in Houston. (Mayo Clinic's Proton Beam Therapy Program opened in 2015.) A scan after the treatment concluded showed the cancer was no longer in Addy's spinal fluid.

"When Addy finished treatment, Dr. Rao said, 'She's doing well. It's time to go live your life,'" says Zidlicky. "We're living life now and just want to enjoy Addy and experience things she hasn't experienced. The further we get from cancer, the better the chances are. We know Addy can get her cancer back or secondary cancer, but we take it a day at a time and live it to the fullest.

"Mayo Clinic saved her life. They're like our family. It's obvious they support us and want our daughter to succeed."

Dr. Nageswara Rao says Addy's survival may be due to several factors — her Mayo team's evolving expertise in brain tumors, her participation in a clinical trial and her own good fortune in overcoming many obstacles.

Preschooler Addy can't grasp with her right hand and wears an ankle brace for support. Despite these challenges, Zidlicky describes her daughter as a social butterfly.

That's music to Dr. Nageswara Rao's ears. "This work has changed my attitude about life. The things that were big no longer are. I focus on how happy the child is today.

"I get a lot from these patients. They face challenges a regular child doesn't go through. I see families reprioritize their lives. I see them laugh and play. Their battles are much greater than mine. I feel privileged and lucky to be on their journeys." ◆



Nathan Cordes and Michele Zidlicky of Wanamingo, Minnesota, are grateful to Mayo Clinic for daughter Addyson's brain tumor care.

Phase I clinical trial in pediatric cancer focuses on virus-based therapy

Mayo Clinic has begun a new phase I clinical trial in pediatric cancer, and it focuses on a virus-based therapy.

The trial is testing the safety and maximum dosing of the virus-based drug Reolysin used in combination with granulocyte-macrophage colony stimulating factor (GM-CSF). Reolysin is produced from a reovirus, a benign virus that may cause little or no flu-like symptoms. Reovirus has been shown to preferentially infect and kill many different types of tumors. GM-CSF may promote the tumor cell-killing effects of Reolysin.

Potential beneficiaries are young people ages 10 to 21 with relapsed or refractory high-grade brain tumors including anaplastic astrocytoma, glioblastoma multiforme, medulloblastoma, atypical teratoid/rhabdoid tumor (ATRT), diffuse intrinsic pontine glioma (DIPG) and primitive neuroectodermal tumor (PNET).

Impetus for trial

Shannon O'Hara was treated for a DIPG at Mayo Clinic in 2011. When her tumor recurred later that year, she was referred to St. Jude Children's Research Hospital in Memphis, Tennessee, for a clinical trial overseen by Mayo alumna Cynthia Wetmore, M.D., Ph.D. (PD '02) (now director of the Center for Clinical and Translational Research at Children's Healthcare of Atlanta, Georgia).

Although Shannon was unable to complete the trial due to tumor growth and loss of function, she and her





parents wanted to donate her tumor cells to research. When Shannon died in Rochester in 2012 at age 13, Dr. Wetmore worked with Mayo Clinic pathology to harvest the cells so they could be sent to her.

Richard Vile, Ph.D. (NMED '98), departments of Molecular Medicine and Immunology at Mayo Clinic in Rochester, attended Shannon's funeral. His son had played tennis with her. Learning about Shannon's story and seeing her parents' pain had a profound effect on Dr. Vile. He refocused his research on using immunotherapy to treat DIPGs. His work led to the phase I reovirus clinical trial.

"DIPGs are universally fatal in children," says Dr. Vile, the Richard M. Schulze Family Foundation Professor. "Dr. Wetmore sent us some of Shannon's cancer cells to use in our research. To date, we've treated three patients in our new trial, with a goal of 15. We hope to have a treatment that we can use more routinely in patients in four to five years."

Dr. Vile collaborated with pediatric hematologist/ oncologist Richard Bram, M.D., Ph.D. (PD '98), and neurooncologist Amulya Nageswara Rao, M.B.B.S., to bring the trial to the Pediatric Brain Tumor Clinic.

Mayo Clinic clinical trials

> mayo.edu/research/clinical-trials

GAME CHANGER

Working to make colorectal cancer an uncommon disease

avid Ahlquist, M.D. (MED '77, I '80, GI '83), Division of Gastroenterology and Hepatology at Mayo Clinic in Rochester and the Carol M. Gatton Professor of Digestive Diseases Research Honoring Peter Carryer, M.D., has devoted his career to finding ways to detect gastrointestinal (GI) cancers early.

Initially his work focused on finding better ways to detect blood in stool — the go-to screening methodology for colorectal cancer for the last four decades. He validated the HemoQuant test, which is still used to quantify blood lost in the GI tract.

But Dr. Ahlquist eventually concluded that blood was a suboptimal marker for colorectal cancer, and he began to explore other detection methods.

"In the face of screening efforts over the last three decades, colorectal cancer remains the second-leading cancer killer in the United States," says Dr. Ahlquist. "We know it's completely curable and preventable if cancer is detected early or if premalignant polyps can be found. But the sad reality is that only about half of the

population that should be screened is actually being screened. In part, that's because screening options are invasive, require time away from work and may not be readily accessible. A large part of our population lives paycheck to paycheck and cannot afford to take off the requisite two days to prepare for and have a colonoscopy."

To help fill this gap, Dr. Ahlquist began a quest to develop an accurate, noninvasive tool that requires no bowel preparation or time off from work and has no diet or medication restrictions. The resulting test, Cologuard, relies on DNA — not blood — shed into stool. Introduced in late 2014, Cologuard is significantly more accurate than stool blood testing and rivals colonosocopy for detection of curable-stage colorectal cancer.

Dr. Ahlquist worked for years to determine which DNA signaled precancer or cancer. He collaborated with Exact Sciences of Madison, Wisconsin, to develop Cologuard. The company had new technology that allowed them to examine stool more easily to find the DNA markers.



We wanted to do for colorectal cancer what the Pap test did for cervical cancer — facilitate early and regular screening to prevent cancer and death."

- David Ahlquist, M.D.



"We wanted to do for colorectal cancer what the Pap test did for cervical cancer — facilitate early and regular screening to prevent cancer and death," says Dr. Ahlquist of the new stool DNA test. "Polyps and cancer continuously shed cells that end up in stool. Cologuard can recover cancer or polyp-related DNA in those exfoliated cells and determine the presence or absence of the molecular signature of a target lesion."

Proof

In 2014 *The New England Journal of Medicine* published the pivotal study in this research that showed the effectiveness of stool DNA testing in a clinical trial of more than 10,000 subjects at 90 centers in the U.S. and Canada. The trial compared the stool DNA test and the fecal immunochemical test (FIT, the most commonly used fecal occult blood test) to colonoscopy. Cologuard accurately detected cancers and advanced adenomas more often than FIT.

Major findings from clinical trial

Sensitivity for colorectal cancer

Cologuard	overall		92%
	earliest-stage cancer		94%
FIT	overall	74 %	
	earliest-stage cancer	70%	

Detection rates, polyps with high-grade dysplasia



Detection rates, serrated sessile polyps larger than 2 centimeters

Cologuard		67 %
FIT	11%	

False-positive rates per year

Cologuard (recommended every 3 years) 3-4%
FIT (recommended every year) 5%

Dr. Ahlquist says the 94 percent detection rate for the earliest stage cancers compares very well with the reported detection rates by colonoscopy, which are in the 92 to 96 percent range. >>



Cologuard was nominated for Best Medical Technology at the Prix Galien in New York City last fall. Dr. Ahlquist (second from right) attended with collaborators from Exact Sciences - (from left) Kevin Conroy, president and CEO; Graham Lidgard, Ph.D., chief science officer; and Maneesh Arora, chief operating officer.

Further proof

Cologuard may offer improved access to screening for communities that lack medical facilities.

Dr. Ahlquist, in conjunction with researchers from the Alaska Native Tribal Health Consortium, tested Cologuard among Alaska Native people. In this study Cologuard detected 100 percent of the colorectal cancers and was significantly more sensitive than FIT for polyp detection.

The high detection rates for cancer and large polyps by Cologuard in the Alaska study were remarkably similar to those demonstrated in the 10,000-patient screening study of the general U.S population reported in The New England Journal of Medicine.

Approval

Cologuard was approved by the Food and Drug Administration (FDA) and Centers for Medicare & Medicaid Services (CMS) in 2014. Cologuard was the first product appraised through a parallel FDA-CMS review to reduce the time between FDA approval and Medicare coverage. The American Cancer Society also includes Cologuard in its colorectal cancer screening guidelines.

The United States Preventive Services Task Force (USPSTF), however, has not yet fully recommended Cologuard, citing lack of long-term evidence to support the method. Instead, the Task Force's preliminary position was to designate Cologuard as an alternative rather than frontline screening approach. In alliance with the American Cancer



How Cologuard works

- A physician must prescribe Cologuard, a self-contained collection kit, which is sent to the patient's home.
- The test is painless and noninvasive. No dietary or medication changes are necessary, and no preparation
- for hemoglobin and certain mutations associated with colorectal cancer.
- Results of the test are sent to the prescribing physician.
- If the test is positive, the patient is advised to have a diagnostic colonoscopy.
- If the test is negative, the patient should repeat it every three years.



Cologuard is available at all three Mayo Clinic campuses and has rolled out to many large health care organizations and systems. Private practice physicians can register directly with the manufacturer.

Society Cancer Action Network, Mayo Clinic has challenged the USPSTF position.

Robert Diasio, M.D. (MPET '06), director of the Mayo Clinic Cancer Center, asked the USPSTF to allow patients unfettered access to this new stool DNA test based on its clearly demonstrated performance merits.

Mayo Clinic president and CEO John Noseworthy, M.D. (N '90), also addressed the USPSTF: "There is compelling scientific evidence that this innovative approach can increase screening accuracy and potentially save lives. We need to remove cost, culture, location and other barriers to improve access to effective screening."

Adoption

Mayo Clinic has made Cologuard available as a primary screening method for its patients. "Part of our aim in adopting this screening method was to increase screening access and compliance, and this approach does both," says Vijay Shah, M.D. (GI '98), chair, Division of Gastroenterology and Hepatology. "We want our patients to benefit from this test's high detection rates of early-stage cancer and polyps at greatest risk of progression, which is unprecedented for noninvasive tests."

Exact Sciences runs the commercial laboratory that distributes Cologuard and tests samples that are mailed in. Among the first 100,000 patients to send in tests, 42 percent had never before been screened for colorectal cancer by any approach.

"That's exactly what we were hoping for — moving the unscreened to the screened category," says Dr. Ahlquist. "Statistically, among 100,000 people, there would be 500 new cancer diagnoses. If we can continue this trend and screen the half of the population that remains unscreened, colon cancer could become an uncommon disease. Cervical cancer used to be the leading cancer killer of women and is now uncommon with regular Pap smears. Cologuard may be an even more sensitive screening tool than the Pap test. The possibilities are exciting and far-reaching."

Future

Dr. Ahlquist and his research team are working on refining stool DNA testing to screen for other cancers in the digestive tract. Together, cancers of the throat, esophagus, stomach, pancreas, liver, bile duct, gallbladder and small bowel cause twice as many deaths

Applications for the esophagus

Prasad Iyer, M.D. (GI '06, CTSC '07), Division of Gastroenterology and Hepatology, is collaborating with Dr. Ahlquist on a noninvasive technique for the early detection of esophageal neoplasia in Barrett's esophagus. Dr. Iyer and his team are studying DNA biomarkers

obtained in a swab capsule on a string that a patient swallows and is then pulled out. Early data show very high rates of sensitivity and specificity.

as colorectal cancer, but cancers in these upper GI organs aren't screened, in part, due to a lack of effective, affordable screening tools.

"The current cancer screening approach is clunky
— one organ at a time," says Dr. Ahlquist. "Molecular
technology allows us to reimagine screening — multiple
organs at a time for more efficient, personal screening of
people instead of organs."

Dr. Ahlquist envisions stool DNA tests to do the following:

- Early detection of cancers above the colon in addition to colorectal cancers
- Cancer screening of multiple organs, rather than just one organ, with a single noninvasive test
- Prediction of cancer location with DNA markers that are specific to tumor site
- Prevention of cancer through detection of premalignant lesions, including pancreatic cancer

"With my colleague Dr. John Kisiel (I '07, CMR '08, GIH-N '09, GI '12, CTSA '13) and others, we have a multicenter study underway to look at stool DNA testing to detect cancer and precancer (dysplasia) in patients with inflammatory bowel disease," says Dr. Ahlquist. "Early results suggest outstanding detection rates. Patients with this condition are advised to have colonoscopy every year or every other year, but the compliance rate is low. Our goal is to improve outcomes in this group at high risk for colorectal cancer with this accurate and noninvasive test that may be more convenient to many." •

Prasad Wer, M

MAJOR MILESTONE

A vaccine to prevent recurrent breast cancer

leven years after joining the staff of Mayo Clinic in Florida, Keith Knutson, Ph.D. (IMM '05), is another big step closer to realizing his career-long research goal. He's just begun a phase II clinical trial for a new vaccine to prevent recurrent breast cancer.

This folate receptor alpha vaccine exploits the need of triple-negative breast cancer to take in folic acid to grow. Triple-negative tumors overproduce the folate receptor alpha, which latches on to folic acid in the tumor's microenvironment. The vaccine is designed to boost the immune system to rapidly react to the presence of the receptor on cancer cells early in the course of tumor recurrence.

A previous phase I clinical trial conducted at Mayo Clinic in Rochester found the vaccine safely induced tumor-specific immune responses and did not induce autoimmunity like some vaccines do.

"Triple-negative breast cancer has a poor prognosis, and these patients have a high risk of a relapse of their cancer," says Dr. Knutson, professor of immunology and director of Mayo Clinic in Florida's Cancer Research Program. "The only available treatment is toxic chemotherapy, so there's a significant need to identify targeted approaches.

"We believe this vaccine will provide a much more robust and sustained immune response to these receptors, which will improve the body's ability to kill the tumor if it begins to re-emerge. If successful, this vaccine will reduce exposure of patients to subsequent life-threatening therapies."

Dr. Knutson hopes to have a phase III trial at the end of five years and, within 10 years, have vaccines to prevent breast, ovarian and possibly other cancers.

"One of my most important goals has been to move my discoveries from the laboratory to patients," says Dr. Knutson. "I am pleased to have had that opportunity due, for the most part, to the collaborative and fostering environment at Mayo Clinic."

Support, funding and eligibility

The vaccine was developed at Mayo Clinic, with support from Mayo Clinic Ventures to file patents and find a vaccine technologies company for licensing and phase I clinical trial funding.

The phase II clinical trial is funded by a five-year, \$13.3 million federal grant — a Breakthrough Award from the U.S. Department of Defense's Breast Cancer Research Program.

Dr. Knutson hopes to have a phase III trial at the end of five years and, within 10 years, have vaccines to prevent breast, ovarian and possibly other cancers.



The trial will involve 280 patients from all three Mayo Clinic campuses and select sites in Mayo Clinic's Academic and Community Cancer Research United, a clinical research network of more than 65 academic institutions and community-based cancer treatment practices in the U.S. and Canada. Eligible patients are those with resected or removed triple-negative breast cancer whose tumors express the folate receptor alpha protein.

'One of our most important research goals'

Edith Perez, M.D. (HEMO '95), Mayo Clinic Cancer Center in Florida, is a principal investigator on the trial with Dr. Knutson.

"Unlike most forms of breast cancer, triple-negative isn't fueled by estrogen and can't be treated with estrogen blockers such as Tamoxifen," says Dr. Perez. "We want to wake up the immune system so the patient's own body fights any cancer cells remaining after standard chemotherapy treatment. Continued improvement in therapies for patients with triplenegative breast cancer is one of our most important research goals." •

Mayo Clinic clinical trials

mayo.edu/research/clinical-trials

Issue 2 • 2016 21

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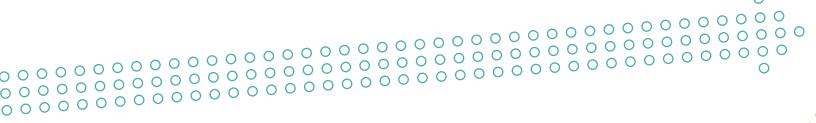
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PRECISION MEDICINE

Choline C-11 — Mayo Clinic's first NDA



hen prostate cancer recurs after treatment, it's difficult, if not impossible, for physicians to know where the cancer has spread.

Further treatment, then, involves a certain amount of speculation. As a result of the ambiguity, some of the 100,000 men whose prostate-specific antigen (PSA) levels rise after initial treatment remain on hormone medication for life.

But the landscape of recurrent prostate cancer treatment is changing due to an advance pioneered by Mayo Clinic. In 2012 Mayo Clinic was approved by the Food and Drug Administration (FDA) for a new drug application (NDA) — Mayo Clinic's first. The drug approved, initially for Mayo Clinic use exclusively, is choline C-11 in primary, recurrent and metastatic prostate cancer.

Choline C-11 uses a radioactive form of the vitamin choline, which is readily absorbed by cancer cells. The drug is injected into the patient, who has a positron emission tomography (PET) scan to see where the drug collects in any prostate cancer tumors regardless of location.



Choline C-11 lets us pinpoint at a very early interval where the cancer is returning."

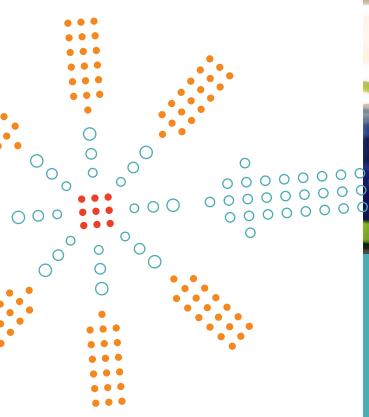
- Eugene Kwon, M.D.

Earliest detection method

"Choline C-11 lets us pinpoint at a very early interval where the cancer is returning," says Eugene Kwon, M.D. (U '02), Department of Urology, Mayo Clinic in Rochester. "Based on what we see in the PET scan, we can more intelligently assign the patient's next therapy."

Dr. Kwon says choline C-11 can identify prostate cancer about seven years before any other form of conventional scanning, including MRI, bone and CT. To date Mayo Clinic has used the new imaging agent for more than 3,500 patients from around the world to identify the site of their relapse and determine the next form of treatment.





Non-proprietary

Mayo Clinic chose not to protect its NDA so other institutions could use choline C-11 to help patients. "We're interested in the best care for patients around the world," says Dr. Kwon. "We cracked the ice on this imaging advancement and are eager for others to adopt our newly optimized approaches for prostate cancer treatment."

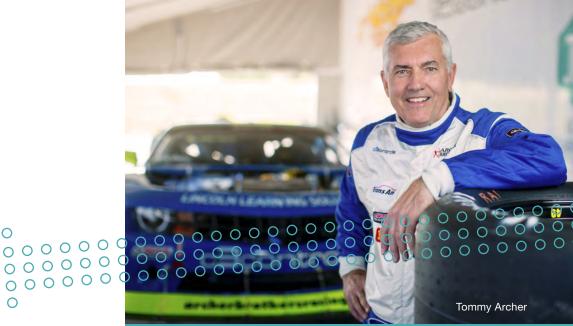
Optimal setup

Choline C-11 has a half-life of 20 minutes and must be made individually for each patient and administered within minutes.

"We've been successful in using choline C-11 because our production facility is located below our PET scanners," says Dr. Kwon. "If these structures were far apart or our campus were more spread out, we couldn't do this. Our excellent facilities and campus layout are ideal for this form of imaging."

Dr. Kwon credits Val Lowe, M.D. (R-NUC '99), and Joseph Hung, Ph.D. (R-D '88), Department of Radiology, and Mark Jacobson, Division of Nuclear Medicine, with establishing the new technology at Mayo Clinic.

According to Dr. Kwon, using choline C-11 in prostate cancer patients has incidentally identified other cancers. "We'd like to explore using it for other cancers," he says.



Life in the fast lane possible again due to change in prostate cancer detection

Professional race car driver Tommy Archer began racing when he was 16 and has tried not to slow down. He's won more than 40 championships in more than three decades of racing.

His 180 miles-per-hour lifestyle came to a screeching halt when he was diagnosed with prostate cancer in 2012. He had prostate removal surgery at Mayo Clinic in Rochester and a year of treatment with hormone medication. When he stopped taking the medication, his PSA level began to rise, indicating recurrence of cancer. His physicians suggested he resume the medication.

"I didn't like taking the medication because it subdues your testosterone and your feelings overall," says Archer. "I certainly didn't look forward to taking the medication for the rest of my life."

Timing was on Archer's side. Last year he had choline C-11 PET scanning, which identified a lymph node with prostate cancer in his pelvis. The node was surgically removed, and Archer was able to resume racing with only four months of downtime.

"We knew his cancer had returned from the increase in PSA levels, but it was like a smoke signal — we didn't know where the cancer was," says Eugene Kwon, M.D., Department of Urology, Mayo Clinic in Rochester. "Fortunately, Mr. Archer was able to have well-informed treatment and get back to his normal life."

Archer's PSA level rose again last summer, indicating his cancer had returned. He had radiation therapy at Mayo Clinic and is once again taking hormone medication. He resumed racing a few months ago.

Mayo Clinic Young Investigators Research Symposium

Connecting disparate Investigators

ayo Clinic's biennial Young Investigators
Research Symposium in March attracted
266 attendees. Graduate students, medical
students, residents, clinical fellows, postdoctoral fellows
and junior faculty made poster and oral presentations in
basic, translational and clinical research. The symposium
integrates basic and clinical research and provides a
forum for younger researchers to gain knowledge from
expert Mayo Clinic investigators.

Elizabeth Vogel, M.D., Ph.D. (I-1 '12, BME '15), an anesthesiology resident at Mayo Clinic in Rochester, participated in the 2014 symposium. She made a valuable connection that contributed to the research that was the basis of her Ph.D. thesis and the subject of upcoming publications.

"I was working on a signaling pathway in the lungs and found someone doing similar research in kidneys," she says. "We discussed how this signaling pathway affected our respective organs of interest, which led me to new pathway inhibitor possibilities and options for protein knockouts that I otherwise might not have thought of. "If not for the symposium, our paths would not have crossed. Usually, research conferences and presentations are subdivided by organ system or area of interest. But this symposium puts everyone together in the same room, allowing for unique collaborative opportunities."

'An exceptional occasion'

Meghan Painter, Ph.D. (NSCI '15), a research fellow in the Department of Neuroscience at Mayo Clinic in Florida, presented posters at the 2012 and 2014 symposiums.

"My current work is to understand how genetic mutations increase the risk of developing Alzheimer's disease," she says. "We use patient samples to study basic pathogenic mechanisms associated with neurodegeneration and rely heavily on collaborations with our clinical colleagues from all three Mayo locations.

"As a translational scientist, I understand now more than ever that the symposium is an exceptional occasion to interact simultaneously with scientists, physicians and statisticians. Participants can practice presenting and refine their content before advancing to external conferences." •



Elizabeth Vogel, M.D., Ph.D.



Meghan Painter, Ph.D.



Winners of the Young Investigators Research Symposium poster competition included clinical and post-doctoral fellows, residents, and graduate and medical students.



2016 Mayo Clinic Young Investigators Research Symposium

- Established in 2010 and held biennially
- For graduate students, medical students, residents, clinical fellows, postdoctoral fellows and junior faculty
- Poster session and oral presentations
- Organized by Mayo Fellows' Association and Mayo Research Fellows Association
- External speakers included:
- Grégoire Courtine, Ph.D., Swiss Federal Institute of Technology, "Locomotor Prosthetics"
- Mari Dallas, M.D., St. Jude Children's Research Hospital, "Immunogenetics of Gamma Delta T Cells in Patients with Leukemia Before and After HSCT"
- Paige Geiger, Ph.D. (ANES '01, PHYS '01),
 University of Kansas, "Obesity, Insulin
- Resistance and Diabetes: Sex
 Differences and the Role of Estrogen
 Receptors"
- Randy Levinson, Ph.D., Senior Editor, Nature Medicine, "Navigating the Publishing Process at High-Impact Journals"
- Keith Lindor, M.D. (MED '79, GI '86),
 Arizona State University, "An Update on Managing Cholestatic Liver Disease"

2016 Mayo Clinic Alumni Association

Donald C. Balfour Award for Meritorious Research

Putting his energy to good use

isit Cheungpasitporn, M.D. (NEPH '16), describes himself as having been a very inquisitive child — always running around, climbing and accidentally breaking things. The energy and curiosity that characterized his youth don't seem to have faded. Mentors who nominated him for the Donald C. Balfour Award for Meritorious Research mention his insatiable eagerness and tenacity. "There is never a dull day in the clinic when Dr. Cheungpasitporn is present," said one.

Most academically productive fellow ever in division

Dr. Cheungpasitporn's unbridled enthusiasm has served him well in his medical career. He's the most academically productive fellow who has ever trained in the Division of Nephrology and Hypertension at Mayo Clinic in Rochester. To date he's contributed to 55 peerreviewed publications — 28 as the first author. His work already has been recognized internationally through research awards for abstracts presented at national specialty meetings. He also is an assistant professor of medicine — rare for a Mayo Clinic trainee. Additionally, he completed the Center for Clinical and Translational Science Postdoctoral Certificate Program during his nephrology fellowship, which he finished in June 2016.

Diverse research interests

His research interests include acute kidney injury (AKI), kidney transplantation and glomerulonephritis. The research he conducted during his nephrology fellowship was wide-ranging:

 Characterizing the epidemiology of AKI after transcatheter or surgical aortic valve replacement

- Exploring admission variables, such as uric acid and magnesium levels, associated with a higher risk for in-hospital AKI
- Quantifying the mortality and likelihood of renal recovery when continuous renal replacement therapy is required for AKI after cardiac surgery
- Determining whether high sugar intake or alcoholic beverage consumption is associated with development of chronic kidney disease
- Further defining the widely accepted recommendation of the importance of high fluid intake in patients with kidney stones
- Identifying an association between renal cell and transitional cell carcinoma in patients with a history of kidney stones
- Characterizing the course of immunoglobulin nephropathy in patients 65 years and older

Wisit Cheungpasitporn, M.D.

Fellow, Renal Transplant Assistant Professor of Medicine Mayo Clinic in Rochester

- Fellowships: Renal Transplant, Nephrology,
 Mayo School of Graduate Medical Education
- Postgraduate: Clinical and Translational Science, Mayo Graduate School
- Residency: Internal Medicine, Bassett Medical Center, Cooperstown, New York
- Medical School: Chulalongkorn University, Thailand
- Undergraduate: Chulalongkorn University
- Native of: Bangkok, Thailand

- Reporting four novel cases of unusual manifestations of renal parenchymal diseases, three of which are related to drugs that are part of recent advances in treatment of other conditions (bortezomib and antivascular endothelial growth factor)
- Describing outcomes of living kidney donors with pre-existing comorbidities of medullary sponge kidney and rheumatoid arthritis

A rising star

"Dr. Cheungpasitporn aspires to have a career as a successful clinical researcher and mentor," says Suzanne Norby, M.D. (I '98, NEPH '01), program director of the Nephrology Fellowship Program. "Undoubtedly, he has the drive and skills to achieve this."

Stephen Erickson, M.D. (I '76, NEPH '78), Division of Nephrology and Hypertension, directed Dr. Cheungpasitporn in a weekly outpatient nephrology clinic. "In the process of producing his meta-analysis on the treatment of kidney stones with high fluid consumption, he had to review more than 2,200 articles to find nine that fit his strict inclusion criteria. For some fellows, this would take the entire fellowship. Dr. Cheungpasitporn did that in one weekend. To say that he is driven by his love of research would be an understatement. He is clearly a rising star in clinical research. In my 42-year tenure at Mayo Clinic, he is quite simply the best fellow I have ever seen.

"You might think he could be difficult to work with, given his many accomplishments. To the contrary, he is extraordinarily humble. It is rare that we meet and he does not thank me for my mentorship. 'Gratitude' should be his middle name."

Even with his full academic medical career, Dr. Cheungpasitporn has energy to burn. He runs, hikes, camps and sings karaoke with friends.

Humble and grateful

Dr. Cheungpasitporn, who recently began a one-year renal transplant fellowship at Mayo Clinic, shares the credit for the Balfour Award. "It is not a representation of my work alone but the accumulation of all the valuable advice and support that I have received from my program director, mentors, and the Division of Nephrology and Hypertension. I enjoy clinical research because it combines my love of science and caring for patients — ultimately to improve their outcomes and quality of life.



"Every day when I wake up, I am excited because I know I am going to learn something new. Our consultants not only are excellent teachers and leaders in their respective areas but also are approachable and supportive."

A destiny, a dream

In addition to crediting his mentors with his success, Dr. Cheungpasitporn credits his grandfather with guiding him toward medicine. "Since I was born, he told me it was my destiny to become a doctor. As a child I did not understand his reasons for saying that, but I held onto those words as if they were clear fact and worked toward becoming what I believed I was meant to be.

"When my grandfather became ill with lung cancer and died after a mere three months of being admitted to a hospital, I understood the true importance of becoming a person who can help others in their time of need. I wanted to be that man in the white coat who works hard to alleviate pain, bring good news to families and help them work through bad news. I enrolled in medical school in my home country of Thailand and began the long journey of realizing my dream." •

2016 Mayo Clinic Alumni Association Edward C. Kendall Award for Meritorious Research

The pathway to independence

acqueline Limberg, Ph.D. (ANES '16), is the 2016 recipient of the Edward C. Kendall Award for Meritorious Research from the Mayo Clinic Alumni Association. Her work has focused on blood flow control and blood pressure regulation in obesity-related conditions, especially as it involves the sympathetic nervous system. Dr. Limberg's novel research has the potential to affect the well-being of a very large patient population — by 2030 the majority of Americans are projected to be obese, according to a report by the Trust for America's Health and the Robert Wood Johnson Foundation.

She received an independent American Heart Association Scientist Development Grant and a Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral Fellowship (Parent F32) from the National Heart, Lung, and Blood Institute, and has 21 original research publications. Dr. Limberg developed a novel program exploring what causes sympathetic nervous activity to be high in obesity and how this affects human health, including blood pressure and blood sugar.

Small-town roots embedded confidence

Dr. Limberg credits having grown up in a town of only 450 people with giving her confidence to believe she could do and be anything.

"I went to a very small school and was in almost every sport and club," she says. "That allowed me to build confidence.

"I fell in love with science when a science teacher in sixth grade challenged me. For what seemed like the first time, I was really forced to think. I enjoyed conducting experiments, and I liked starting with a question and coming up with my own answer."

Summer program fostered love of research, sports promoted fast thinking

Dr. Limberg says she was unsure where a career in science would lead her. "The summer after my junior year of college, Marquette offered a new summer undergraduate research program. I signed up, and it was the best summer I ever had. I worked with a researcher studying muscle fatigue in patients with multiple sclerosis. My friend's mom has MS and I saw how fatigue impacted her life, so it was personal for me. I became fascinated with research and changed my plan for my senior year. I got my master's degree and Ph.D., and came to Mayo Clinic in 2012."

She credits playing collegiate and competitive rugby during graduate school with developing her ability to

Jacqueline Limberg, Ph.D.

Research Fellow, Human Integrative Physiology Lab Associate Consultant, Physiology and Biomedical Engineering, Department of Anesthesiology Assistant Professor of Physiology

Mayo Clinic in Rochester

- Research Fellowship: Human Integrative Physiology, Mayo School of Graduate Medical
- Graduate: Ph.D., Kinesiology, University of Wisconsin-Madison; Master's Degree, Anatomy, Palmer College, Davenport, Iowa
- Undergraduate: Marquette University, Milwaukee, Wisconsin
- Native of: St. Cloud, Wisconsin

read the field, anticipate what will happen and make effective split-second decisions.

Joining up, striking out

Dr. Limberg joined the lab of Michael Joyner, M.D. (ANES '92), Department of Anesthesiology and the Frank R. and Shari Caywood Professor of Anesthesiology. His lab studies human response to physical and mental stress during activity. "Dr. Joyner has a reputation for mentoring trainees that go on to have successful research programs in academic medical centers," says Dr. Limberg.

Dr. Joyner describes her as someone who is independent, takes risks and pursues her own vision. Dr. Limberg attributes those qualities, in part, to being a first-generation college student. "No one in my family had gone to college prior to me," she says. "I had to establish my own path.

"I wanted to strike out on my own at Mayo Clinic. Dr. Joyner showed me areas that could be beneficial to pursue, but I had to decide my course."

Role models contributed to success

Dr. Limberg says she's benefited from strong role models in her career. They include Barbara Morgan, Ph.D., Department of Orthopedics and Rehabilitation, and Bill Schrage, Ph.D., Department of Kinesiology, at the University of Wisconsin-Madison, and, in particular, Dr. Joyner.

"I couldn't have done what I've done without his support and flexibility. When I told him I was expecting my first child, he was excited and said our field needs people who have successful families and careers. He said, 'Let's make sure this works for you.'"

Dr. Limberg recently welcomed her second child. She also just received a National Institutes of Health Pathway to Independence Award (K99/R00). These grants are designed to facilitate transition from a mentored postdoctoral research position to a stable independent research position with NIH or other research support at an earlier stage than is the norm. The award provides up to five years of support in two phases — an initial phase of one to two years of mentored support and a second phase of up to three years of independent support contingent on securing a tenure-track or equivalent research position.

She will remain at Mayo Clinic for another year and then begin at the University of Missouri as an assistant professor in the Department of Nutrition



and Exercise Physiology. Her research under the new grant will focus on the relationship between sleep apnea and high blood pressure.

Success defined by research and personal achievement

As she develops in her research career, Dr. Limberg aims to be a good role model. "I want to be an example of a successful woman researcher who has a family and healthy life balance," she says. "Typically, women with families aren't well represented in large research universities. In higher-level graduate courses, few full-time research faculty are women. We need women role models in the classroom and in labs."

Dr. Limberg is a board member of Women in Science and Engineering Research (WiSER) at Mayo Clinic, a group that envisions Mayo Clinic as an institution where gender doesn't hinder advancement of a career in science and engineering research.



Know your Board

Mayo Clinic Alumni Association Board of Directors

Provides leadership | Makes policy decisions | Decides strategic direction and vision



David Skillrud, M.D. (I '82, THD '85)

Board Member

- Private Practice, Pulmonary and Sleep Medicine, Normal and Morton, Illinois
- Fellowship: Thoracic Disease, Mayo School of Graduate Medical Education
- Residency: Internal Medicine, Mayo School of Graduate Medical Education
- Medical School: Southern Illinois University School of Medicine, Springfield
- Undergraduate: Illinois Wesleyan University, Bloomington, Illinois
- Native of: Bloomington, Illinois

Why did you decide to pursue medicine?

I liked science and interacting with people in high school and

thought medicine would be a nice combination of the two. In high school I worked part time at a medical lab. When there was a phone call for me I often joked, "Is that Mayo Clinic calling for me again?"

Why did you train at Mayo Clinic?

My family is from Minnesota, so I was very familiar with the area. Mayo has a wonderful reputation, and it felt like home.

How does Mayo Clinic influence your practice?

I was diagnosed with multiple sclerosis — fortunately mild — during my training at Mayo Clinic. I learned so much about being a patient. I think every doctor ought to be a patient at some point. I recall a hematologist at Mayo carefully reviewing every page of my medical record with me when seeing me just for a temporary platelet reduction associated with a neurology drug.

I treat every patient that way, reviewing page after page of medical history that may or may not be applicable to their current condition. I know what it feels like when your doctor is thorough.

My years at Mayo — 1979 to 1985 — were the most important years of my life. I didn't go to Mayo intending to be a pulmonologist.

I started in internal medicine. When I rotated through pulmonology, I was really taken not just with how thorough the department physicians were but also with what wonderful, fun and complete persons they were. Thirty years later, I'm still in touch with some of them.

What do you contribute to the Mayo Clinic Alumni Association?

My love for Mayo and my loyalty. I've been a member of the Doctors Mayo Society since I completed my training.

What do you do in your spare time?

I have six children, including two still in high school, parents who are still lively in their late 80s and siblings who are all in town, so I spend a lot of time on family activities.

What would people be surprised to know about you?

I like to perform — piano, some singing and 260 medical talks during my career. In February I did stand-up comedy at a local community college fund-raising event and won first place. ◆

Mayo Update

Mayo Clinic begins to develop Zika virus vaccine

Mayo Clinic's Vaccine Research Group has begun to develop a vaccine to protect against the Zika virus. Gregory Poland, M.D. (GIM '88), Mayo Clinic Cancer Center and Division of Internal Medicine, is leading the effort in collaboration with the Butantan Institute in Brazil — the largest immunobiology lab in Latin America.

Mayo Clinic's Vaccine Research Group has been active in advancing discoveries in influenza, rubella, measles and smallpox. Currently there is no vaccine for the Zika virus, which was first reported in Brazil in 2015 and has spread to many Latin American countries.



Mayo Clinic names new executive dean for education

Fredric Meyer, M.D. (NS '87), was selected as the Juanita Kious Waugh Executive Dean for Education, Mayo Clinic College of Medicine. Dr. Meyer is enterprise chair of the Department of Neurosurgery and continues in that role. He also is the Alfred Uihlein Family Professor of Neurologic Surgery.

Dr. Meyer leads the educational strategies and direction for the five schools of the Mayo Clinic College of Medicine — Mayo Medical School, Mayo School of Graduate Medical Education, Mayo School of Health Sciences, Mayo Graduate School and Mayo School of Continuous Professional Development —

along with academic support units. These schools span across Mayo sites in Arizona, Florida, Rochester and Mayo Clinic Health System.

Dr. Meyer completed his residency at Mayo Clinic and joined the staff in 1987. He has been named Teacher of the Year in the Mayo Clinic College of Medicine 14 times and received the Distinguished Educator Award — Mayo's highest honor in education — in 2011. He has served as program director of the Neurologic Surgery Program at Mayo School of Graduate Medical Education. He is a past member of the Accreditation Council for Graduate Medical Education, past president of the American Academy of Neurological Surgery and past chair of the American Board of Neurological Surgery. He is the executive director of the American Board of Neurological Surgery.

Dr. Meyer succeeds Mark Warner, M.D. (ANES '80), the Walter and Leonore Annenberg Professor of Anesthesiology in Honor of Daniel R. Brown, M.D., Ph.D. Dr. Warner served as executive dean since 2012 and returned to clinical practice. In his new role, Dr. Meyer also assumed the role of Mayo Medical School dean, succeeding Michele Halyard, M.D. (RADO '89), who has served as interim dean since May 2015. She continues as the Suzanne Hanson Poole Vice Dean for the medical school.



As executive dean for education,
Dr. Meyer leads the educational strategies and direction for the five schools of the Mayo Clinic College of Medicine.



Mayo Clinic in Florida opens new nanotechnology research lab

Mayo Clinic in Florida has opened a new laboratory for nanotechnology research — a key part of Mayo Clinic's new Translational Nanomedicine Program. The lab is focused on developing, testing and applying tiny materials to diagnose and treat patients, especially those with cancer.

Nanoparticles may be useful in delivering therapeutic drugs to cells and helping diagnose, treat and monitor disease from within. Potential uses for nanomedicine include:

- Injecting nanoparticles into tumors and heating them via magnetic fields, X-ray or light to destroy cancer cells
- Using nanoparticles to deliver tiny amounts of chemotherapy drugs or gene therapies directly to cancer cells, minimizing side effects on healthy tissue
- Developing new technologies to help in early detection of cancer and other diseases, and determining whether treatments were effective

Debabrata (Dev) Mukhopadhyay, Ph.D. (MBIO '03), Department of Biochemistry and Molecular Biology and Department of Physiology and Biomedical Engineering, is director of the new lab. "Nanotechnology in medicine is going to have a major impact on patient care, with more effective and targeted therapy," he says.

The Translational Nanomedicine Program aims to bring new solutions to patients of Mayo Clinic's Comprehensive Cancer Center. The new center is supported by the state of Florida and is expected to benefit the entire southeastern United States.

New Department of Clinical Genomics established

Mayo Clinic has introduced a new Department of Clinical Genomics, the clinical arm of the Center for Individualized Medicine, which will provide support for subspecialty genetics and genomics activities.

The new department has nine clinical geneticists, 12 genetic counselors and allied health support employees across the institution. The department chair is Dusica Babovic-Vuksanovic, M.D. (PD '96, MGEN '98), Department of Medical Genetics, Department of Pediatric

and Adolescent Medicine, and Department of Laboratory Medicine and Pathology.

"The creation of this new department is an important step for the Center for Individualized Medicine as we seek to better integrate genomics-enabled health care for our patients," says Keith Stewart, M.B., Ch.B. (HEMO '05), the Carlson and Nelson Endowed Director of the Center for Individualized Medicine, and the Vasek and Anna Maria Polak Professor of Cancer Research.



Mayo Clinic Florida neurogeneticist receives Potamkin Prize for Research

Rosa Rademakers, Ph.D. (NS '07), Department of Neuroscience at Mayo Clinic in Florida and the Mildred A. and Henry Uihlein II Professor of Medical Research, received the 2016 Potamkin Prize for Research in Pick's, Alzheimer's and Related Diseases. This prize — one of the highest honors in neuroscience — is awarded annually by the American Academy of Neurology (AAN) and the American Brain Foundation for advancing dementia research.

She received the \$100,000 award in April at the AAN's 68th Annual Meeting in Vancouver, British Columbia, the world's largest gathering of neurologists.

Dr. Rademakers' research laboratory has made significant discoveries in the molecular genetics of neurological diseases including Alzheimer's disease, frontotemporal dementia (FTD), amyotrophic lateral sclerosis (ALS) and Parkinson's disease-related syndromes.

In 2011 her lab identified that an unusual mutation of the C9orf72 gene is the most common cause of ALS and FTD. This finding explained the disease in more than 30 percent of ALS patients and about 25 percent of FTD patients who have other family members with dementia or ALS. Dr. Rademakers' lab has since discovered several genetic factors that help explain why some people with the mutation develop ALS while others develop FTD.

In 2009 her lab played a key role in the discovery of mutations in the progranulin gene, another major cause of FTD. Her lab developed a highly predictive blood test to detect progranulin mutations in dementia patients and provided important insight into the regulation of the progranulin protein.

Discoveries of genetic targets such as C9orf72 and progranulin form the basis of diagnostic testing and therapies, and provide insight into how diseases develop and how to prevent them.

Dr. Rademakers is the fifth researcher from Mayo Clinic to

receive the Potamkin Prize. The others are:

- 1995, Steven Younkin, M.D., Ph.D. (PHAR '95), Department of Neuroscience, Mayo Clinic in Florida
- 2005, Ronald C. Petersen, M.D., Ph.D. (MED '80, N '84), Department of Neurology, Mayo Clinic in Rochester
- 2008, Clifford Jack Jr., M.D. (R-NEU '84), Department of Radiology, Mayo Clinic in Rochester
- 2011, Dennis Dickson, M.D. (PATH '97), Department of Laboratory Medicine and Pathology, and Neuro-Oncology Program, Mayo Clinic in Florida



Mayo Clinic CEO honored for research advocacy

In the last decade Mayo Clinic has increased its self-funded investment in research from \$100 million to \$300 million.

To honor Mayo Clinic's commitment to research, Research! America, the national advocacy organization for medical research, selected John Noseworthy, M.D. (I '90), president and CEO of Mayo Clinic, for the Geoffrey Beene Builders of Science Award. This recognition honors effective advancement of the nation's commitment to research.

The announcement of the award from Research! America stated that

Dr. Noseworthy "has focused his career on advancing research to meet the needs of individual patients and has enhanced Mayo Clinic's ability to conduct research and provide evidence-based care."



Research at Mayo Clinic

In 2015 Mayo Clinic:

- Was conducting more than 11,000 active clinical studies
- Launched 2,723 new human studies
- Had 4,685 research grants and contracts
- Had 1,000 medical scientists and researchers and 3,392 full-time research personnel
- Had approximately 80 percent of its physicians involved in some type of research
- Had a total research budget of almost \$700 million, including government grants



Mayo Clinic tests one-of-a-kind 3T compact MRI scanner

For more than eight years, Mayo Clinic has been involved in a partnership with GE Global Research, funded through a National Institutes of Health Bioengineering Research Partnership grant, to develop and test a new kind of MRI machine — a compact 3 Tesla MRI scanner. The one-of-a-kind prototype machine is an investigational device for research, and is located at the Charlton North building in the Department of Radiology.

The machine is much smaller than a conventional whole-body MRI scanner, with a bore size of 37 centimeters compared to 60 to 70 centimeters. The compact scanner weighs one-third as much as a conventional MRI magnet. Because of its smaller bore size, the compact MRI scanner doesn't perform scans of the adult trunk, but it can accommodate almost half of the clinical MRI exams done at Mayo Clinic. The initial focus of the research is on scanning the head; the machine also can be useful for scanning extremities such as wrists and feet and for infants.

The compact MRI machine is easier and less expensive to place:

- Standard MRI machines use large amounts of liquid helium, an expensive, nonrenewable resource that recently experienced worldwide shortages. The compact MRI scanner uses only about 12 liters of liquid helium compared with approximately 2,000 liters for a traditional whole-body MRI scanner.
- Because of its large quantity of liquid helium, a conventional MRI scanner requires a reinforced vent stack that leads outside of a building. The compact MRI scanner uses much less helium, so its installation at Mayo didn't require a vent stack, greatly simplifying the process.

The compact machine is easier to transport and install because of its reduced size and weight, possibly making it advantageous in locations and areas of the world that lack adequate MRI capabilities.

According to medical physicist Matt Bernstein, Ph.D. (R-D '98), Department of Radiology at Mayo Clinic in Rochester, his lab has developed methods to improve image quality for compact scanners. One of these reduces distortion near the edge of the field of view in images. These corrections are important for all MRI images but especially so for compact scanners because the patient's head fills up a greater fraction of the bore.

Alumni Association Board members receive ACGME awards

Two Board members of the Mayo Clinic Alumni Association received awards at the annual educational conference of the Accreditation Council for Graduate Medical Education (ACGME) in February:

- Steven Rose, M.D. (MED '81, I '82, ANES '84), dean of Mayo School of Graduate Medical Education, was one of two recipients of the Parker J. Palmer Courage to Lead award, given to designated institutional officials who have demonstrated strong leadership and astute resource management and have encouraged innovation and improvement in residency programs and their sponsoring institution.
- Olufunso (Funso) Odunukan, M.B.B.S. (I '12, CV '16), a fellow in the Division of Cardiovascular Diseases at Mayo Clinic in Florida, was one of two recipients of the David C. Leach Award the only award given to residents and fellows.

Dr. Odunukan's award recognizes residents and fellows who have fostered innovation and improvement in their residency programs, advanced humanism in medicine, and increased efficiency and emphasis on educational outcomes.

Dr. Odunukan led his colleagues in the Mayo Fellows' Association in pioneering the Fellows and Residents' Health and Wellness Initiative. They joined forces with the Lyndra P. Daniel Center for Humanities in Medicine at Mayo Clinic in Florida in an initiative to combat symptoms of resident physician burnout by providing creative outlets using arts and the humanities. Dr. Odunukan created a pilot project that revealed that internal medicine residents who participated in one hour of art class were less fatigued and had improved work-related motivation when compared to their colleagues who participated in the usual noon conference. He also conducted a randomized crossover study that compared the effects of art and meditation, which showed that group participation in arts led to improved bonding with colleagues and that meditation was more effective for lowering stress and fatigue. As a result, Mayo Clinic





in Florida now designates one noon conference per month as Humanities Thursday for facilitated discussions of artwork, guided visual imagery and art projects.

Dr. Odunukan was part of a panel at the American Medical Association's (AMA) 2015 annual meeting to discuss solutions to stress and burnout among graduate medical trainees. The project is highlighted in the AMA's resident wellness program (stepsforward.org/modules/physician-wellness).

Obituaries

John Camp Jr., M.D. (R-D '62), died Dec. 19, 2015.

William Crawford, M.D. (OPH '61), died March 3, 2016.

James Gay, M.D. (SGPA '84), died March 2, 2016.

James McCully, M.D. (R-D '72), died July 23, 2015.

Robert Pittelkow, M.D. (DERM '56), died March 26, 2016.

John Timmons Jr., M.D. (U '74), died Feb. 17, 2016.

Lewis Vadheim, M.D. (S '51), died Jan. 5, 2016.

Jon Weingart, M.D. (I '64, N '69), died Dec. 11, 2015.

• <u>alumniassociation.mayo.edu/people</u> for complete obituaries and alumni news

Mayo Clinic neurologist awarded John Dystel Prize for Multiple Sclerosis Research

Claudia Lucchinetti, M.D. (N '94, NIMM '95), chair of the Department of Neurology at Mayo Clinic in Rochester and the Eugene and Marcia Applebaum Professor of Neuroscieces, received the John Dystel Prize for Multiple Sclerosis Research for her contributions to understanding and treating multiple sclerosis (MS). The award is given by the National MS Society and the American Academy of Neurology (AAN).

She received the \$15,000 award in April at the AAN annual meeting.

Dr. Lucchinetti is one of only a few neurologists in the world with expertise in neuroinflammation. Her research has led to shifts in understanding of central nervous system (CNS) demyelinating diseases in the past two decades. Her research focuses on mechanisms of demyelination — damage to the protective covering that surrounds nerve fibers in the brain and spinal cord. She also focuses on tissue injury among the family of CNS inflammatory demyelinating disorders. Dr. Lucchinetti began to collect and analyze MS lesion brain biopsies 20 years ago and has created the world's largest tissue bank of MS lesions in her quest to find effective treatments.

Her research has shown that the pattern of damage in brain tissue differs between patients with MS but remains the same for any given patient. This suggested for the first time that MS is a disease with fundamentally



different targets and mechanisms of tissue damage in different patients.

She subsequently demonstrated that therapies may need to be individualized for patients on the basis of their specific tissue injury patterns, underscoring for the first time the importance of personalized medicine approaches in the treatment of MS.

This is the second time a Mayo Clinic neurologist has won this prize. Brian Weinshenker, M.D. (N '92), received it in 2011.

Alumni Connect matches alumni mentors with medical students

The Mayo Clinic Alumni Association has started a new mentorship program, Alumni Connect, to match alumni with Mayo Medical School students.

"Current students who are exploring residency options would love to gain the insights of our alumni around the world," says Dawn Marie Davis, M.D. (PD '03, DERM '06), medical director, Alumni

Center. "Mentors will get the chance to know students' interests, share their experiences and help them navigate the interview process.

"Mayo alumni recognize that mentorship is an important responsibility and historically have been pleased to help our students. Formalizing the process will give more students this valuable opportunity."

Register to mentor

To register to be a mentor for Alumni Connect:

- Visit <u>alumniassociation.mayo.edu/</u> <u>mentorship/</u>.
- Activate your account with your alumni ID.
- Complete the mentorship form.
- Matches will be made based on specialty, geography and other criteria.



"I owe my profession to the incredible kindness shown toward me by caring, selfless mentors. I consider it a great honor to mentor young colleagues."

- Gerardo Colon-Otero, M.D. (I '82, HEM '84), Associate Dean, Mayo Medical School

Mayo Clinic Alumni magazine is published quarterly and mailed free of charge to physicians, scientists and medical educators who studied and/or trained at Mayo Clinic, and to Mayo consulting staff. The magazine reports on Mayo Clinic alumni, staff and students, and informs readers about newsworthy activities throughout Mayo Clinic.

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Mayo Clinic is committed to creating and sustaining an environment that respects and supports diversity in staff and patient populations.

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