

Mayo Alumni 2014 | No.3

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Expanding medicine's evidence base

Mayo Alumni

Features

2 Leading the charge in women's health and sex differences True evidence-based individualized medicine requires research and education to understand female physiology and pathophysiology. Virginia Miller, Ph.D., a pioneer in sex differences and equality in medicine, has helped to put Mayo Clinic in the forefront of sex and gender medicine.

12 On the shoulders of giants

Mayo Clinic is heralded for its rich tradition of training the next generation — a practice that thrives today. David Skillrud, M.D., describes how Howard Andersen, M.D., Ed Rosenow III, M.D., George Morrow, M.D., and Richard DeRemee, M.D., influenced him.

Jill Barnes, Ph.D. — scientist's diligence and drive propel her to take risks

A close-up look at the recipient of the 2014 Edward C. Kendall Mayo Clinic Alumni Association Award for Meritorious Research.

16 Arthur Beyder, M.D., Ph.D. – physician-scientist combines love of molecules and patient care

A close-up look at the recipient of the 2014 Donald C. Balfour Mayo Clinic Alumni Association Award for Meritorious Research.

18 Young Investigators Research Symposium

This biennial event helps to jump-start young research careers by connecting people with similar interests and allowing faculty and other experts to provide instruction and inspiration.

21 Know your Mayo Clinic Alumni Association Board of Directors Learn more about Douglas Chyatte, M.D., Gene Siegal, M.D., Ph.D., Steven Rose, M.D., and Suzanne Ildstad, M.D.

Mayo Update

24 Honor Roll of Alumni Benefactors, obituaries, Sesquicentennial books

A Letter from the Secretary-Treasurer

esearch is an integral part of Mayo Clinic and our emphasis on translational medicine and improving patient care as quickly as possible. This issue of *Mayo Alumni* focuses on research endeavors that exemplify the richness of this shield.

First and foremost is a look at women's health research and the formidable efforts of Virginia Miller, Ph.D., who has led this charge at Mayo Clinic and gained national and international recognition. In the look at the BIRCWH scholars, it's clear that Virginia also is inspiring the next generation of researchers interested in sex differences in medicine. As Virginia says so eloquently, "Studying only one sex and applying it to the other without testing is poor science."

This issue also features our 2014 Balfour and Kendall award recipients and examines what drives these promising researchers.

A new tradition at Mayo Clinic is the Young Investigators Research Symposium, which is partially sponsored by the Alumni Association. This biennial event is designed as a springboard for young research careers and has been wildly successful. Because so many of our programs are longstanding, it's exciting to see a new activity take shape, gather momentum and develop a healthy following.

Thank you for following us by reading the *Mayo Alumni* and sending your thoughts and comments.

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Peter C. Amadio, M.D. Secretary-Treasurer Mayo Clinic Alumni Association

Lloyd A. and Barbara A. Amundson Professor of Orthopedics

Mayo Clinic Alumni Association 69th Biennial Meeting

October 15–17, 2015 / Mayo Clinic, Phoenix 🔳

The meeting will celebrate the 100th anniversary of the Alumni Association's formal incorporation in 1915. Details to come.





WOMEN'S HEALTH

Mayo Clinic leads in research and education in women's health and sex differences

ne size doesn't fit all when it comes to research and clinical care. Some diseases look different in women compared to men. Some tests are different. Women may have more side effects from drugs than men. Too often, research studies don't analyze results separately by sex. The National Institutes of Health (NIH) recently introduced a policy to end routine gender bias in basic research, warning scientists to also test theories in female lab animals, tissues and cells. NIH grant reviewers will take into account this male-female balance in study design.

"Studying only one sex and applying it to the other without testing is poor science," says Virginia Miller, Ph.D. (PHYS '86, S '91), departments of Surgery and Physiology and Biomedical Engineering and principal investigator of Mayo Clinic's Specialized Center of Research (SCOR) on Sex Differences. "Female is not simply a variation of male. Every cell has a sex, and sex does matter in strategies to prevent, diagnose and treat disease. If we want to improve care for all people, we need to understand if an intervention, drug, device or surgery works the same or differently in men and women. Accounting for sex is fundamental to individualized and evidence-based medicine, and it starts at the basic science level."

Dr. Miller is a pioneer in sex differences and equality in medicine. She received the 2014 Bernadine Healy Award for Visionary Leadership in Women's Health. Dr. Healy was the first woman director of the NIH (1991–1993). Dr. Miller's work has put Mayo Clinic in the forefront of sex and gender medicine.



"Mayo is now on the map in this area because we've endeavored to bring our work in sex and gender medicine in all three shields to the national and international stage," says Dr. Miller. "In research, we're working with the NIH Office of Research on Women's Health and segments of the FDA. Clinically, we're gaining prominence in providing evidence-based medicine spearheaded through our Women's Health Research Center and Women's Health Clinic. And in education, we've published an analysis of medical school student knowledge of sex and gender topics in curriculum and are working with other groups to pilot new curriculum as a result."

Dr. Miller describes the imperative in women's health research, practice and education. >>

To practice true evidence-based, individualized medicine, we must move forward with research and education to understand female physiology and pathophysiology. " – Virginia Miller, Ph.D.

"Mayo Clinic is known for practicing evidence-based medicine," she says. "To date, however, the evidence base for how women have been treated has been based on a male model. To practice true evidence-based, individualized medicine, we must move forward with research and education to understand female physiology and pathophysiology. We're on the right track, and the progress we've made is exciting and encouraging."

Office of Women's Health established to compete in national arena

Dr. Miller was the first director of Mayo Clinic's Office of Women's Health, established in 2001. The office was created in response to the NIH initiating specialized centers of excellence in women's health in the 1990s.

"Creating our own Office of Women's Health was a necessity if we wanted to be in the national forefront of providing excellent care for women," says Dr. Miller. "Mayo has always offered women's health services, but they were diffuse."

The early charge of the Office of Women's Health was to improve interdepartmental collaboration in women's health — diseases that occur uniquely in women, more frequently in women or affect women differently from men.

The office took a big step toward realizing this charge in 2005 when Dr. Miller became a principal investigator in the multicenter KEEPS (Kronos Early Estrogen Prevention Study) trial, which was designed to evaluate the effects of hormone replacement in recently menopausal women a group not included in other large prospective studies of hormone treatments.

"We hadn't been involved in other multicenter clinical trials in women's health, so KEEPS was a wonderful opportunity for us to gain a national presence in research," says Dr. Miller. "KEEPS brought together Mayo colleagues across disciplines interested in women's health research in a new way, creating momentum and breaking down barriers to true integration."

The KEEPS trial colleagues formed a working group, which became an incubator to spur research in other women's health specialties including cardiovascular disease, brain function, bone health, breast pain and sleep disorders.

KEEPS also linked Mayo with a network of collaborators and investigators with strong traditions in women's health research and was a springboard to involvement in joint efforts and national programs including SCOR on sex differences research funded through the National Institute on Aging. Mayo Clinic is one of 11 centers in the country with this P50 grant. Dr. Miller leads Mayo's SCOR efforts, which focus on two life stages for women — menopause and pregnancy — and their effects on later risk of cardiovascular disease and cognitive aging.

"We learned how to collaborate to compete in the national arena for grants in sex differences research," says Dr. Miller. "The KEEPS trial was a major building block for what's happened since then in women's health at Mayo Clinic."

Office of Women's Health coordinates, integrates, educates

Today, the Office of Women's Health is directed by Lynne Shuster, M.D. (MMS '87, I '90, ADGM '91), Division of General Internal Medicine. The office serves in an administrative role to:

- Provide a central point of coordination for women's health programs and facilitate integration of women's health care practices
- Provide women's health education to health care providers, patients and the community

- Facilitate women's health research opportunities through faculty training, development and mentoring
- Identify and support implementation of best practices to deliver safe, consistent, high-quality and fiscally responsible care for all women
- Develop women's health practice metrics to measure outcomes of clinical care, quality, safety and patient satisfaction

"We want Mayo's activities across the three shields to be coordinated and inclusive," says Dr. Shuster. "The Office of Women's Health provides a central point of connection."

Women's Health Research Center aims to understand and improve women's health

A long-term vision of the Office of Women's Health was to create a multidisciplinary Women's Health Research Center. This was achieved in 2011, with the goals of:

- Understanding and improving the health of women across their life span
- Advancing research in women's health-related areas
- Addressing disparities between the sexes in diagnosis, treatment and outcomes of many diseases
- Gaining national recognition for translational research that improves the health and care of women

The Women's Health Research Center complements and builds on Mayo Clinic's strong base of women's healthrelated research, education and patient care activities. The center coordinates efforts by researchers involved in the SCOR grant, BIRCWH (Building Interdisciplinary Research Careers in Women's Health) training program grant (page 8) and women's health research activities beyond those already served by the well-established women's cancer program. Today, more than 1,400 research studies related to women's health are underway across Mayo Clinic campuses.

Focus areas for the Women's Health Research Center include women-specific issues and sex differences in four program areas:

- Mother and baby health and disease
- Brain, mind and mood
- Living well with chronic disease
- Menopause and healthy aging >>

We want Mayo's activities across the three shields to be coordinated and inclusive. The Office of Women's Health provides a central point of connection." – Lynne Shuster, M.D.





Research in basic and translational science is necessary so that we can continue to move discoveries into the clinic." – Rebecca Bahn, M.D.

"The Women's Health Research Center is in the early stages of evolving into what we envision as a truly integrated research incubator to help us understand and improve women's health across the life span," says Rebecca Bahn, M.D. (MMS '81, I '84, IMM '88, ENDO '88), director, Women's Health Research Center. "Research in basic and translational science is necessary so that we can continue to move discoveries into the clinic."

Sharing knowledge is critical to improve education, research and patient care

An essential component of realizing the value in sex- and gender-based differences initiatives is the dissemination of information. Mayo Clinic shares the knowledge it gains in its women's health efforts to promote inclusion of sex and gender considerations into research and clinical care settings. Dissemination efforts include:

• Curriculum development in sex and gender medicine: Mayo Medical School is revising its curriculum and developing targeted programs for postgraduate education in partnership with Mayo Clinic's Center for Clinical and Translational Science.

- **Clinical rotation:** Mayo medical students, and residents and fellows from many specialties rotate through the Women's Health Clinic and Breast Clinic.
- Women's Health Training Track, General Internal Medicine Fellowship (Rochester): This postgraduate program provides interdisciplinary clinical training in areas relevant to women's health, focusing on prevention and treatment of diseases prevalent in women through adulthood. The training program was created more than a decade ago to develop leaders in the evolving field of women's health and to improve health care outcomes for women; directed by Nicole Sandhu, M.D., Ph.D. (MBIO '00, I '04).
- BIRCWH (Building Interdisciplinary Research Careers in Women's Health) training program grant: Mayo Clinic's Interdisciplinary Women's Health Research Program is funded by this award from the NIH for junior faculty to receive advanced research training in interdisciplinary women's health fields (page 8).
- "Controversies in Women's Health:" Annual educational symposium in Chicago currently directed by Stephanie

Faubion, M.D. (GIM '96), and Douglas Creedon, M.D., Ph.D. (MMS '01, OBG '05), and sponsored by the Mayo Clinic Office of Women's Health.

- "Multidisciplinary Update in Breast Diseases:" Annual Mayo Clinic state-of-the-art conference on benign and malignant breast diseases; directed by Sandhya Pruthi, M.D. (FM '94), Barbara Pockaj, M.D. (S '95), and Edith Perez, M.D. (HEMO '95).
- "Update on Women's Health:" Annual course that addresses the unique needs of female patients and their health care providers; held in Scottsdale.
- "OB/GYN Clinical Reviews, Advancing Women's Health:" Continuing medical education course that addresses relevant and controversial topics facing patients and their health care providers; directed by Dr. Creedon, Shannon Laughlin-Tommaso, M.D. (OBG '09), Lois McGuire, R.N., C.N.P., and Myra Wick, M.D., Ph.D. (LABM '94, MMS '04, OBG '08, MGEN '10).

"The tests we order and treatments we recommend may differ based on sex and gender differences, so it's essential that we communicate this information to others to help make sure everyone gets the best care," says Dr. Faubion, Division of General Internal Medicine and director of the Mayo Clinic Women's Health Clinic. >>

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Women's clinical programs

Mayo Clinic's women's health research efforts are translated into patient care in clinical programs, including:

- Women's Health Clinic Stephanie Faubion, M.D. (GIM '96), director; provides care for sexual health, menopause, cancer survivorship
- Breast Clinic
 Karthik Ghosh, M.D. (GIM '01), director
- Women's Heart Clinic
 Sharon Mulvagh, M.D. (CV '90), director
- Women's Cancer Program James Ingle, M.D. (ONC '76), Betty J. Foust, M.D. and Parents' Professor; and Sean Dowdy, M.D. (OBG '01, GYNO '04), co-directors



BIRCWH scholars Advancing individualized medicine

Mayo Clinic has had nine BIRCWH (Building Interdisciplinary Research Careers in Women's Health) scholars since it received a training grant from the Office of Research on Women's Health (NIH) in 2010.

Mayo Alumni profiles three current or former BIRCWH scholars.

Jamie Bakkum-Gamez, M.D., Division of Gynecologic Surgery, Department of Obstetrics & Gynecology

Developing a screening test for endometrial cancer

Dr. Bakkum-Gamez (ONG '06, GYNO '09) was a BIRCWH scholar from 2011 to 2013. Her research focused on marrying a minimally invasive testing modality (a tampon) with sensitive molecular testing (DNA methylation) to detect endometrial cancer. She has continued this work with funding from Mayo Clinic and the National Cancer Institute.

Her unique research could develop a first-ever screening or early-detection test for endometrial cancer. A clinical trial is underway for women at high risk for the disease.

"Mayo Clinic is a major national and international site for endometrial cancer research, and an NIH collaborator approached Mayo in 2009 to see if we'd be interested in exploring this work," says Dr. Bakkum-Gamez. "It dovetailed with research we were involved in, and I pursued it for my BIRCWH project.

"The results have been promising. We've identified new genes not previously identified in endometrial cancer that can potentially be used as biomarkers for early detection and screening. These biomarkers may also play a role in causing endometrial cancer. The Pap test as a screening test changed the lives of millions of women. A screening test for endometrial cancer could do the same, and that's an exciting development to be involved in."

Dr. Bakkum-Gamez points out an additional benefit of this screening tool. "We know that there are racial and socioeconomic disparities in mortality of endometrial cancer," she says. "A low-cost, easy-to-access screening test could help to address these discrepancies." >>

We've identified new genes not previously identified in endometrial cancer that can potentially be used as biomarkers for early detection and screening." – Jamie Bakkum-Gamez, M.D.





(From left) Melissa Morrow, Ph.D., Jamie Bakkum-Gamez, M.D., and Stacey Winham, Ph.D., are among more than 500 junior faculty at 39 institutions across the United States who have benefitted from the BIRCWH career development program that supports interest in women's health and sex differences research.

Melissa Morrow, Ph.D., Division of Orthopedic Research, Department of Orthopedic Surgery

Determining female-specific risk factors for knee osteoarthritis

Dr. Morrow (BME '09, CTSA '12, OR '12) was a BIRCWH scholar from 2011 to 2013. Her degrees are in biomedical engineering and clinical and translational science, and her fellowship was in rehabilitation sciences. Her research focused on characterizing the differences in disease severity, manifestation and outcomes between men and women with knee osteoarthritis.

"Women have a higher prevalence and incidence of knee osteoarthritis than men, but in reviewing the literature I noticed a lack of detail in the reporting of how the disease differs in women from men," says Dr. Morrow. "We've found a potential difference in the frequency of loading on the knee throughout the day — the number of steps we take and higher cadence — and we're continuing research to help answer these questions."

Dr. Morrow says she wants to be more of a voice in professional orthopedic biomechanics societies about the importance of studying sex differences. "I was aware of this issue before becoming a BIRCWH scholar, but my interest has grown," she says. "Sex is just another level of analysis but a very necessary one. We need to be mindful about an equitable process in recruiting for studies. Sex as an important variable is still a new topic for many investigators to even consider."

Dr. Morrow cites Virginia Miller, Ph.D. (page 3), as a driving force in waking up the scientific community about these differences. "She's been a strong voice talking about this for a long time and is just now receiving the attention and platform she deserves," says Dr. Morrow. "Dr. Miller has provided a forum for many young researchers to have someone to talk to about these issues."

Stacey Winham, Ph.D.,

Division of Biomedical Statistics and Informatics, Department of Health Sciences Research

Studying X chromosome inactivation in ovarian cancer

D^r. Winham (HSR '12) began her BIRCWH scholarship in 2013. Her research focuses on identifying sex-specific genetic effects, with a particular interest in integrating

We need to be mindful about an equitable process in recruiting for studies. Sex as an important variable is still a new topic for many investigators to even consider." – Melissa Morrow, Ph.D.



the X chromosome into genetic analyses and studying X chromosome inactivation.

"BIRCWH provides funding and dedicated time to focus on data analysis, but also networking and presentation opportunities, and an internal group of other BIRCWH scholars and the executive committee — a team to help me accomplish my goals," she says.

Dr. Winham has developed a data-mining method to analyze high-dimensional genetic data that integrates X chromosome data and hopes to complete a study of X chromosome inactivation in ovarian cancer during her BIRCWH scholarship.

"My area of research is new at Mayo and to the research community in general because the X chromosome is typically excluded from genetic association studies," says Dr. Winham. "I was already interested in the X chromosome but, through BIRCWH, I've learned of its importance and how often it has been ignored. Others with whom I'm collaborating have realized applications to their own research projects, which is exciting. I hope this work helps move us along the path to individualized medicine and brings attention to sex differences in genetic studies."

What is **BIRCWH**?

BIRCWH (Building Interdisciplinary Research Careers in Women's Health) is a mentored career development program that funds research time for junior faculty (BIRCWH scholars) and connects them to senior faculty with shared interest in women's health and sex differences research.

Since 2000, the national BIRCWH program has awarded 77 grants to 39 institutions to support more than 542 junior faculty.

Who is eligible for BIRCWH?

Junior faculty, who may be male or female, must have recently completed clinical training or a postdoctoral fellowship and plan to conduct interdisciplinary basic, translational, behavioral, clinical or health services research relevant to women's health.

Many BIRCWH scholars obtain independent NIH grant funding after participation in the program.

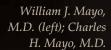
My area of research is new at Mayo and to the research community in general because the X chromosome is typically excluded from genetic association studies." – Stacey Winham, Ph.D.



On the Shoulders of Giants

"If I have seen further it is by standing on the shoulders of giants." — Sir Isaac Newton

his feature shares vignettes of Mayo Clinic alumni who describe the influence of mentors in that unique Mayo way — active ideal of service, primary and sincere concern for the care of the individual patient, unselfish interest in every member of the group, guidance without pampering, help without mentoring.







(Clockwise from lower left) Richard DeRemee, M.D., Ed Rosenow III, M.D., George Morrow, M.D., and Howard Andersen, M.D.

The faces of my mentors in these pictures remind me every day of the class-act physicians who trained me and represented Mayo Clinic so wonderfully."





Photographic reminders of mentors w

David Skillrud, M.D. (I '82, THD '85), a pulmonologist in Bloomington–Normal and central Illinois, was 24 when he arrived at Mayo Clinic. "The next six years were the most important of my life. My mentors and Mayo Clinic changed everything for me and established my career for the rest of my life," he says. "The people I met were incredible. You know, great doctors can be found everywhere. But at Mayo, there are great doctors in every area, and the system in which they operate is phenomenal."

To honor those who inspired and taught him, Dr. Skillrud has black-andwhite framed photos of his favorite and most-respected Mayo Clinic mentors hanging in his exam room. Pictured are Howard Andersen, M.D. (S '49, I '51), Ed Rosenow III, M.D. (I '65, THD '65), George Morrow, M.D. (I '57), and Richard DeRemee, M.D. (I '66). A photo of Drs. Will and Charlie Mayo adorns an adjacent wall alongside his degree certificates.

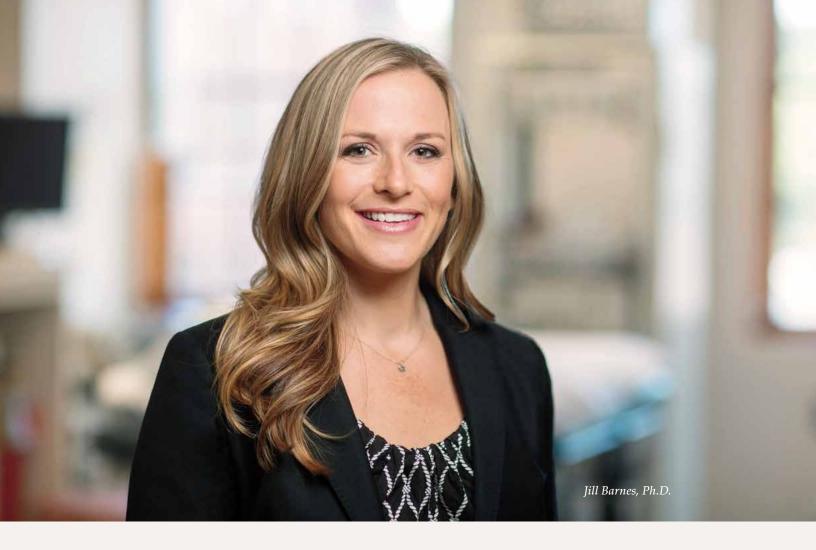
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"I have seen more than 23,000 different chest and sleep medicine patients since leaving Mayo Clinic in 1985, and every one of them assessed in the office setting sees these pictures," he says. "The faces of my mentors in these pictures remind me every day of the class-act physicians who trained me and represented Mayo Clinic so wonderfully." Ulrud, M. D. Sleep Medicine

The inscriptions on three of the four photos are still legible:"David, I'm very proud to have played even a very small part in your

- education." (Dr. Rosenow)
- "To David Skillrud, with expectations for an outstanding medical career." (Dr. Morrow)
- "To David, a colleague in medicine, a comrade in music, a friend in the world." (Dr. DeRemee)

"I feel so blessed that they were part of my training and of my life," says Dr. Skillrud.



'Highly original'

Diligence and drive propel scientist to take risks and earn awards

s an undergraduate student at the University of Michigan, Ann Arbor, Jill Barnes, Ph.D. (ANES '13), had to work harder to compete.

"I'd gone to a small community high school with open teaching and few college prep courses," she says. "At Michigan, incoming freshmen had semesters of college credit under their belts, and their families had spent a lot of time and effort on their education. I felt like I had to work harder than everyone else or produce off-the-wall ideas. Sometimes those ideas pan out. "I thrive when my curiosity can just run. I love to read about the latest research, generate questions, narrow down what will be useful and productive, and search for the answers. Having to really apply myself to compete gave me a certain drive."

'A shining star'

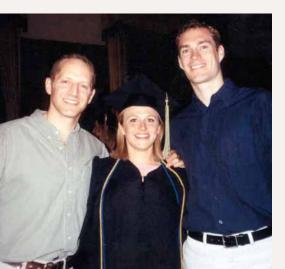
Diligence and drive have paid off. Dr. Barnes has racked up awards for academic achievement, accomplishments and professional involvement. Recently, she received the 2014 Edward C. Kendall Mayo Clinic Alumni Association Award for Meritorious Research. Her Ph.D. program mentor at the University of Texas at Austin, Hirofumi Tanaka, Ph.D., director, Cardiovascular Aging Research Laboratory, describes her as the most driven student he has supervised. "Aggressiveness is a very important trait in the increasingly competitive area of academic research," he says. "Jill will be a shining star in the field of cardiovascular and exercise physiology in the future."

Dr. Barnes has received an independent NIH K99/R00 award, has authored 33 original publications in peer-reviewed journals, received an individual NIH NRSA (F32) from the National Institute of Aging, was instrumental in obtaining a pilot feasibility grant from the Mayo Alzheimer's Disease Research Center, and is collaborating with other principal investigators on a newly funded NIH P50 Specialized Center for Research to study sex-specific differences in cognitive decline. She developed a novel and independent research program exploring the interactions of aging, sex differences and cerebral blood flow regulation in humans.

'A taste for risk-taking'

"Jill's ideas about aging, cognition and blood flow are highly original," says Michael Joyner, M.D. (ANES '92), a consultant in the Department of Anesthesiology and the Frank R. and Shari Caywood Professor of Anesthesiology at Mayo Clinic in Rochester. "Rather than plug into a successful ongoing area of investigation in the lab, Jill struck out on her own. She has a taste for intellectual and professional risk-taking and the skills to obtain the input and resources needed to pursue her vision."

Dr. Barnes says she was surprised at the collaborative possibilities at Mayo Clinic. "I thought that as a fellow I wouldn't have a lot of opportunities," she says. "I was able to do things I never imagined — working across



departments, writing editorials and review articles, partaking in large collaborative studies with industry and other funding sources. The intellectual capital on this campus is impressive. It's a very collaborative research community."

A move to a state away

Dr. Barnes' intellectual capital will soon grace the University of Wisconsin–Madison campus. In January, she will begin her tenuretrack faculty appointment in the Department of Kinesiology.

"My experience at Mayo was great, and I'd love to have spent my career in Rochester. But there's more opportunity for a career path as a scientist at Wisconsin," she says. "Even though I'm a state away, I hope to continue to collaborate with Mayo Clinic at least until studies I'm involved with are complete, including Dr. Virginia Miller's SCOR [Specialized Centers of Research] grant on sex differences.

"Being on a college campus presents other facets of diseases such as dementia and Alzheimer's that I hadn't previously considered, including the sociological aspects of the health and wellness of caretakers. I look forward to new collaborations and exploration."

Jill Barnes, Ph.D., at her graduation from the University of Michigan in 2003. She's pictured with her undergraduate thesis mentor, Jeff Horowitz, Ph.D. (left), professor of movement science at the University of Michigan, and Nick Knuth, Ph.D., then a Ph.D. student in Dr. Horowitz's lab and now an assistant professor in the Department of Kinesiology at Towson University in Towson, Md.

Jill Barnes, Ph.D.

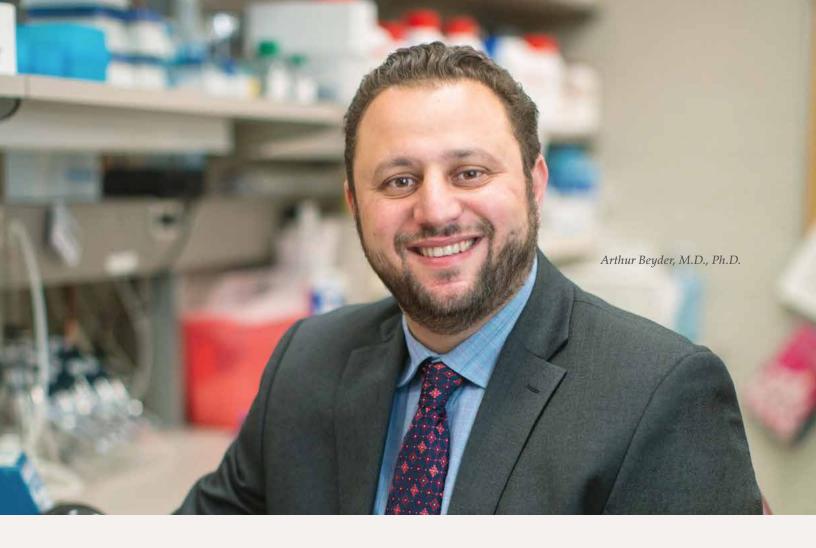
Associate Consultant, Department of Anesthesiology, Mayo Clinic in Rochester; Assistant Professor, Department of Physiology and Biomedical Engineering, Mayo Clinic College of Medicine

Fellowship: Human and Integrative Physiology and Pharmacology Laboratory, Mayo School of Graduate Medical Education

Graduate: Ph.D., Kinesiology– Cardiovascular Physiology, Master's Degree, Cardiovascular Physiology, University of Texas at Austin

Undergraduate: University of Michigan, Ann Arbor

G Jill will be a shining star in the field of cardiovascular and exercise physiology in the future." – Hirofumi Tanaka, Ph.D.



Two sides of a coin

Physician-scientist combines love of molecules with patient care

His mother was an engineer. His mother was a family physician. He felt drawn to both worlds.

"If you are the firstborn in a physician family in Russia, you are basically donated to clinical medicine — you are going to be a physician," says Arthur Beyder, M.D., Ph.D. (I '10, CI '12, GI '14), a consultant in the Division of Gastroenterology and Hepatology at Mayo Clinic in Rochester. "On house calls with my mom, I saw how much personal contact and human touch mean to patients. My dad, on the other hand, was the consummate logical thinker. He taught me brute deconstruction of problems and helped to shape the part of me that loves working on unsolved problems.

"I get to exercise both of those interests at Mayo Clinic. No matter how deep you are into the microscope, you still see patients. You never forget that your research needs to link back to the patient."

Dr. Beyder's family moved to the United States when he was 13. His mother had died four years earlier.

"She was ill for years, and no one could figure out the problem," he says. "I accompanied her on house calls because she had blackouts. Ultimately, her doctors treated her for what they thought was an arterial thrombus. They gave a strong thrombolytic and inadvertently caused a fatal stroke. It was only much later that we found out she had Takayasu's arteritis, an inflammatory condition of her vessels, which required a completely different therapy. Without strong diagnostic tools, you're limited in therapies, and both were lacking in my mother's case. My childhood experiences drive my quest for better diagnostic tools and therapies for patients."

Problem-solving pays off in a 'major achievement'

Recently, Dr. Beyder's diligent problem solving revealed a novel

way of correcting a patient's gastrointestinal problem.

In the Mayo Clinic laboratory of Gianrico Farrugia, M.D. (I '91, GI '94), Dr. Beyder and others were working on a long-standing question — the link between a particular sodium ion channel (NaV1.5) and irritable bowel syndrome (IBS). The group identified several mutations in this gene in patients with IBS, but the mechanisms of disease are not understood and treatments, therefore, cannot be targeted.

Dr. Beyder characterized these mutations and found that the majority had a considerable loss of function at the molecular level. Focusing on one of the most severe mutations, the group found that the anti-arrhythmic medication mexiletine repaired the underlying defect in vitro. They secured a Clinical and Science Translational Award (CTSA) grant and treated the patient with mexiletine. The patient's constipation-predominant IBS was completely reversed by treatment.

As a result of this research, the group has begun to understand the mechanisms of disease in a well-defined subset of IBS patients which, for the first time, allowed for a disease-targeted — instead of symptom-targeted — treatment.

"This was a major achievement," says Dr. Farrugia, Carlson and Nelson Endowed Director, Center for Individualized Medicine and consultant in the Division of Gastroenterology and Hepatology. "For the first time, we've identified an ion channel genetic basis for a defined subset of patients with IBS. We corrected the problem in a patient with a drug that had never been used before with this particular disease. Dr. Beyder is one of the ever-decreasing breed of physicians who is also a superb basic scientist."

Dr. Beyder's accomplishments garnered him the 2014 Donald C. Balfour Mayo Clinic Alumni Association Award for Meritorious Research and 2014 Arnold J. Bargen Research Award from the Division of Gastroenterology and Hepatology.

'We have the perfect environment' to achieve a lot

Dr. Beyder says this discovery is just the tip of the iceberg in terms of what is needed for the prevalent functional conditions in gastroenterology that may not be fatal but cause significant morbidity and numerous physician and hospital visits for millions of people. These conditions are difficult to diagnose and treat because they are multisystemic.

"What we are doing requires expertise in disciplines including neurology, cardiology, internal medicine and gastroenterology," says Dr. Beyder. "I want to solve problems in functional gastroenterology and

motility disorders — that's why I came to Mayo Clinic.

Arthur Beyder, M.D., Ph.D., in 1978 at age 2 in Kharkov, Ukraine, with his engineer father, Alexander, and physician mother, Lina.

Arthur Beyder, M.D., Ph.D.

Consultant, Division of Gastroenterology and Hepatology, Mayo Clinic in Rochester; Assistant Professor, Department of Medicine, Mayo Clinic College of Medicine

Fellowship: Gastroenterology and Hepatology, Mayo School of Graduate Medical Education

Residency: Internal Medicine, Mayo School of Graduate Medical Education

Medical School: M.D./Ph.D., University at Buffalo, State University of New York

Undergraduate: SUNY Buffalo

Dr. Farrugia and my other mentors have molded my training so that I have the tools to answer these important questions. Research in other fields such as cardiology and neurology will help illuminate our path and allow us to translate findings to patient care. The work we're doing in GI at Mayo simply hasn't been done before because it requires collaboration across multiple disciplines.

"Twenty years ago, we couldn't have answered these questions or performed these experiments because the tools didn't exist. Now, at Mayo Clinic, we have the perfect environment. We know the questions to ask, and we have the tools to answer them. I believe you achieve more as a group. Working together, we're going to achieve a lot."

17





How do trainees learn how to jump-start the research aspect of their careers?

The Mayo Clinic Young Investigators Research Symposium was established in 2010 to help researchers in the early stage of their careers learn the ABCs of research and provide a way for them to interact with research colleagues and possible mentors.

In March, 335 residents, fellows, postdoctoral fellows, students, junior faculty and allied health professional researchers participated in the third biennial Young Investigators Research Symposium at Mayo Clinic in Rochester. Most were from a Mayo campus, but those from other institutions — including visiting scientists and clinicians — also took part. Senior faculty members judged posters and oral presentations, and speakers from within and outside Mayo Clinic addressed participants about research career development.

The origin

The concept for the symposium originated with the Mayo Fellows' Association and Mayo Research Fellows Association, who sought ways to promote networking between the clinical and research sides, present and promote research data, and obtain feedback. Members of these groups plan the biennial event and select speaker topics.

"The trainees saw an opportunity to take greater advantage of faculty resources on our campus to improve the quality of their research and presentation skills," says Steven Rose, M.D. (MMS '81, I '82, ANES '84), dean, Mayo School of Graduate Medical Education. "The symposium provides a rich environment for communication among people with similar interests who might not connect otherwise, and a chance for our faculty and other experts to give instruction and inspiration to young people beginning their research careers. As Mayo Clinic grows, there are fewer traditional opportunities for interaction with colleagues across disciplines.

"Our faculty has been enthusiastic and generous with their time and expertise. They are passionate about research and recognize the importance of mentoring. We demonstrate our responsibility to fulfill the Mayo Clinic mission when we invest in education and research and advance all three shields."



Dr. Rose says the symposium can be compared to experiential learning in simulation training. "It provides a supportive, low-risk environment for clinical residents and fellows to present their research work, receive feedback, interact with the basic scientific community and improve their performance," he says. "It's preparation for being more effective in disseminating their work more broadly."

The scene

This year, 212 researchers were selected for poster presentations and 12 for oral presentations — a new feature. Submissions covered randomized trials, outcome studies, practice innovations and descriptive analyses. Winners from the Rochester Regional Science Fair (grades 6–12) also displayed research at the event.

"The symposium has become a key event for putting together research teams for the future," says Bruce Horazdovsky, Ph.D. (MBIO '02), associate dean, Mayo Graduate School. "The Gonda atrium bustles with young investigators networking across all of the schools and beyond, practicing elevator speeches and learning how to develop their scientific career from its earliest stage."

Sarah Greising, Ph.D. (PHYS '15), president of the Mayo Research Fellows Association, co-chaired the event with Jeffrey Wang, M.D. (S '10, U '14), president of the Mayo Fellows' Association. "For many participants, it's the first time presenting

The symposium is an important training ground that demonstrates Mayo's commitment to and support for young scientists and clinician-scientists." – Sarah Greising, Ph.D.



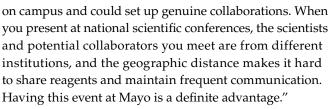
G I received advice from world-renowned investigators right here on campus and could set up genuine collaborations." – Meghan Painter

their work," says Dr. Greising, Department of Physiology and Biomedical Engineering. "The symposium is an important training ground that demonstrates Mayo's commitment to and support for young scientists and clinician-scientists."

The experience

Meghan Painter (NSCI '15), a doctoral candidate at Mayo Graduate School, presented posters at the 2012 and 2014 events and received an award for her poster at the recent symposium. Her research focuses on how a transgene boosts host innate immunity in a transgenic mouse that is resistant to viral infection. Understanding this protective pathway can allow drugs to be designed that will activate the pathway to fight human disease caused by viruses.

"The symposium is the perfect venue in which to practice before presenting at external conferences," says Painter. "I received advice from world-renowned investigators right here



Katharina Hopp, Ph.D. (BMB '13, NEPH '15), a member of the symposium planning committee, says she was impressed with the time senior principal investigators at Mayo Clinic provide for the event. "Eighty established PIs interacted with young investigators in a co-peer informal environment and provided true feedback," says Dr. Hopp, Division of Nephrology and Hypertension. "Most PIs at Mayo are interested in advancing the next generation, infusing them with enthusiasm and steering them toward translation in their research. These are the young investigators who will take their spots one day. This event molds the next generation of researchers."

Most PIs at Mayo are interested in advancing the next generation, infusing them with enthusiasm and steering them toward translation in their research." – Katharina Hopp, Ph.D.



Know your Board

Recent issues of Mayo Alumni magazine have featured profiles of members of the Mayo Clinic Alumni Association Board of Directors, and this issue includes more.

Mayo Clinic Alumni Association Board of Directors

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



Douglas Chyatte, M.D. (NS '85)

Board Member

- Professor of Neurosurgery
- Mayo Clinic College of Medicine
- Mayo Clinic Health System, Southwestern Minnesota Region
- Residency: Neurosurgery, Mayo School of Graduate Medical Education
- Medical School: Northwestern University Honors Program in Medical Education, Evanston, III.
- Undergraduate: Northwestern University
- Native of: Oak Park, III.

Why did you decide to pursue medicine?

I have always enjoyed the sciences and working with people. I decided to pursue medicine in high school largely because of a part-time job I had in a hospital laboratory.

Why did you train at Mayo Clinic?

When I looked into places to train, Mayo unquestionably had the best neurosurgery training program in the world. Mayo Clinic is unlike any other health care organization on the planet in terms of depth, expertise and organization.

My training at Mayo was a genuine boot-camp experience in a positive sense. I came to Mayo a medical school graduate and left a physician.

What valuable lesson did you learn at Mayo Clinic?

Spend a little extra time just listening to your patients and what they have to tell you. It's simple to do, doesn't cost very much and is one of the most effective things you can do.

How do you contribute to the Mayo Clinic Alumni Association?

When I trained in neurosurgery, the Rochester campus was Mayo Clinic. Now, Mayo spans a broad geography and diverse set of practices. To some extent, I represent the diversity that is now Mayo Clinic.

What do you do in your spare time?

For the last several years, I've been honing my skills as a private pilot. I gave back a little to the aviation community through volunteer service with the Civil Air Patrol and the Young Eagles program.

What would people be surprised to know about you?

I seriously considered a career in astronomy before deciding on medicine. >>



Gene Siegal, M.D., Ph.D. (PATH '79)

Board Member

- Robert W. Mowry Endowed Professor of Pathology
- Professor of Surgery
- Professor of Cell, Developmental, & Integrative Biology
- UAB School of Medicine, Birmingham, Ala.
- Director, Division of Anatomic Pathology, UAB
- Executive Vice Chair, Pathology, UAB Medicine
- Fellowship: Surgical Pathology, University of Minnesota Medical School, Minneapolis; Pathology Research, Mayo School of Graduate Medical Education
- Residency: Anatomic Pathology, Mayo School of Graduate Medical Education
- Graduate Degree: Ph.D., University of Minnesota, Minneapolis
- Medical School: University of Louisville, Ky.
- Undergraduate: Adelphi University, Garden City, N.Y.
- Native of: Plainview, N.Y.

Why did you train at Mayo Clinic?

My dream was to pursue a clinicianscientist program, and Mayo had just instituted such a program in the Department of Pathology. I viewed it as an opportunity too great to pass up. I looked at approximately 25 programs that allowed me to pursue a Ph.D. along with a residency in pathology. Mayo had the mystique, and I had the outstanding good fortune to find Dr. Harold L. Moses (PATH '73), who was a young faculty member in the Department of Pathology. He agreed to take me under his wing, and the rest is history.

What was your first impression of Mayo Clinic?

Mayo helped solidify my belief that one could do high-quality diagnostic pathology in parallel with competitive extramurally funded basic research. My mentors showed me that it could be done, and I was pleased to try to follow in their large footsteps.

What valuable lesson have you learned at Mayo Clinic?

Mayo is the ultimate company town in the best sense of the words. My years there taught me the value that every member of the health care team brings to patient care along with a strong sense of loyalty that this engenders among the thousands of employees in the Mayo system and the institution that sustains them.

Mayo does an extraordinary number of things exceedingly well, but it was rewarding to me after almost six years at Mayo to complete my training at other institutions. This helped round out my experience and let me better understand the huge diversity that is American medicine.

How do you contribute to the Mayo Clinic Alumni Association?

I would hope to bring a balance to the discussion between those in academia

and those many distinguished members of the Alumni Association who have achieved great success in community practice and other forms of high-quality health care and basic research.

What do you do in your spare time?

I enjoy traveling with my wife, reading and spending time with my children and, more recently, my four grandchildren.



Steven Rose, M.D. (MMS '81, I '82, ANES '84)

Board Member, Executive Committee

- Professor of Anesthesiology, Mayo Clinic College of Medicine
- Department of Anesthesiology
- Dean and Designated Institutional Official, Mayo School of Graduate Medical Education
- Fellowship: Mayo Foundation Scholar, Cape Town, South Africa, and London
- Residency: Anesthesiology, Mayo School of Graduate Medical Education
- Medical School: Mayo Medical School
- Undergraduate: Concordia College, Moorhead, Minn.

G I assimilated the attitudes of many mentors who strove for excellence in all their activities. The opportunities Mayo Clinic provided to grow as a clinician, administrator and educator are the core of my professional identity." – Steven Rose, M.D.

Why did you decide to pursue medicine?

I elected to pursue medicine while I was in high school based on my admiration for a local physician and my interest in science.

Why did you train at Mayo Clinic?

I was thrilled to be admitted to Mayo Medical School after having been impressed by the institution during the interview process. The highly professional patient-oriented atmosphere was very attractive.

What valuable lesson did you learn at Mayo Clinic?

Focus on the best care for every patient. Regardless of status or background, every patient is a VIP deserving of our greatest effort and attention.

I assimilated the attitudes of many mentors who strove for excellence in all their activities. The opportunities Mayo Clinic provided to grow as a clinician, administrator and educator are the core of my professional identity.

How do you contribute to the Mayo Clinic Alumni Association?

My contributions are based on my long experience at Mayo Clinic, engagement with our current and past residents and fellows, and desire to maintain a strong connection with those who trained at Mayo Clinic and share similar values.

What do you do in your spare time? I enjoy Alpine skiing, reading, golf and travel.

What would people be surprised to know about you?

I enjoy and collect Western paintings and sculpture.



Suzanne Ildstad, M.D. (MMS '78)

Board Member

- Director, Institute for Cellular Therapeutics
- Jewish Hospital Distinguished Professor of Transplantation
- Professor of Surgery, Physiology, Immunology
- University of Louisville
- CEO, Regenerex, LLC, Louisville, Ky.
- Fellowship: Pediatric Surgery, Cincinnati Children's Hospital Medical Center; Transplantation Biology Section, Immunology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Md.
- Residency: General Surgery, Massachusetts General Hospital, Boston

- Medical School: Mayo Medical School
- Undergraduate: University of Minnesota, Minneapolis
- Native of: Edina, Minn.

Why did you decide to pursue medicine?

My mother and grandmother were both graduates of Saint Marys School of Nursing in Rochester. I grew up attending their reunions at Mayo Clinic and was exposed to medicine at an early age. I knew by age 5 that I wanted to be a physician.

I chose Mayo Medical School for its excellence and quality of education. I have always respected Mayo Clinic's quality of care and respect for the patient.

I became interested in surgery mainly because of Dr. Ollie Beahrs (S '50), who became a valuable mentor.

What do you do in your spare time?

We are translating our basic research to the clinic and have more than five FDAregulated clinical trials. Much of my time is occupied with that, and it's very rewarding. We have kidney transplant recipients who do not need to take immunosuppression.

What would people be surprised to know about you?

I am the CEO of a biotech startup company in addition to a transplant surgeon.

Mayo Update

Honor Roll of Alumni Benefactors

Each year, the Department of Development recognizes alumni who have made philanthropic gifts to Mayo Clinic via an online, interactive Honor Roll of Alumni Benefactors.

Visit mayoclinic.org/giving-tomayo-clinic/ways-to-give/alumni-giving to see the 2013 Honor Roll of Alumni Benefactors, which includes more than 3,000 names.

Obituaries

John Geisler, M.D. (I '66, P '69), died April 19, 2014.

John Leigh, M.D. (S '60), died Aug. 14, 2014.

George Porretta, M.D. (S' 59), died July 3, 2014.

John Robinson, M.D. (I '56), died April 25, 2014.

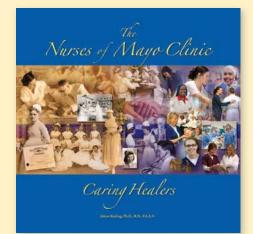
Jeffrey Wilwert, M.D. (FM '89), died June 29, 2014.

Complete obituaries and the Update section, with alumni and staff news, are available on the Mayo Clinic Alumni Association website, alumniconnections.com/olc/pub/MAYO/.

Two new books available for Mayo Clinic Sesquicentennial

The Nurses of Mayo Clinic: Caring Healers

- Hardcover with embossed cover and dust jacket, 152 pages
- First-ever coffee table book about the history of Mayo Clinic nursing, including Minnesota, Arizona, Florida and Mayo Clinic Health System
- Author Arlene Keeling, R.N., Ph.D., a fellow in the American Academy of Nursing and internationally recognized author and scholar in the history of nursing
- Funded with support from benefactors including Saint Marys and



Rochester Methodist volunteers and Methodist-Kahler School of Nursing alumni; leadership gift from John Guider in memory of his mother, Emma C. Lieser, R.N.; Saint Marys Hospital School of Nursing Class of 1932

Art & Healing at Mayo Clinic

- Softcover, 175 pages
- First-ever coffee table book about art at Mayo Clinic
- High-quality color photos of the Mayo art collection in Minnesota, Florida, Arizona and Mayo Clinic Health System
- Funded with a gift from The Barry Foundation
- Letter of endorsement of the Mayo Clinic art collection by Stephen Lash, Mayo Clinic patient, chairman emeritus of Christie's and an internationally recognized specialist in art



The books, \$19.95 each, are available exclusively by Mayo Clinic retailers. To order, visit: <u>http://150years.mayoclinic.org/gift-items.php</u>

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For information about alumni meetings and receptions, visit mayo.edu/alumni

Alumni Philanthropy

Contact: Terri Burkel 800-297-1185 / 507-538-0055 DoctorsMayoSociety@mayo.edu

Mayo 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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Mayo Clinic earns top rank in the nation on *U.S. News & World Report* Honor Roll

Mayo Clinic achieved the highest honor in the 2014–2015 *U.S. News & World Report* ranking of top hospitals, with more number-one rankings than any other provider. Mayo Clinic ranked number one or number two in 11 of the 12 specialties based on reputation, services and volume, safety and clinical outcomes. U.S. News & World Report ranked Mayo Clinic number one in eight specialties including diabetes and endocrinology; ear, nose and throat; gastroenterology and GI surgery, geriatrics; gynecology; nephrology; neurology and neurosurgery; and pulmonology.

No. 1

diabetes and endocrinology ear, nose and throat gastroenterology and GI surgery geriatrics > gynecology

nephrology

neurology and neurosurgery

pulmonology