Medicine@Yale

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Advancing Biomedical Science, Education, and Health Care

Medical school scientist named a Howard Hughes investigator

Immunobiologist studies defenses against pathogens at mucosal points of entry

It was announced on May 9 that Akiko Iwasaki, PH.D., professor of immunobiology and of molecular, cellular, and developmental biology, has been selected as a Howard Hughes Medical Institute (HHMI) investigator.

In addition to receiving one of the most prestigious designations in biomedical science, HHMI investigators are given the support necessary to move their research forward in creative new directions. HHMI provides each investigator with his or her full salary, benefits, and a research budget over an initial five-year appointment.

The institute also covers other expenses, including research space and the purchase of critical equipment. Investigator appointments may be renewed for additional five-year terms, each contingent on a successful scientific review.

Iwasaki is one of 27 top researchers, selected for their individual scientific excellence from a group of 1,155 applicants, to be named HHMI investigators this year.

"HHMI has a very simple mission," said HHMI President Robert Tjian, PH.D., when this year's group of new investigators was announced. "We find the best original-thinking scientists and give them the resources to follow their instincts in discovering basic biological processes that may one day lead to better medical outcomes . . . And while we cannot predict where their research will take them, we're eager to help them move science forward."

Responding to the news of her new appointment, Iwasaki said, "Funding from HHMI will enable my lab to pursue // HHMI *(page 6)*

KIKE CALVO

Akiko Iwasaki is one of 27 top researchers nationwide named investigators by the Howard Hughes Medical Institute.

A 'theory of everything' for disease?

$10 million grant is awarded by the Blavatnik Family Foundation to explore inflammation's role in diverse illnesses

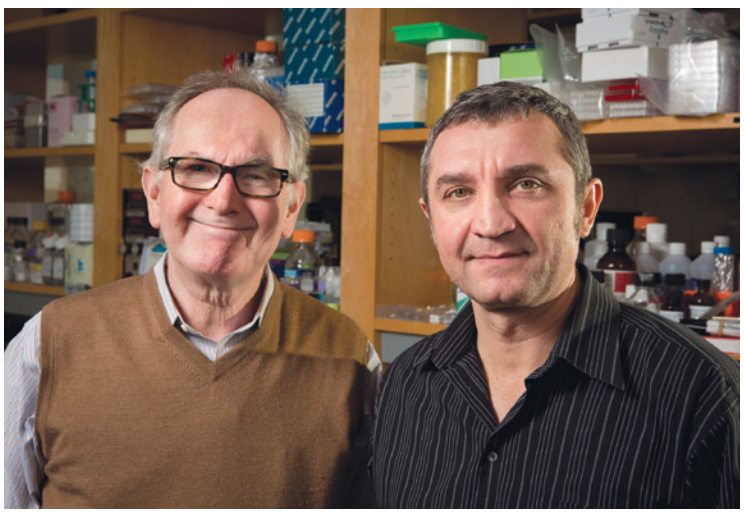
Theoretical physicists have long sought a grand "theory of everything," which would account for all the physical phenomena in the universe by unifying Einstein's general relativity with the so-called standard model based on quantum mechanics.

In recent years, some biomedical scientists, including School of Medicine immunobiologists Richard A. Flavell, PH.D., and Ruslan M. Medzhitov, PH.D., have proposed that deeply understanding inflammatory processes might provide similar unifying insights into a great range of seemingly dissimilar chronic diseases: heart disease, cancer, type 2 diabetes, Alzheimer's disease, and more.

Thanks to a $10 million grant from the Blavatnik Family Foundation, a charitable organization started by American industrialist and philanthropist Leonard Blavatnik, Flavell and Medzhitov will now have the opportunity to put their ideas to the test. "The Blavatnik Family Foundation is proud to support breakthrough scientific discoveries that accelerate the impact of biomedical research," Blavatnik says. "The theory proposed by Drs. Flavell and Medzhitov represents a paradigm shift in the science of chronic diseases and may lead to new prevention strategies, treatments, and even cures for many disorders."

The healthy human body regulates its own tissues and organs to maintain key physiological variables in a beneficial balance, a steady state that scientists call homeostasis. The body even gets some outside help from microbes, or commensal microorganisms, that reside on the skin and in the digestive tract and play a part in maintaining core body temperature, blood pressure, blood sugar, sleep patterns, and a host of metabolic processes needed for fitness and survival.

When infection or tissue damage occurs, the body's innate immune system activates inflammatory mechanisms that help to combat these dangers and restore a proper balance, at least in the short term. Flavell, // Blavatnik *(page 6)*



HAROLD SHAPIRO

The theory advanced by Richard Flavell (left) and Ruslan Medzhitov is a potential "paradigm shift in the science of chronic diseases," says philanthropist Leonard Blavatnik.

Life cut short by war inspires new gift for clinical education

In memory of a spirited young School of Medicine alumnus who died in the Vietnam War just as his academic career was about to begin, clinical-skills teaching at the School of Medicine has received an unprecedented boost.

To mark what would have been her late husband's 50th medical school reunion, Cynthia Livingston, M.A.T., has made a gift of $580,000 to the medical school to establish the Peter B. Livingston, M.D. '63 Fund for Excellence in Teaching, the first School of Medicine fund dedicated to teaching and mentorship in clinical skills. Income from the fund will support faculty efforts to create clinical-skills curricula and to mentor students as they develop those skills.

"Peter had a good experience at Yale, and I've always wanted to honor his memory," says Cynthia Livingston, who earned her Master of Arts in Teaching at Yale in 1963. "I know that Yale places great emphasis on the basic sciences in medical education, which is a wonderful thing, but I just want to make sure // Livingston *(page 7)*

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INSIDE THIS ISSUE

ALSO

TERRY DAGRADI

School of Medicine CIO Daniel Barchi says his experience as a naval officer gave him the confidence to "jump into almost any role," flexibility that has come in handy as he manages the complexities of Yale's implementation of the $250 million Epic electronic medical record system. Barchi says the new system will provide good service for the next two or three decades.

Sailing into a new platform

School's CIO launches electronic medical records with military efficiency

As a surface warfare officer with the U.S. Navy in the 1990s, Daniel Barchi sailed the world in American efforts to intervene in international conflicts. During the Bosnian War in 1994, his ship stationed in the Adriatic Sea, Barchi led armed boarding parties that searched ships for weapons and contraband in support of NATO sanctions.

"My ship carried Tomahawk missiles," Barchi says. "During one of our deployments we were ordered to make a high-speed transit through the Suez Canal into the Red Sea." Although his crew never had to take action, the ship spent several weeks stationed in the middle of the Red Sea, calmly patrolling in case conflict arose.

Barchi himself is calm, polite, and businesslike, with a military bearing and a spartan, orderly office. Now chief information officer (CIO) for the School of Medicine and the Yale-New Haven Health System, he says military life gave him "the ability to jump into almost any role."

After leaving the Navy, Barchi worked for the telecommunications company MCI WorldComm, and then was president of the Carilion Biomedical Institute in Roanoke, Va., before joining Carilion Health System as CIO.

"I had never done IT before," says Barchi, who relied on central principles of leadership in solving a basic problem: Carilion was using multiple electronic tools that didn't work together.

Barchi's strategy was to introduce a single software system that would unite these disparate tools. Today Barchi is managing the rollout of that same system, Epic, at Yale, an ongoing project since his arrival in 2010.

At Yale, installing Epic means introducing electronic medical records (EMRs) for all patients. The system, which cost more than $250 million, went live at Yale-New Haven Hospital (YNHH) at midnight on February 1, and was in operation the following day—with operating and imaging suites heavily booked—just in time for the next monthly billing cycle.

"It went really well," says Barchi, attributing the smooth transition to well-coordinated training sessions, talented medical staff, and the work of IT support teams that included many workers from outside organizations.

Another lesson Barchi learned in the Navy: "Good leadership is about asking appropriate questions." Until recently, however, health information technology was ill-equipped to provide useful answers. Early EMRs were merely digital versions of paper records, he says, and systems were designed primarily for billing, limiting the availability of data needed to answer clinical or research questions.

By providing a single platform for all Yale users, Epic opens doors to numerous new possibilities. For instance, the system can offer prompts to physicians when a given patient might qualify for a clinical trial—a feature that has enabled the Cleveland Clinic to recruit more than 10,000 new research volunteers.

Bridgeport Hospital and the Saint Raphael campus of YNHH will come online later this year, and Epic will be fully implemented at Yale and the Yale New Haven Health System by early 2014. "Now we're focused on using the tool well," Barchi says, adding that he hopes that Epic will serve Yale for another 20 to 30 years.

Importantly, Epic also allows patients to access important health information—quickly, and from any computer. Increasingly, Barchi predicts, the U.S. government will insist that patients have immediate access to health information. If history is any measure, under Barchi's watch, Yale will be prepared.

Connecticut Mental Health Center opens new Wellness Center

The Connecticut Mental Health Center (CMHC), a New Haven-based community mental health center co-administered by the State of Connecticut Department of Mental Health & Addiction services and the medical school's Department of Psychiatry, has opened a new Wellness Center in partnership with the Cornell Scott-Hill Health Center.

The Wellness Center, which serves mainly low-income residents of New Haven who face challenges associated with serious mental illness or substance abuse disorders, opened in February and will serve as a medical home to 600 patients annually.

"Our patients deal with extraordinary challenges daily," said Michael J. Sernyak Jr., M.D., professor of psychiatry and CEO of CMHC.

Benefits for patients include annual check-ups, prevention plans, sick visits, referrals to specialists, and consultations with medical professionals about health concerns. The availability of basic medical care will be one in a growing list of services CMHC offers some 5,000 patients per year in the greater New Haven area.

Patients being treated for chronic mental illness and substance abuse problems also have access to a network of community programs that include housing and residential services, employment services, and social rehabilitation.

Michael Sernyak

Community-based medical partner Cornell Scott-Hill Health Center will provide primary care services at the Center together with CMHC staff.

The Wellness Center is supported in part by a $1.6 million grant from the Substance Abuse and Mental Health Services Administration Center for Integrated Health Solutions.

Emergency Medicine chair lauded for research

Gail D'Onofrio

Gail D'Onofrio, M.D., M.S., professor and chair of the Department of Emergency Medicine, has been honored with the 2013 Society for Academic Emergency Medicine (SAEM) Excellence in Research Award. The award, given for the first time to a woman, honors D'Onofrio's accumulated body of research as well as her influence as a leader in academic Emergency Medicine.

D'Onofrio's research, funded by the National Institute on Drug Abuse and the National Institute on Alcohol Abuse and Alcoholism, has focused on perfecting interventions for Emergency Department (ED) patients who misuse drugs and alcohol, and has led to effective, empirically tested techniques that have influenced intervention models across the U.S.

D'Onofrio is a mentor to medical students, trainees, and junior faculty in Emergency Medicine at Yale, and is also the principal investigator on a training grant funded by the Substance Abuse and Mental Health Services Administration to train residents in drug and alcohol intervention techniques in all medical settings.

D'Onofrio earned her bachelor's degree at Duke University, her M.S. at Boston University, and her M.D. at Boston University School of Medicine. She completed a residency in emergency medicine at Boston City Hospital, and a fellowship with the Substance Abuse and Mental Health Services Administration. She serves as physician-in-chief of Yale-New Haven Hospital's ED, and is a founding member of the American Board of Addiction Medicine.

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ADVANCES
Health & Science News

Making an old brain young again


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It doesn't take a neuroscientist to observe that old and young brains differ: children and adolescents can learn new things more easily and more quickly than adults, and their brains can recover more fully from injury. Underlying these differences is Nogo Receptor 1 (NgR1), a protein that fixes brain circuits in place in adulthood to ensure stable functioning.

Stephen M. Strittmatter, M.D., PH.D., Vincent Coates Professor of Neurology and professor of neurobiology, teamed up with William B. Cafferty, PH.D., assistant professor of neurology, and colleagues to study NgR1's role in brain plasticity—the brain's ability to rearrange its connections based on new experiences.

In the March 6 issue of *Neuron,* the group reports that adult mice lacking NgR1 exhibited plasticity at levels typically seen in much younger mice; the mice were more adept than control mice at learning new tasks, and were more able to recover from trauma. The findings, they say, could lead to new ways to treat brain injuries, such as stroke, or memory loss in humans.

A microscopic syringe to deliver vaccines

Sometimes there's a goof-up when bacteria divide, and one cell, called a "minicell," contains no chromosomal DNA. Minicells can't replicate (or cause infection), and scientists can tweak them to carry proteins, making them a safe vehicle for vaccines.

Jorge E. Galán, PH.D., D.V.M., chair and Lucille P. Markey Professor and chair of Microbial Pathogenesis and professor of cell biology, had previously shown that a needle-like machine possessed by the bacterium *Salmonella typhimurium* could be engineered to inject into human cells any particle that scientists wanted the body's immune system to attack. But using this syringe mechanism meant setting a small number of bacteria loose in the body, which can be risky in some patient populations.

In a new study, published March 12 in *Nature Communications*, Galán and colleagues isolated minicells from a strain of *Salmonella* and engineered them to contain all the components of the injection system. When administered to mice, the minicells elicited an immune response but did not generate a full-blown infection, the ideal response to a vaccine.

The system could be used to combat cancer as well as a wide variety of infectious diseases, says Galán.

Making a real-world impact for elders

By taking multiple health issues of elderly patients into account, Yale researchers are improving quality of life and independence

The number of Americans aged 90 and older has tripled in the past three decades and will quadruple again over the next four, according to the U.S. Census Bureau, and the majority of people in this age group have one or more disabilities. But medical studies typically seek volunteers with one—and only one—disease so that variables can be eliminated from research data.

"Those people don't exist!" says geriatric medicine expert Leo M. Cooney Jr., M.D., Humana Professor of Medicine—at least not among the patients he treats. In other words, there is a rapidly growing segment of the population that health researchers have historically made a point of excluding from studies. But that is changing, and the Yale Program on Aging (POA), founded by Mary E. Tinetti, M.D., in 1991 and now one of the most respected research programs on health and aging in the U.S., has led the way.

The POA has developed research methodologies that take into account the multiple health issues that seniors typically face to examine how these problems interact and to develop evidence-based interventions that promote quality of life and independence.

"We have the opportunity of potentially solving some of the most vexing issues in our society," says Thomas M. Gill, M.D., Humana Professor of Medicine, and current director of the POA and the affiliated Claude D. Pepper Older Americans Independence Center, which was launched at the School of Medicine in 1992.

"Rather than adapt our research questions to the available methodology, we really adapted the methodology to the clinical questions," says Tinetti, the Gladys Phillips Crofoot Professor of Medicine and professor of epidemiology and investigative medicine.

The program is home to a team of biostatisticians sought after throughout the medical school for their ability to apply rigor to out-of-the-box questions. "We have one of the best biostatistics cores in the country," says Cooney.

Tinetti has worked with this team to develop ways to explore complex issues in the lives of older people. Her work has focused on falls, an area that many researchers would have seen as hopelessly broad. Many physical factors play into falls, as do furniture arrangement, poor lighting, and other factors. But falls cause 95 percent of hip fractures and kill more than 20,000 elderly Americans a year, according to the Centers for Disease Control, so Tinetti saw falls as a major public health issue that was worth pursuing.

Tinetti's research proved that falls, once thought an inevitable part of aging, could be predicted and prevented, and that fall-prevention programs offer significant health care savings.

Demonstrating the success and cost-effectiveness of interventions has been a hallmark of POA research, which has led to widespread adoption of the fall-prevention strategies Tinetti championed, and of strategies to prevent delirium during hospital stays, devised by former POA member Sharon Inouye, M.D., adjunct professor of internal medicine and assistant clinical professor of nursing.

"We have taken our research to the next step that a lot of researchers don't," says Tinetti. "Not a publication in a top journal or a presentation at a national meeting. The next step is working with the clinical community and the community at large."

Tinetti's work has received wide praise, and earned her a MacArthur Fellowship (or "Genius Grant") in 2009. But she maintains that research on aging remains "unglamorous," so the POA makes a point of aggressively recruiting medical students and young physicians for training. "We make major investments in young investigators," and not all are geriatricians, says Gill, also professor of public health. The program works with doctors who specialize in cardiology, infectious disease, or any other areas that come into play in the health of older people. Increasingly, basic scientists are collaborating with clinical researchers.

The necessary element is that collaborators be "brave enough to embrace the complexity" of the field, says Gill, who was once a trainee in the program himself, working under Tinetti. He credits her with revealing this complexity—the "almost overwhelming" interrelationships among the health problems facing seniors. But complexity has its advantages, he adds, often leading to multiple strategies to help elderly patients stay independent. For example, though numerous factors contribute to falls, by addressing just a few of these causes, clinicians have been able to make great progress in their prevention. **// Aging** *(page 7)*


CARL KAUFMAN

Mary Tinetti (front row, left), Thomas Gill (back row, fourth from left), and Leo Cooney (back row, second from right) are part of a diverse and talented group of Yale researchers, clinicians, statisticians, and nurses specializing in geriatrics.

Bringing young physicians into research on aging


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Researchers at the School of Medicine are leading the way to improve the quality of life and independence of older Americans by developing effective, proven solutions to the health problems faced by seniors.

Because these Yale innovations are also cost-effective, they have been widely adopted across the country. Your support for continuing this work is crucial as the number of Americans reaching age 90 and beyond is increasing at a rapid rate.

To secure the future, we must attract young physicians to geriatric research and care of the elderly, and gifts that support their work will have a lasting impact for seniors.

Current-use gifts can be targeted to support specific projects; *endowments* can generate perpetual support for investigators just launching their careers.

For information about these and other ways to support the School of Medicine, contact Jancy Houck, associate vice president for development and director, medical development, at (203) 436-8560 or jancy.houck@yale.edu

OUT & ABOUT

January 2 The **Yale Psychiatry Wellness Initiative** joined forces with New Haven's Miya's Sushi for a dinner to benefit the Immanuel Baptist Shelter for homeless men. (Front, from left) Third-year psychiatry resident **Beth Grunschel**, M.D.; **C.J. Algarin-Cruz**, a student at Common Ground High School; **Meredith Siefert**, Miya's Sushi intern; Common Ground students **Jenny Edge** and **Janet Sakouvogui**; second-year psychiatry resident **Ayana Jordan**, M.D., PH.D.; and third-year psychiatry resident **Yauss Safavi**, M.D. (Back, from left) **Bun Lai**, chef and owner of Miya's Sushi, and **David Ross**, M.D., PH.D., assistant professor of psychiatry.

SHANE SEGER

CARL KAUFMAN (2)

February 25 Members of the Yale medical community convened for a ribbon-cutting ceremony marking the **opening of the Wellness Center at the Connecticut Mental Health Center** (CMHC; see related story, page 2). **1.** (From left) **John H. Krystal**, M.D., Robert L. McNeil Jr. Professor of Translational Research, chair of the Department of Psychiatry, and chief of psychiatry at Yale-New Haven Hospital; **Robert J. Alpern**, M.D., dean and Ensign Professor of Medicine; **Nancy Wyman**, lieutenant governor of Connecticut; **Michael Taylor**, interim CEO of Cornell Scott-Hill Health Center; **Patricia Rehmer**, MSN, commissioner of Connecticut's Department of Mental Health and Addiction Services; **Michael J. Sernyak**, M.D., professor of psychiatry and CEO of CMHC. **2.** (From left) **Larry Davidson**, PH.D., professor of psychiatry; **Robert A. Cole**, M.H.S.A., COO of CMHC; **Gale M. Banks**, APRN, the CMHC's staff liaison to the Wellness Center; **Aniyizhai Annamalai**, M.D., assistant professor of psychiatry and medicine and director of the Wellness Center; **Chyrell D. Bellamy**, PH.D., assistant professor of psychiatry; **Edwin F. Renaud**, LCSW, PH.D., associate director of clinical services at CMHC; **Rebecca A. Miller**, PH.D., instructor in psychiatry and director of peer support at CMHC; **Jeanne L. Steiner**, D.O., associate professor of psychiatry and CMHC medical director.

TERRY DAGRADI

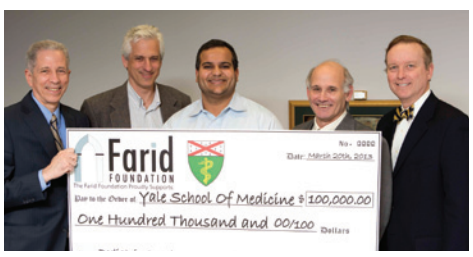
March 15 On **Match Day** each year, graduating medical students around the U.S. learn where they'll head for residencies following their time in medical school. At the School of Medicine this year, 91 members of the Class of 2013 "matched." **Charles Odonkor** (left), who matched in internal medicine at Yale-New Haven Hospital, followed by physical medicine and rehabilitation at Johns Hopkins Hospital, savored the moment with his friend **Richard Arthur**, M.P.H., a 2012 graduate of the School of Public Health.

February 22 Members of the medical school's Class of 2015 performed in the annual **Second Year Show** in Harkness Auditorium, an evening of theatre in which students poke fun at their professors with skits and choreographed musical numbers. Proceeds from this year's zombie-themed show, titled "The Walking Med," were donated to the New Haven-based charities New Haven Community Soup Kitchen, Liberty Community Services, Continuum of Care, Inc., and the Yale Community Health Care Van. **1. Amanda King** performed in "Escape to Histology Lab." **2.** (From left) **Pierre Martin**, **Sean Bickerton**, **Lauren Krumeich**, King, and **Alex Scherer** in "I'll Make a Doc Out of You." **3.** (From left) Scherer and King in the same number. **4.** (From left) **Veronica Shi**, Scherer, and **Adam Kundishora** in "Nowhere to Hide." **5.** (From left) **Luis Rubio**, **Jared Sun**, and **Alex Svoronos** in the show's curtain call.

TERRY DAGRADI (5)

HAROLD SHAPIRO (3)

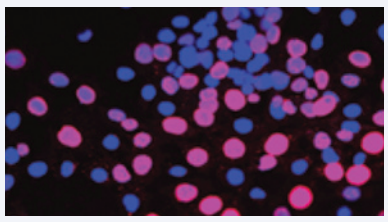
March 16 Patients of the Yale Children's Diabetes Program and their families attended the annual **Family Day Symposium**. The half-day event, held on Yale's West Campus, included lectures, discussions, and interactive programs for adults and children. **1. Eda Cengiz**, M.D., associate professor of pediatrics. **2. Amanda Rossi** (left) and **Jailene Lobo**. **3.** (From left) **William V. Tamborlane**, M.D., professor of pediatrics and chief of the Section of Pediatric Endocrinology, with **Jon Borkowski** and **Chris Frataza**, sales representatives of the health care company Novo Nordisk. **4.** (From left) **Susan Berson** and **Jennifer L. Sher**, M.D., PH.D., instructor in pediatrics.



HAROLD SHAPIRO

March 20 The **Farid Foundation** made a $100,000 gift to support pediatric oncology at the School of Medicine. The Connecticut-based philanthropic foundation was established in 2005 by brothers Tariq and Kamran Farid, founders of Edible Arrangements. (From left) **Robert J. Alpern**, M.D., dean and Ensign Professor of Medicine; **Gary Kupfer**, M.D., professor of pediatrics and pathology and chief of the Section of Pediatric Hematology/Oncology at Smilow Cancer Hospital at Yale-New Haven; **Kamran Farid**; **George Lister**, M.D., Jean McLean Wallace Professor and chair of the Department of Pediatrics and professor of cellular and molecular physiology; **Clifford W. Bogue**, M.D., associate professor of pediatrics, chief of the Section of Pediatric Critical Care Medicine, and physician-in-chief at Yale-New Haven Children's Hospital.

Applying muscle to muscular dystrophy



COURTESY OF ANTON BENNETT

A protein newly described by Yale researchers puts the brakes on the creation of new muscle cells; when this protein is inactivated muscle stem cells make muscle. Using a mouse model of Duchenne muscular dystrophy (DMD), a disease of progressive muscle loss, the group discovered that switching this protein off reduced symptoms of the disease.

In humans, DMD primarily affects boys, with symptoms of muscle weakness as early as infancy leading to an average lifespan of only 25 years. There is no treatment for the disease.

In the April 1 issue of the *Journal of Clinical Investigation*, a team led by Anton M. Bennett, PH.D., associate professor of pharmacology and comparative medicine, reports that the protein Mkp5 keeps muscle stem cells in a state of readiness, poised to make new muscle when needed. When Mkp5 is removed, these stem cells are activated and embark on generating new muscle. DMD mice lacking Mkp5 showed both higher levels of new muscle cell creation (pink in photo) and lower rates of muscle degeneration. The team says that drugs that block Mkp5 in humans may open new avenues of therapy for DMD.

Cellular gatekeepers of inflammation

When a tissue in the body becomes injured or infected, white blood cells rush from nearby blood vessels to launch an immune response, generally a positive first step in the healing process. But if too many of these first responders arrive on the scene, inflammation can result, so it's vital that the response is tightly regulated.

A team of scientists led by Anjelica Gonzalez, PH.D., assistant professor of biomedical engineering, and Jordan S. Pober, M.D., PH.D., the Bayer Professor of Translational Medicine and professor of immunobiology, dermatology, and pathology, suspected that cells called pericytes, which form the outermost layer of blood vessels, might act as gatekeepers that manage the release of white blood cells into tissue.

The team created a model of blood vessels with discrete layers of human pericytes and endothelial cells, which line the interior of vessels. They found that pericytes precisely and selectively restrict the number of white blood cells that exit vessels into injured tissues. The finding will help researchers build better *in vitro* models of blood vessels, and could lead to new drugs to treat inflammatory diseases, especially those that affect the lungs, eyes, and skin, which have high levels of pericytes.

Salt is new culprit in autoimmunity

In a surprising finding, high salt levels are found to spur the growth of immune cells involved in numerous autoimmune disorders

The health risks of eating high amounts of salt make up quite a laundry list: high blood pressure, heart attacks, stroke, and kidney stones, to name a few. Now, School of Medicine scientists have discovered another potential detriment of a high-salt diet. Salt, they've found, may drive the progression and severity of autoimmune diseases, through its interactions with certain immune molecules in the gut.

The research, which appeared in the March 6, 2013 issue of *Nature*, is based on experiments with mice, but likely applies to human autoimmune diseases, including multiple sclerosis, says David A. Hafler, M.D., Gilbert H. Glaser Professor and chair of Neurology, professor of immunobiology, and senior author on the new paper.

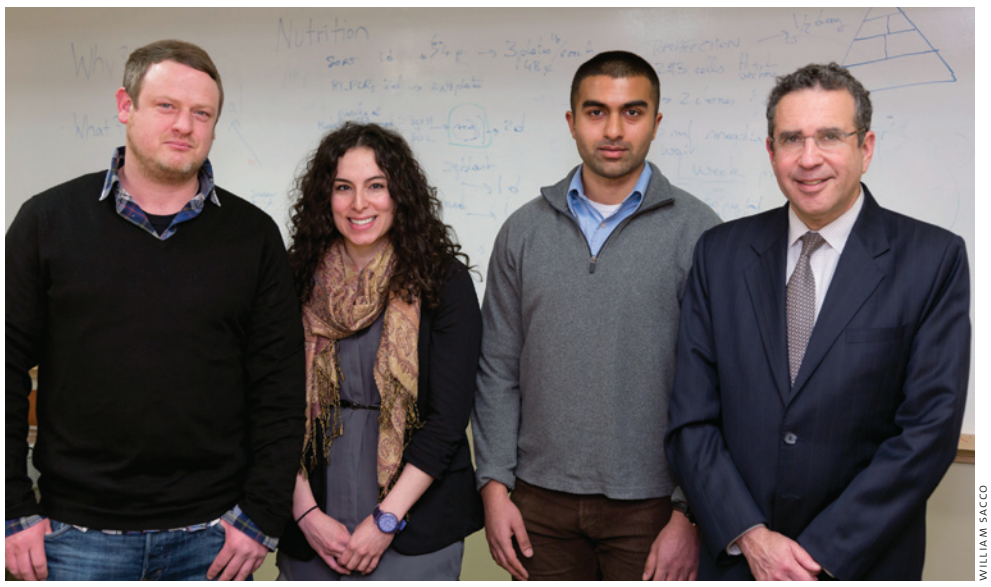
"This goes to show that the immune system may well be linked to what you eat, in unexpected ways," Hafler says. He is confident enough in the findings, he adds, that he is already recommending that his patients who are prone to autoimmune disease reduce their salt intake.

Scientists have long known that a type of immune cell, called T helper 17 (TH17) cells, is involved in several autoimmune diseases, including multiple sclerosis, psoriasis, type 1 diabetes, and rheumatoid arthritis. Patients with these conditions, scientists have shown, have higher levels of TH17 cells, which helps to explain why their immune systems are more likely to attack their bodies' own cells.

But over the past 50 years, the incidence of these autoimmune diseases has increased, and first author Markus Kleinewietfeld, PH.D., associate research scientist, Hafler, and colleagues wondered whether there was something in the environment that affected TH17 cells. When they followed the diets of patients, something jumped out at them. "People who are at a fast-food restaurant more than once a week had higher levels of TH17 cells," Hafler says.

To test whether it was the high levels of salt in most fast food that accounted for this difference—rather than levels of fat or other compounds—the researchers first tested TH17 cells growing in the lab. When they added salt to the culture surrounding these cells, more than 10 times as many cells matured.

Hafler's group then tested the implications of this finding in a strain of mice prone to developing a version of multiple sclerosis. When they added moderate amounts of extra salt to the diets of these mice, the severity of their disease increased. Normally, salt levels are much lower in the blood than in surrounding tissues. While a high-salt diet doesn't drastically increase the level of salt in the blood, it does increase the salt that's free in the gut, // Salt *(page 7)*



WILLIAM SACCO

(From left) Associate research scientist Markus Kleinewietfeld, M.D./PH.D. student Amanda Hernandez, and postdoctoral associate Mansoor Zaidi are exploring the potential effects of dietary salt on autoimmune diseases in the laboratory of David Hafler (right).

Prostate cancer: moving beyond 'watchful waiting'

Prostate cancer is the second-leading cause of cancer death in American men: the American Cancer Society expects the disease will claim nearly 30,000 lives in 2013. The disease mainly affects older men—the median age of diagnosis is 67—and it's a slow-growing cancer, so most men diagnosed with the disease are likely to die of other causes.

Brad Davis, a veterinarian with a family history of prostate cancer, was diagnosed at age 54. A blood test he had taken showed elevated levels of prostate-specific antigen (PSA), a protein that may indicate the presence of the disease, and a biopsy confirmed the diagnosis.

"This put me in a quandary," says. Davis, who knew he had many active years still ahead, and was concerned that surgery or radiation could compromise them. Still, he was young enough that the cancer, if left unchecked, could eventually kill him.

Just a few years ago Davis's options would have been limited to "watchful waiting" (close monitoring by a doctor with treatment postponed until deemed necessary) or prostatectomy to remove part or all of his prostate. But thanks to advances in prostate cancer treatment, his Yale doctors were able to offer a relatively new, middle-of-the-road approach called active surveillance.

When Peter G. Schulam, M.D., PH.D., came to Yale from the University of California at Los Angeles (UCLA) in 2012 as professor and chair of the School of Medicine's newly formed Department of Urology, one of his first actions was to assemble the team and equipment necessary to perform active surveillance.

Schulam, who directs Yale Cancer Center's Prostate and Urologic Cancer Program, had seen good results with active surveillance in California, but the approach is so new that there are not yet any national guidelines for the protocol.

At Yale, patients like Davis who have a high PSA result or an abnormal digital exam have a baseline biopsy, then a repeat biopsy after six months, and a subsequent biopsy every two or three years—or more frequently if indicated.

One reason biopsies are a preferred diagnostic tool in prostate cancer is that the prostate is "the only solid organ in the body in which we cannot image cancer," Schulam says.

ROBERT LISAK

Peter Schulam and colleagues in the Department of Urology offer "active surveillance" to men diagnosed with prostate cancer.

So if a magnetic resonance imaging scan reveals suspicious lesions in the prostate, Yale doctors providing active surveillance perform what is known as a fusion biopsy using the Artemis device, a 3D imaging and navigation system that tracks the disease's progress with great precision.

"We use Artemis and fusion biopsy to take // Prostate *(page 6)*

// Blavatnik *(from page 1)* chair and Sterling Professor of Immunobiology, and Medzhitov, the David Wallace Professor of Immunobiology, postulate that these same inflammatory mechanisms can have a cumulative damaging effect on homeostatic controls—an effect they believe is a root cause of many serious health disorders. With the new grant from the Blavatnik Family Foundation, the scientists plan a detailed study to define the molecular links between inflammation, commensal microorganisms, and chronic disease.

Yale President-elect Peter Salovey expressed the University's gratitude to the Blavatnik Family Foundation for what he called "an extremely generous and far-sighted" contribution. "The research now under way in the Medzhitov and Flavell laboratories has the potential to transform our understanding of human biology and our approaches to the most intractable diseases. This grant will accelerate their work at Yale's Department of Immunobiology, which is world-renowned for leading major advances in innate and adaptive immunity," Salovey said.

Medzhitov and Flavell, both of whom are Howard Hughes Medical Institute investigators, have led pioneering studies on the control of inflammation by the innate immune system.

Medzhitov is widely recognized for classic studies he conducted in the late 1990s with the late Charles A. Janeway Jr., M.D., that clarified the functions and importance of the innate immune system, work for which he received a Blavatnik Award for Young Scientists in 2007. In February, Medzhitov and Flavell were jointly awarded the 2013 Vilcek Prize for Biomedical Science.

Robert J. Alpern, M.D., dean of the School of Medicine, believes that a unified theory of inflammation and chronic disease will be a game-changer. "This work offers a whole new way to look at the causes of many chronic illnesses, including cardiovascular disease, type 2 diabetes, autoimmune diseases, asthma and allergies, neurodegenerative diseases such as Alzheimer's disease, and cancer," Alpern says. "A few years from now, I am optimistic that we will be in a position to develop new therapeutics that can broadly impact human health and quality of life."

The founder and chair of Access Industries, Leonard Blavatnik is deeply committed to supporting innovation in biomedical research and higher education. In 2007, the Blavatnik Family Foundation established the Blavatnik Awards for Young Scientists, awarded through the New York Academy of Sciences, to recognize innovative and high-impact accomplishments in the life sciences, physical sciences, mathematics, and engineering. Blavatnik has supported the Broad Institute at Harvard University and MIT, and he has provided seed funding at Harvard for highly promising, early-stage research in the life sciences. In 2010, he contributed more than $115 million to the University of Oxford to establish the Blavatnik School of Government.

// HHMI *(from page 1)* questions that are risky but potentially very rewarding. We will be able to understand the types of immune responses generated by sensing different levels of danger associated with infections, and to determine how the bacteria and viruses that inhabit our body influence the immune system. Ultimately, we hope to design vaccines that effectively prevent diseases caused by viruses that enter through mucosal sites."

Iwasaki's body of research has addressed the mechanisms of innate recognition of viruses and the initiation of antiviral immunity.

Her lab focuses on sites where a virus encounters mucosal surfaces. Until now, most efforts to develop vaccines have focused on the immune system's antibodies, or T cells, circulating through the body.

But efforts to harness these circulating T cells have not been effective in organs such as the vagina, intestines, lung airways, and central nervous system, which restrict the entry of these "memory" T cells.

Iwasaki's research has thrown light on the crucial role of dendritic cells, a special class of white blood cells that form part of an early warning system against infection, in protecting the body from certain viruses.

Dendritic cells are abundant in skin and mucosal surfaces, where they act as sentinels against foreign invaders.

In a study recently published in *Nature*, Iwasaki's team developed a new model for vaccination against genital herpes, a disease for which there is no effective immunization, and no cure. The researchers focused on peripheral tissue in the female genital tract, where viral exposure occurs.

Working with mice, they explored a two-part vaccine strategy they call "prime and pull": The priming involves conventional vaccination to elicit a system-wide T cell response. The pulling involves recruitment of activated T cells directly into the vaginal tissue, via topical application of chemokines—substances that help mobilize the immune cells.

Iwasaki and colleagues found that the recruited T cells were able to establish a long-term niche and offer protective immunity against genital herpes by reducing the spread of herpes simplex virus into sensory neurons.

Other recent research by Iwasaki, published in *Proceedings of the National Academy of Sciences*, showed that, following influenza infection, the relationships among bacteria in the gut critically regulates the generation of the immune response's virus-specific CD4 and CD8 T cells and antibody responses.

Her results revealed the importance of commensal ("good") microbes in regulating immunity in the respiratory mucosa through the proper activation of multiprotein complexes known as inflammasomes.

A non-profit medical research organization with an endowment of more than $16 billion, HHMI was founded by businessman Howard Hughes in 1953.

// Prostate *(from page 5)* pictures and overlap them with real-time ultrasound images to help us guide where our needles go," explains Preston Sprenkle, M.D., assistant professor of urology. This method allows doctors to take future biopsies from the exact same spot in the prostate where previous lesions were found, allowing them to better monitor the most troublesome part of the gland.

So far the evidence in favor of systems like Artemis is promising. A study published in January by UCLA researchers in the *Journal of Urology* found that targeted biopsies were three times likelier than conventional biopsies to detect cancer, and there is hope that tools like Artemis may enable doctors to treat prostate cancer more efficiently.

"We overtreat prostate cancer in the United States," says Schulam. Most cases are not life-threatening, but a vast majority of men with prostate cancer diagnoses undergo aggressive treatments—there are between 100,000 and 120,000 radical prostatectomy surgeries per year in the U.S. In 2012, the U.S. Preventive Services Task Force recommended against PSA-based screening for prostate cancer, reasoning that too many patients were being treated for asymptomatic disease. The recommendation "charges us as urologists to better differentiate those who need treatment from those who don't," Schulam says.

The patients referred to Yale who benefit most from active surveillance are at a low risk of developing symptoms. Normally, Sprenkle says, he would recommend radiation or surgery in patients who, like Davis, are in their 50s.

"The chance their cancer is going to progress over the next 30 to 40 years is very high," says Schulam, adding that men in their 60s are more likely to find that active surveillance is an attractive treatment option.

Doctors also assign a Gleason score to prostate cancers, a measure of the likelihood a cancer will spread based on its appearance under a microscope. Men with a Gleason score of 6 or below and with cancer in only a few biopsy samples are also good candidates for active surveillance, Sprenkle says. Davis says that his Gleason score of 6, in only 20 percent of one core biopsy—confirmed in a secondary biopsy with Artemis—contributed to his decision.

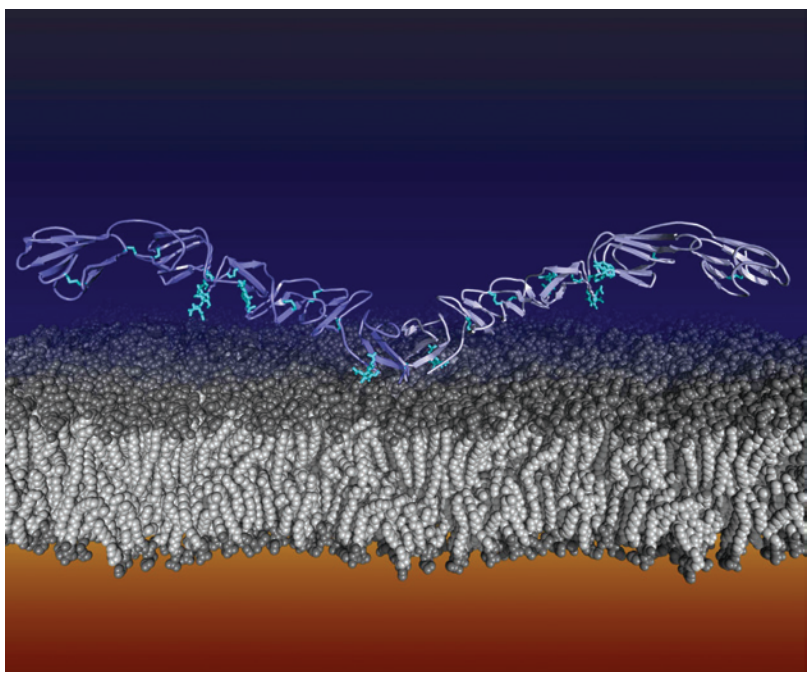
ROBERT LISAK

(From left) Urologists Peter Schulam and Preston Sprenkle discuss a patient's case using the Artemis system, which offers new flexibility to men diagnosed with prostate cancer who are not ready to pursue surgical treatment.

Davis, now 55, was the first patient in Yale's active surveillance program, and he is happy to have had the choice available to him.

When interviewed for this article, Davis was symptom-free, his PSA level was at 3 and not a cause for concern, and he had "some benign hyperplasia"—prostate enlargement—"that's not real significant," he said. "The reality is many men diagnosed in their 60s may have lesions for years like mine before detection."

Eye for Science



COURTESY OF YORGO MODIS

Pestiviruses, animal pathogens related to hepatitis C virus, are a major global health threat. They deliver their genome into hosts' cells by fusing their envelope with the cell membrane. In April, in *Proceedings of the National Academy of Sciences,* Associate Professor of Molecular Biophysics and Biochemistry Yorgo Modis and colleagues published the crystal structure of glycoprotein E2 from a pestivirus known as BVDV. Here, the glycoprotein (blue and purple) is seen on the viral envelope (gray), poised to fuse with a host cell membrane.

AAAS Fellows

Four School of Medicine faculty members have been elected fellows of the American Association for the Advancement of Science (AAAS), an international nonprofit organization dedicated to advancing science around the world.

Lynn Cooley, PH.D., the C.N.H. Long Professor of Genetics, is renowned for her work on egg development in the fruit fly *Drosophila melanogaster.* Also professor of cell biology and of molecular, cellular, and developmental biology, Cooley directs Yale's Combined Program in the Biological and Biomedical Sciences.

Pietro De Camilli, M.D., Eugene Higgins Professor of Cell Biology and professor of neurobiology, is one of the world's leading researchers in the cell biology of the synapse. De Camilli is also a director of the Program in Cellular Neuroscience, Neurodegeneration, and Repair, and a Howard Hughes Medical Institute investigator.

Mark W. Hochstrasser, PH.D., Eugene Higgins Professor of Molecular Biophysics and Biochemistry, works to understand the mechanisms by which some specific proteins are rapidly degraded within cells while most others are spared. Hochstrasser is also professor of molecular, cellular, and developmental biology.

David A. McCormick, PH.D., the Dorys McConnell Duberg Professor of Neurobiology and vice director of the Kavli Institute for Neuroscience at Yale, is an authority on the organization and function of the cellular networks of the brain's cerebral cortex and thalamus.

// Gift *(from page 1)* that the clinical side of things has its own support."

Born in 1937, Peter Livingston died on November 19, 1968 after months of providing psychiatric care to soldiers at a division-level hospital at Long Binh Post, a major command center for the U.S. Army. He had been about to join Cynthia and their baby son for a leave in Hawaii when his helicopter was shot down.

His wife's gift honors a man whom his friends say was broadly educated, energetic, and warm—and one who had the makings of a dedicated teacher himself. Livingston majored in English at Tufts University in Medford, Mass., where he wrote and published poetry. In medical school, full of what his friend and Yale alumna Sharon Meltzer M.A., PH.D., calls "nervous keenness," he was profoundly influenced by the ecumenical approach to medicine championed by Frederick "Fritz" Redlich, M.D., then chair of the Department of Psychiatry. Livingston took graduate seminars at Yale in philosophy and ethics and greatly admired the university's legendary chaplain, William Sloane Coffin Jr.

For his psychiatry residency, Livingston went to the Massachusetts Mental Health Center (MMHC) in Boston, where he taught Harvard medical students with enthusiasm, recalls School of Medicine classmate and fellow Harvard resident James S. Dalsimer, M.D., now a psychoanalyst in Boston. MMHC's overall learning atmosphere was "a treat beyond treats," says Dalsimer, and it was there that Livingston published his first two papers and decided to pursue schizophrenia research.

But while still a resident, Livingston was drafted into the Army. Though Livingston opposed the Vietnam War, says another medical school classmate, Herb Meltzer M.D., who is now a research psychiatrist at Northwestern University, he took his deployment gracefully. "He mastered whatever feelings he had about the bad luck he had in being sent over there," says Meltzer, "and did the job he was supposed to do."

Much of that job involved teaching, and Livingston wrote to his wife about the daily teaching marathons he undertook in the Army hospital. "He said by the end of these things he'd be hoarse but happy," recalls Cynthia. While still in Vietnam, he was accepted as a fellow at Cambridge University, where he planned to continue his studies of schizophrenia. He was preparing a third paper on psychosis at the time of his death. Had he lived, says Meltzer, "I would imagine Peter would have been a professor of psychiatry at a leading medical school."

If so, he might have found it challenging to find time to teach clinical skills, as many practicing physicians and researchers do. The new Livingston Fund is expected to relieve some of that time pressure.

"We're very grateful to Cynthia, especially for her appreciation of the effort that's involved in teaching mentoring and curriculum development, and the importance of attention to clinical skill-building in the education of future physicians," says Deputy

COURTESY OF CYNTHIA LIVINGSTON

Peter Livingston, of the School of Medicine's Class of 1963, died in the Vietnam War. On the occasion of the 50th reunion of his class, his widow, Cynthia Livingston, has endowed a fund to support the teaching of clinical skills.

Dean for Education Richard Belitsky, M.D., a psychiatrist and Harold W. Jockers Associate Professor of Medical Education. "It is through her generosity that our faculty will have the time and resources needed to design and implement innovative approaches to clinical education."

That's just what Livingston is hoping for. A retired teacher herself, she has fond memories of joining her husband to hear superb discussions at Grand Rounds while he was in medical school. And their son, Oliver M. L. Bacon, M.D., M.P.H., who graduated from Yale College in 1988 and from the School of Medicine in 1996, is now a clinical faculty member at the University of California–San Francisco.

"As medicine changes in the 21st century and becomes a little more abstract, I think the clinical skills that are passed on are still really important," Livingston says. "Freeing up some time for teaching clinical skills is essential."

// Salt *(from page 5)* and Hafler believes that a high-salt diet could activate TH17 cells there. Such a diet also could change the balance of bacteria living in the gut, which could likewise affect the immune system.

There are more than 150 genes linked to autoimmune disease risk in humans, and when Hafler took a fresh look at the genes on the list, he discovered that almost 30 percent of these genes were activated by salt, further supporting the connection.

"This really opens up a whole new area of investigation," Hafler says, adding that there are likely to be environmental factors other than salt that are responsible for the increased prevalence of autoimmune disease, so there are numerous avenues of research yet to be followed.

David Fox, M.D., a rheumatologist at the University of Michigan, calls Hafler's results "exciting" but agrees that more research is needed. "The story may be more complicated than it seems," Fox says. "I don't think this one paper completely proves that there is a link between diet and multiple sclerosis."

Moreover, he points out, the effect of salt on TH17 cells is unlikely to have the same impact on all autoimmune diseases. The incidence of rheumatoid arthritis, for example, has not risen over the time period that multiple sclerosis has, so it may not be as affected by diet.

John O'Shea, M.D., chief of the National Institutes of Health's Molecular Immunology and Inflammation Branch, agrees. Changing official dietary recommendations without clinical trials would be premature, he says, but also points out that low-salt diets are already recommended for some patients with risk factors for other disorders.

"The findings are interesting and provocative, but we don't know if this is pertinent to humans with autoimmunity," says O'Shea. "Lots more work needs to be done to establish this point. Nonetheless, the study raises an exciting possibility for intervention."

Motivated by that possibility, Hafler and colleagues are beginning a new dietary study in humans to more firmly establish the link between salt intake and autoimmunity.

But in his role as a physician, Hafler says, he's not waiting to suggest dietary changes to his patients.

"If you have a high susceptibility to autoimmune disease in your family, especially if you have an infant, I would recommend trying to keep salt levels low,"says Hafler. "We have to be careful in extrapolating this to human disease at this point," but, like O'Shea, he believes the potential benefits of a low-salt diet outweigh any risks.

// Aging *(from page 3)* Gill's work focuses on disability in the elderly (also once thought to be part and parcel of aging) and how relatively simple interventions might slow or prevent it. He is the primary investigator at Yale for the Lifestyle Interventions and Independence for Elders (LIFE) study, a multi-site project funded primarily by the National Institutes of Health's National Institute on Aging, in which researchers are examining how physical activity affects people who are sedentary and at risk of disabling illnesses and injuries.

When a patient named Richard (a pseudonym) first joined the LIFE study, he was recovering from hip surgery, and walking for 20 minutes was a challenge. "I was really out of shape," he remembers.

Now, less than three years later, Richard arrives early for his twice-weekly sessions on a walking track so he can get in a full hour. "It's definitely helped me," says Richard, who at 83 reports that he's healthy and takes long neighborhood walks on days he doesn't report to the LIFE study.

If the intervention proves effective, it could be widely and easily adopted by existing facilities, such as senior centers or YMCAs. "This society generally and policymakers specifically are really looking for cost-effective interventions to decrease the rate of increase in the Medicare budget," says Gill. Tinetti agrees, saying, "We spend an awful lot of health care dollars on things that don't work."

Cooney first became interested in geriatrics in 1969 at Boston City Hospital. "I started seeing older patients who I felt were not being very well cared for." The level of disability in the elderly population has dropped since then, he says, and there is a growing awareness among physicians of the need to treat "people, not diseases."

Tinetti believes that there is a hopeful trend of rejecting the idea that quality of life must decline sharply with age. "The baby boomers won't stand for that," she says.

Inaugural Lurie Prize awarded to School of Medicine scientist

In a May 14 ceremony at Northwestern University's Feinberg School of Medicine, Yale immunobiologist Ruslan M. Medzhitov, PH.D., was awarded the inaugural Lurie Prize in the Biomedical Sciences from the Foundation for the National Institutes of Health (FNIH).

The newly instituted award, which honors early-career researchers whose findings have advanced basic biomedical science, was given to Medzhitov, the David W. Wallace Professor of Immunobiology and a Howard Hughes Medical Institute investigator, for his groundbreaking studies of the innate immune system, the body's first line of defense against bacteria and viruses (see related story, page 1).

A jury of scientists headed by Solomon H. Snyder, M.D., of Johns Hopkins School of Medicine, selected Medzhitov from a group of 154 nominees for the award, which carries an honorarium of $100,000.

Medzhitov, elected to the National Academy of Sciences in 2010, came to Yale in 1994 from Moscow, Russia, having been inspired by the then-controversial theories of innate immunity championed by the late Yale immunobiologist Charles A. Janeway Jr., M.D.

At that time the innate immune system was receiving little scientific attention, but by 1997 Medzhitov, Janeway, and colleagues had established that innate immune system components known as toll-like


Ruslan Medzhitov

receptors (TLRs) act as a pathogen-detecting sentinel and activate adaptive immunity. Since then, TLRs have become the subject of intense research activity in laboratories around the world.

"Dr. Medzhitov's painstaking studies paved the way for the identification of multiple TLR family members and their respective ligands, which help bind molecules forming larger complexes, advancing the entire field of immunology and opening the way for the development of new vaccines and treatments," Snyder said in an announcement of Medzhitov's selection. "He is a true pioneer of medical science."

The prize was established by Chicago philanthropist Ann Lurie "to reward and acknowledge a scientist who makes a discovery that is clearly a game changer in terms of medical and biological research."

In accepting the prize, Medzhitov said, "This award is a tremendous honor, and I am very grateful to all my colleagues, teachers, and trainees. I am especially grateful to the FNIH and its scientific jury for recognizing the tremendous progress in the field of innate immunity to which so many of my colleagues have contributed."

Expert in minimally invasive, image-guided pediatric surgery is new Pritzker Professor

Pediatric surgeon Michael G. Caty, M.D., M.M.M., has been named the Robert Pritzker Professor of Pediatric Surgery. Also professor of pediatrics and chief of pediatric surgery at Yale-New Haven Children's Hospital, Caty's clinical interests include neonatal surgery, thoracic surgery, intestinal motility disorders, pediatric surgical oncology, pediatric laparoscopy, and minimally invasive thoracic surgery.

Prior to his arrival at Yale in 2012 Caty was professor of surgery and pediatrics at the University of Buffalo School of Medicine and Biomedical Sciences, and surgeon-in-chief, division director of pediatric surgery, and program director in pediatric surgery at Women & Children's Hospital of Buffalo.

Caty is an expert in minimally invasive surgical techniques, as well as the development of an imaging technique called "augmented reality," three-dimensional models that


Michael Caty

surgeons use to see the insides of organs. He is also working to develop prototypes that will make it possible to repair esophageal atresia with an endoscopic approach.

He earned his bachelor's degree at Boston College and his M.D. at the University of Massachusetts, then completed general surgery training at the University of Michigan and finished his residency in pediatric surgery at Children's Hospital of Boston and Harvard Medical School. Additionally, he holds a master's degree in medical management from Carnegie Mellon University's Heinz School of Public Policy, and is a member of the American College of Surgeons, the Society of University Surgeons, the American Academy of Pediatrics, and the American Surgical Association.

Chair of pediatrics, critical care medicine specialist, is appointed as Wallace Professor

George Lister, M.D., chair of the Department of Pediatrics, chief of pediatrics at Yale-New Haven Hospital (YNHH), and physician-in-chief at Yale-New Haven Children's Hospital, has been named the Jean McLean Wallace Professor of Pediatrics.

A 1973 graduate of the School of Medicine, Lister focuses his research on the factors affecting infants at risk for Sudden Infant Death Syndrome (SIDS). He was a member of the medical school's Department of Pediatrics for 25 years before moving in 2003 to the University of Texas Southwestern Medical School, where he was professor, the Robert L. Moore Chair of Pediatrics, and associate dean for education until 2011. He also served as pediatrician-in-chief at the Children's Medical Center of Dallas.

Lister completed a residency in pediatrics at YNHH, and a fellowship in pediatric cardiology and neonatology at the University of California-San


George Lister

Francisco. There, he began research that led to his specialization in critical care medicine, a field in its formative stages at the time.

Lister's long-standing research interest in oxygen transport has contributed significantly to the understanding of cardiopulmonary interaction in congenital heart disease and cardiorespiratory control in infants at risk for SIDS.

He has also played an active role in medical education throughout his career. A member of the Institute of Medicine, he has had numerous national leadership roles in pediatric professional organizations and, among other publications, is co-editor of the 21st and 22nd editions of *Rudolph's Pediatrics*, one of the most widely read pediatric textbooks in the world.

Program for Anxiety Disorders director is named Alfred A. Messer Professor

Wendy K. Silverman, PH.D., newly named as the inaugural Alfred A. Messer Professor of Child Psychiatry, focuses her research on developing and evaluating psychosocial interventions for child and adolescent anxiety disorders.


Wendy Silverman

A child and adolescent clinical psychologist, Silverman became director of the Yale Child Study Center's Program for Anxiety Disorders in January. She previously served on the psychology faculty at Florida International University and at the University at Albany, State University of New York (SUNY). A graduate of Binghamton University, SUNY, Silverman received her M.A. and PH.D. in clinical psychology from Case Western Reserve University.

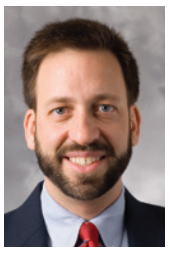
Silverman, who was president of Division 53 (Society of Clinical Child and Adolescent Psychology) of the American Psychological Association from 2006 to 2007, was chair of the National Institute of Mental Health (NIMH) Interventions Committee for Disorders Involving Children and their Families from 2007 to 2010.

She has published numerous scientific papers and chapters in the area of child and adolescent anxiety disorders, and is the author of five books on the topic. She has been principal investigator on NIMH research grants to develop and evaluate treatments for anxiety disorders in children and adolescents for the past 20 years, and has been an invited lecturer both nationally and internationally.

Currently co-editor of *Clinical Psychology Review*, Silverman previously served as editor of the *Journal of Clinical Child and Adolescent Psychology*, as well as associate editor of other major journals in her field. She was recognized with an NIMH mid-career development award (K24) from 2005 to 2010 for her research as well as for her mentorship of trainees in both psychology and psychiatry.

Young Professor, chair of Ob/Gyn, is an expert in uterine development and genetics

Hugh S. Taylor, M.D., has been named the Anita O'Keeffe Young Professor of Obstetrics, Gynecology, and Reproductive Sciences. Taylor, who became chair of the Department of Obstetrics, Gynecology, and Reproductive Sciences in 2012, is a noted clinician, scientist, and educator whose clinical research is in the areas of infertility, endometriosis, menopause, and diethylstilbestrol (DES) exposure.


Hugh Taylor

Also professor of molecular, cellular, and developmental biology and chief of obstetrics and gynecology at Yale-New Haven Hospital (YNHH), Taylor's basic science research focuses on uterine development, the regulation of developmental gene expression by sex steroids, endocrine disruption, and stem cells. His research has been continuously funded for more than 20 years by the National Institutes of Health. As chief of reproductive endocrinology and infertility at YNHH, he has grown the clinical service to one of national renown.

A 1983 graduate of Yale College, Taylor earned his M.D. at the University of Connecticut School of Medicine. He completed his residency in Ob/Gyn at YNHH in 1992, followed by a postdoctoral fellowship in molecular biophysics and biochemistry at Yale and a fellowship in reproductive endocrinology and infertility.

Taylor has been named a Mentor of the Year by the American College of Obstetricians and Gynecologists and Honoree of the Year by the Endometriosis Foundation of America. He received the President's Achievement Award from the Society for Gynecologic Investigation (SGI) in 2008.

He serves as editor-in-chief of the journal *Reproductive Sciences* and editor of *Endocrinology* and is on the board of directors of the American Society for Reproductive Medicine and a member of the governing council of the SGI.