Clifford Bogue is appointed to pediatrics chair after two years in an interim role

Clifford W. Bogue, M.D., professor of pediatrics (critical care), has been appointed chair of the Department of Pediatrics. The appointment became effective August 1. Bogue had been serving as the department’s interim chair since 2015.

“Cliff has been a strong advocate for the department. He is committed to strengthening its research mission, developing a cadre of new leaders in pediatrics, and seeing faculty and staff flourish,” says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine.

Bogue says he would like to raise the stature of Pediatrics so that it is one of the preeminent departments in the country. He plans to accomplish this by bolstering and expanding the range of high-quality clinical services the department delivers in conjunction with Yale New Haven Children’s Hospital and fortifying research within the department and with other programs. Plans are underway, for example, to merge the department’s neurodevelopmental services with the Yale Child Study Center to provide opportunities for joint clinical care and research collaborations.

He also is committed to preparing the next generation of pediatric clinician scientists.

New surgery chair with strong cancer background is coming from Johns Hopkins

Nita Ahuja, M.D., M.B.A., has been named chair of the Department of Surgery at the School of Medicine and chief of surgery at Yale New Haven Hospital, effective February 1.

Ahuja is currently the Jacob C. Handelsman Professor in Abdominal Surgery and professor of surgery, oncology, and urology at the Johns Hopkins University School of Medicine, and chief of surgical oncology at Johns Hopkins Hospital. She also serves as vice chair of academic affairs for the Department of Surgery and associate director of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

“A million-dollar fund will support junior researchers

Donor, an alumnus, sees vast potential in the work of early-career neuroscientists

With a goal of spurring new discoveries in neuroscience by bright young investigators, and supporting the work of the next generation of leaders in the field, Reynold Spector, M.D. ’66, and his wife Michiko Spector have established a $1 million fund to foster the education and training of junior faculty members.

The Reynold and Michiko Spector Fund for Neuroscience celebrates—and looks to help through philanthropy—Yale’s long history of neuroscience discovery, which has contributed a great deal to the understanding of brain anatomy, physiology, and chemistry.

“Yale is a strong place for neuroscience research,” says Reynold Spector. “The university is committed to it, and I am hopeful that bright young scientists will come up with ideas that are new and valuable.”

“The Spectors’ gifts are timely, coming at a moment when young investigators are increasingly valued as indispensable partners for the medical school’s senior faculty,” says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. “We realize more than ever how talented young scientists bring creative and innovative approaches to the school’s research programs.”

As a physician and researcher, Spector has had a strong interest in the neurosciences since his Yale days. He completed his medical school thesis with the late professor and chief of neuropathology Elias Manuelidis, M.D., a world-renowned expert in Creutzfeldt-Jakob disease, a degenerative disease of the nervous system. Spector has also closely followed the work of Manuelidis’ wife, Laura Manuelidis, M.D., professor of surgery (neuropathology).

“Elias Manuelidis thought a little bit differently than many other neuroscientists. He taught me an offbeat approach to things, and that turned out to be exceedingly useful, because I heard my own drummer,” says Spector. “We need strong, smart, young people to foster the education and training of junior faculty members.”

“Nita is widely respected for innovative patient care, renowned for her research on cancer epigenetics, and passionate about mentoring the next generation of surgeon scientists. Her ability to be a collaborative leader will make her a welcome addition to the School of Medicine community,” says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine.

At Johns Hopkins, Ahuja leads the integration and expansion of surgical oncology programs across the health system. Her surgical specialization is in gastric, rectal, and pancreatic cancers. She has developed a strong cancer background in gastric, rectal, and pancreatic cancers.

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Spurring the body to repair itself

Investigator seeks new pathways toward guiding immune system’s ability to heal and restore

Growing up in Buenos Aires, Argentina’s capital city, Carla V. Rothlin, Ph.D., associate professor of immunobiology and of pharmacology, and her three sisters listened to dinnertime conversations steeped in science. Their mother, a physician, regularly shared dermatological case studies from her practice. Their father, a pharmacology researcher, gave incremental progress updates on his lab.

At age 17, Rothlin had to choose her undergraduate specialization before entering the University of Buenos Aires. She did so without hesitation: biochemistry. “I knew it would give me human-oriented biomedical training,” she says, “and also a solid foundation in mathematics, physics, biology, and medicine.”

She remained there for her doctoral studies, also in biochemistry, and met world-renowned scientist Ana Belén Elgoyhen, Ph.D., who became her mentor. At the time, Elgoyhen studied the neurobiological mechanisms of how humans hear and comprehend sound. Fascinated, Rothlin decided to focus her dissertation on biochemical mechanisms that tune the sensitivity of the inner ear.

“Let’s say you and I are in a noisy bar, and you want to focus only on what I am saying,” Rothlin says, “condensing the complex into an everyday analogy as she very frequently does. The brain has a way to signal back to the inner ear and tune it.”

Intrigued by neurobiology’s complexity, Rothlin pursued that field for her postdoctoral fellowship at the Salk Institute for Biological Studies in California under the tutelage of Greg Lemke, Ph.D. At the time, Lemke and his lab team were just beginning to better understand how a family of three receptor tyrosine kinases, called TAM receptors, which Lemke had discovered in the 1990s, are linked to the immune system. Rothlin felt drawn to immunology. She enthusiastically embraced the field and mastered its jargon and major tenets.

“When you are surrounded by smart, experienced researchers, you can take on a challenge like that,” says Rothlin, noting that even with that sudden change in career focus, an important constant remained: Research questions into the “mechanisms that regulate the magnitude, duration, and types of responses in the body” have guided her work throughout, including in the immunobiology lab she established when she arrived at Yale in 2009.

In a short time, Rothlin has been recognized for her basic science work within various autoimmune diseases, including asthma, lupus, Crohn’s disease, and colitis. In 2016, the Howard Hughes Medical Institute (HHMI), the Bill & Melinda Gates Foundation, and the Simons Foundation made Rothlin one of their inaugural group of HHMI Faculty Scholars, part of a program to support early-career scientists who pursue primarily basic research projects. “It’s a huge honor—a very special thing,” Rothlin says of the award, which included funding to support her lab. “Everything I do is with my lab and this award gives us enthusiasm to continue working on basic science.”

Also in 2016, in a paper published in Science, Rothlin and colleagues identified a receptor called TYK2, located on innate immune cells, that controls the strength of the immune response, and could be a potential drug target for treating allergies.

This past May, Rothlin, Sourav Ghosh, Ph.D., associate professor of neurology and of pharmacology, and colleagues detailed in Science how the presence of the cytokine interleukin 4 (IL4) near a damaged site in the body caused macrophages to release growth factors needed to rebuild tissue (see “Advances,” p. 3).

After discovering that significant relationship, Rothlin and her team will now focus on understanding exactly how macrophages, considered sentinels of the innate immune system, coordinate the healing and rebuilding of damaged tissue. “It’s clear that the molecular program that induces different genes and expression of proteins for macrophages to help with tissue repair is a very different program from the one that drives inflammation, the first line of immune defense,” Rothlin says. To untangle that puzzle, Rothlin is “searching for nothing less than how the body heals and rebuilds itself. For Rothlin, it is one more puzzle she wants to solve.”

Yale innovative-thinking center headed by medical school professor

A School of Medicine professor is the inaugural faculty director of the recently opened Tsai Center for Innovative Thinking at Yale (Tsai CITY), where trainees in numerous Yale disciplines are invited to network, interact, and exchange ideas.

G. Schulam, M.D., Ph.D., professor and chair of urology, hopes that Tsai CITY will inspire members of Yale’s health community to think about problems and opportunities in unprecedented ways.

“There’s an opportunity to create relationships based on innovation amongst the entire university bridging relationships between the various schools and leveraging their unique expertise and perspectives,” says Schulam. “Linking the medical school, the medical center, and the Yale [Medicine] Health system to this process will provide a unique opportunity for innovation in health care delivery. At many institutions the medical school is a little bit isolated and separated. I think this is going to be another dimension of collaboration that will be unique for Yale.”

Schulam says President Peter Salovey, //Tsai CITY (page 7)

Accomplishments in primary care earn Leffell Prize

Matthew S. Ellman, M.D., associate professor of medicine (primary care medicine) and director of Yale Internal Medicine Associates, is the 2017 recipient of the David J. Leffell Prize for Clinical Excellence. The prize, established by David J. Leffell, M.D., David P. Smith Professor of Dermatology and professor of surgery (otolaryngology and plastic), and his wife, Cindy, is awarded each year to “an individual who best demonstrates the highest level of clinical expertise, commitment to teaching, and the highest standards of care and compassion for patients.”

Robert J. Alpers, M.D., dean and Ensign Professor of Medicine, presented the award.

In accepting the prize on June 21, Ellman emphasized his passion for primary care medicine, which, he says, gives him “the gift and honor of knowing people over a lifetime, and the ability to partner with them to make life as good as it can be and to help those nearing the end of their life to make that transition.”

Ellman’s “primary care gives me the opportunity to use my mind in concert with my heart.”

In addition to his work as a clinician, Ellman is a scholar and educator in the area of palliative and end-of-life care, in which he first developed a strong interest during the 1980s while a resident at Bellevue Hospital in New York City, where the AIDS epidemic was at its peak and no effective treatments were available.

Ellman earned his M.D. degree at Harvard Medical School and was a Robert Wood Johnson Clinical Scholar at Yale.

Medicine@Yale

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Becomes one of the first U.S. centers to adopt a technology that reveals far more than past methods about the compositions of specimens

When clinicians need diagnostic data across fields as diverse as hematology, transplantation, and tumor immunology, among others, flow cytometry is traditionally the tool they choose to identify cell markers. Investigators use flow cytometry for purposes that include analyzing cells, detecting biomarkers, and protein engineering. The technique has been essential to basic bench researchers and clinicians alike.

The methods and equipment used to probe cellular ques-
tions are rapidly advancing—including, at Yale, through the addition in 2014 of CyTOF, or Cytometry Time-Of-Flight, and this past June of the CyTOF Imaging Mass Cytometer (IMC). The latter acquisition distinguishes Yale as one of the first academic medical centers in this country to host a CyTOF IMC. Both instruments greatly expand upon the types of samples and numbers of components that can be analyzed—30 to 140 different biomarkers—where flow cytom-
ters are more limited and can generally detect only eight. While its own the CyTOF analyzes cells in suspension, the IMC, by contrast, can produce labeled images of tissues with spatial accuracy and provide position details of cells in an intact tissue.

The process of converting a tissue sample to a labeled, spatially accurate, microscopic image begins with a thin cross section of tissue mounted on a glass slide. Researchers add antibod-
ies to the tissue, each antibody tagged with a different heavy metal that lets it be tracked as it binds with a specific protein. The whole assemblage goes into the IMC, where a laser vaporizes the sample from its slide, hurling the heavy metal markers into the CyTOF instrument. Each marker, based on its mass, will have a different “time of flight” to travel through the machine. The instrument translates the times-
of-flight into signals that are mapped back to where they were ablated by the laser—each one corresponding to the protein tagged with the metal—while also measuring the abundance of each protein of interest at a specific tissue location.

The IMC “means that you can detect much more in the same sample, and you can detect it with more certainty,” says Ruth R. Montgomery, Ph.D., as-
so

Aiming cancer meds within the brain

Treating brain tumors can depend on getting drugs into the brain, but the blood-brain barrier makes that difficult. In recent years, researchers have by-
passed the barrier using nanoparticles that function like invisibility cloaks for drugs. Now, W. Mark Saltzman, Ph.D., Goizueta Foundation Professor of Biomedical Engineering and professor of chemical engineering and molecular physiology, and colleagues, are working to ensure that once in the brain, drug-
carrying nanoparticles will actively target tumors—as opposed to either damaging healthy cells or occupying vacant space in the brain with no thera-
pic effect.

Saltzman’s team treated the brains of rats with nanoparticles bearing several different coatings. Some coat-
ings included “stealth properties,” which help the nanoparticles evade the immune system but also can prevent cancer cells from recognizing them. For others, stealth properties were combined with bioadhesive coatings designed to make the nanoparticles stick to cells. As reported on May 17 in Nature Communications, the bioadhesive nanoparticles targeted all cell types at a higher rate than particles with stealth properties alone. Tumor cells internal-
ized the bioadhesive nanoparticles at the highest rates of all. The result may signal a future ability to target therapies far more precisely, and with greater safety and effectiveness.

Yale enhances its cytometry capabilities

ADVANCES

Health & Science News

Activating immune properties that heal

The human body’s macropores—a type of immune cell—not only fight off invading pathogens, but also help repair injured tissue after an infection.

Yale researchers have now discovered what triggers macropores to switch from attack mode to rebuilding mode.

In a study published on June 9 in Sci-
ce, Carla V. Rothlin, Ph.D., associate pro-
fessor of immunobiology and of pharmacology, Seerat Gosh, Ph.D., associate professor of neurology and of pharmacology, and colleagues found that when they blocked the ability of macropores to sense the presence of cells that had died, the macropores no longer switched on genes required to repair tissue, even when the immune molecules IL-3 or IL-4, which help both to activate mac-
ropores and to signal early stages of infection, were also present.

Their finding in mice that signaling molecules and dead cells were both needed to activate cell repair may help scientists learn how better to spur healing after infections, and to develop therapies for chronic inflam-
mary diseases such as colitis.

From a very technical, highly scientific question, all the way to patient care,” Rimm and Schalper do not see the IMC arriving in clinics anytime soon. For now, the instru-
ment is too specialized and expensive for that setting. In its academic realm, however, IMC is used to track tens of variables in tissues—identifying which ones differentiate cancer—ignoring from cancer-fighting ones, for example—and then apply that knowledge to more readily available methods. Once researchers know which variable to look for—thanks to the IMC—the more limited capabilities of standard techniques no longer pose the same restrictions.

“We use all the tools we can to get at the puzzles we’re looking for,” Montgomery says. This includes collaborat-
ing with Yale’s Department of Mathematics and other sources of quantitative expertise, to consolidate the sheer volume of data that IMC produces. The digital image of a single patient’s tissue sample in Rimm’s lab contains 400,000 to 600,000 pixels, and the // Cytometry page 3 //

ABOVE: Ruth Montgomery (center) is director of the Cytometry Time-Of-Flight (CyTOF) facility at the School of Medicine. David Rimm (left) and Kurt Schalper (right) have been primary investigators at the facility’s new Cytometry Imaging Mass Cytometer (IMC) since it came into active use.

LEFT: An image produced by the CyTOF IMC shows T-cells (represented in green) in the stroma of human non-small cell lung carcinoma that are positive for cytokeratin (white). The signal for Ki-67 (red), a proliferation marker, is higher in both viable and stromal cells. Nuclei are shown in blue. This image goes far beyond the detec-
tion capabilities of previous methods of cytometry.
April 25  At an Alumni Grand Rounds event, medical students gathered insights and shared stories with family medicine veterans Richard Gibbs, M.D., ’86, and Tricia Hellman Gibbs, m.d. ’87, both professors of clinical medicine at the University of California, San Francisco, and co-founders of the San Francisco Free Clinic. From left, medical students Zola Chihombori Quao, Class of 2018; Dervin Cunningham, Class of 2019; Aishwarya Pillai, Class of 2020; Richard and Tricia Gibbs; and Nicolas Munoz, Class of 2020.

June 15  The Department of Internal Medicine established the Iva Dostanic Physician-Scientist Trainee Award five years ago to honor a physician researcher who died of ovarian cancer in 2011 while at Yale. The 2017 awardee is Sarah Huen, M.D., Ph.D., then an instructor in medicine (nephrology) and now an assistant professor at the University of Texas Southwestern Medical School. (l-r): Iva Dostanic, parents, Predrag Dostanic, and Dragana Dostanic, M.D.; Gary V. Desir, M.D., chair of internal medicine; Huen; and Peter S. Aronson, M.D., C.H. Long Professor of Medicine and professor of cellular and molecular physiology, and award committee chair.

June 21-22  The 2017 Lung Cancer SPORE Workshop, held at Yale West Campus Conference Center, invited discussion in wide areas of lung cancer. 1. Keynote speaker (with plaque) Tyler Jacks, Ph.D., director of the Koch Institute for Integrative Cancer Research at MIT, stands with fellow researchers, from left, Peter Ujházy, M.D., Ph.D., deputy associate director of the Translational Research Program of the National Cancer Institute; Charles S. Fuchs, M.D., M.P.H., Richard Sackler and Jonathan Sackler Professor of Medicine and director of Yale Cancer Center (YCC); Roy S. Herbst, M.D., Ph.D., Ensign Professor of Medicine and professor of pharmacology, and chief of medical oncology at YCC; Tyler Jacks; Katerina A. Politi, Ph.D., associate professor of pathology at Yale; and Christine M. Lovly, M.D., Ph.D., assistant professor of medicine and of cancer biology at Vanderbilt-Ingram Cancer Center. 2. Ellen Sigal, Ph.D., chair and founder of Friends of Cancer Research, talks with Roy Herbst during a panel discussion.

// Pediatrics (page 3) and has been actively involved in training students, residents, and fellows. He wants to develop a research pathway with expanded infrastructure and mentorship for residents and fellows who are interested in biomedical research. Under his leadership, the department will expand its efforts to enhance the number of faculty and trainees from underrepresented minorities in medicine, an effort that he already has begun.

Bogue, who was named chief medical officer at Yale New Haven Children’s Hospital in 2014, has held a number of medical school and hospital leadership positions since he joined the faculty in 1993. He has served as director of pediatric critical care transport, medical director of the pediatric intensive care unit, director of the pediatric critical care fellowship, chief of pediatric critical care medicine and associate chair for strategic planning.

For more than 20 years he has directed a research program funded by the National Institutes of Health on the developmental biology of the lung, liver, and cardiovascular system. His laboratory has made important contributions to the discovery of genetic pathways involved in embryonic organ development, including the identification of genetic pathways essential to the formation of the liver and biliary system, as well as the cardiovascular system.

Bogue has received the Mac Gailani Jr. Faculty Award, the Norman J. Siegel Faculty Award, and a pediatric fellow teaching award, among other honors. He graduated with distinction from the University of Virginia in 1981 and completed his M.D. at his alma mater in 1984. He was chief resident in pediatrics at Vanderbilt University before completing his fellowship in pediatric critical care medicine at Yale.

June 2-4  At Reunion Weekend, alumni attended research talks, met current medical students, and renewed class ties. 1. Dervin Cunningham, Class of 2019 (right), joins Ahmed About-Zamzam Jr., M.D. ’92, and his wife, Sharon S. Lum, M.D., on a campus tour. 2. Dean Robert J. Alpern, M.D. (left), gives the Distinguished Alumni Service Award to outgoing Alumni Association President Richard Kayne, M.D. ’76, joined by incoming president Harold Mancusi-Ungaro, M.D. ’73. 3. From left, Matt Massicotte, M.D. ’92, Jenny Williams, M.D. ’92, Julie Lund Sharpless, M.D. ’92, and her husband, Ned Sharpless, M.D.
Alzheimer’s damage reversed by a drug

An experimental drug improves the learning and memory skills of mice with Alzheimer’s disease, and reconstitutes their brain cells, according to new Yale-led research. Stephen M. Strittmatter, M.D., Ph.D., professor of neurology and of neurosciences, and colleagues had previously found that the receptor mGluR5, found on the surface of brain cells, was a key to explaining how Alzheimer’s affects the brain. mGluRs, they discovered, transmits the damaging effects of amyloid beta peptides, the proteins trapped in the inside of brain cells, causing the hallmark dysfunctional associates associated with Alzheimer’s.

But mGluR5 is also required for normal brain function, so fully blocking it is not an option to treat disease.

In the new work, published July 5 in Cell Reports, Strittmatter’s team tested the Silent Allosteric Modulator (SAM) drug BMS-984923, which keeps mGluR5 from interacting with amyloid beta peptides, and prion proteins without blocking its normal function. While the drug did not lower levels of the usually damaging proteins, it prevented them from diminishing brain cell function. The treatment also reversed existing Alzheimer’s symptoms in the mice.

Pathway affects blood vessel actions

Blood vessel development depends on the fibroblast growth factor (FGF) signaling pathway, suggests a study published on May 11 in Nature.

Researchers already knew that another growth factor, VEGF, played an integral role in vascular development, so Michael Simons, M.D., Robert W. Berliner Professor of Medicine (Cardiology) and professor of cell biology, investigated whether FGF might do the same. Mouse embryos genetically engineered to lack FGF receptors in their blood vessels developed smaller and less-branched vascular networks than embryos with the receptors, Simons’ team found. The absence of FGF also hampered the development of lymphatic vessels.

Further, blood vessels were found to need FGF receptors in order to metabolize sugars through glycolysis, a process where enzymes break down glucose. FGF receptors are necessary for production of the transcription factor c-Myc, which leads to generation of the essential glycolytic enzyme HK2.

Knowledge of molecules important for vascular development could lead to drugs that block the blood vessel formation that often sustains cancer tumors, Simons says. It may also point the way toward regrowing blood vessels in patients with vascular problems such as coronary artery disease.

Boost for method to curb youth smoking

Video games that have shown effectiveness in trials will have their use expanded through funding from the CVS Health Foundation

Lynn E. Fiellin, M.D., associate professor of medicine and in the Yale Child Study Center, has spent much of her recent career determining how best to use video games to empower adolescents to avoid risky behaviors that affect life outcomes. Fiellin’s work has just received a substantial boost in the form of a $1.4 million gift from the CVS Health Foundation. The three-year gift is a part of “Be The First,” a $50 million commitment by CVS Health to help deliver the first tobacco-free generation.

This gift aims to further smoking prevention by helping to bring smokeSCREEN, a game Fiellin’s group has developed, to a broader audience across the United States. The game, currently played on an iPad, conveys anti-tobacco messaging via character-based graphic novel-like images and multiple-choice learning games. Results of a New Haven- and Los Angeles-based study indicate a significant impact on health risk perceptions and knowledge about both cigarette and electronic cigarette use among young people exposed to smokeSCREEN.

The game is part of a series that has focused on HIV prevention, sexual risk, drugs, alcohol, bullying, and cheating, Fiellin says, and has recently been expanded with additional NIH and Food and Drug Administration funding to significantly emphasize smoking prevention. Among other support, in 2009 the National Institutes of Health (NIH) awarded her a $4 million, five-year grant to support research on using the games to influence adolescent behavior. In 2015, Fiellin founded the Center for Health & Learning Games at the School of Medicine, which focuses on serious game development and evaluation, and their applications to health and behavioral science.

CVS first approached Fiellin in March of this year, two years after it made headlines by announcing plans to ban all cigarette sales at its stores. “That spoke volumes,” Fiellin says. “Freedom from smoking was really the goal, and the carve-out was an option to treat disease.”

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He also had a long career in clinical pharmacology, culminating in a position at Merck, where he oversaw the development of breakthrough medications including Zoro®), Singulair®, Fosamax®, and Cozaar®; and vaccines for human papillomavirus and shingles. Prior to his tenure at Merck, where he served as head of development, Spector conducted neuroscience research at Harvard for seven years, and then at the University of Iowa, where he was director of the university’s Clinical Research Center as well.

The Spectors’ daughter, June T. Spector, M.D., M.P.H., is also a graduate of Yale School of Medicine, Class of 2009. She now is an associate professor of medicine (general internal medicine), and of environmental and occupational health sciences, at the University of Washington. The Spectors view their contribution to Yale as a crucial investment in an institution that has done much for them, and for all of its students. “Both June and I benefited greatly from Yale,” Reynold Spector says, “so we decided to give back.”

From there to here, Spector says, “I believe the Spector Fund Award will greatly contribute to the development of my research program. The award will give me the opportunity to expand my research in new directions with the aim of advancing our understanding of the neurobiology of autism.”

Reynold Spector, now retired, focused his research on understanding the blood-brain and blood-cerebrospinal fluid barriers. He also had a long career in clinical pharmacology, culminating in a position at Merck, where he oversaw the development of breakthrough medications including Zoro®, Singulair®, Fosamax®, and Cozaar®; and vaccines for human papillomavirus and shingles. Prior to his tenure at Merck, where he served as head of development, Spector conducted neuroscience research at Harvard for seven years, and then at the University of Iowa, where he was director of the university’s Clinical Research Center as well.

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CVTometry (page 3) IMC measures 30 to 40 selected proteins within each pixel for more than 60 patients. That adds up to 120 million data points for one small pilot study, so Rimm has recruited Yuval Kluger, Ph.D., associate professor of pathology, a bioinformatics expert affiliated with Yale’s Applied Mathematics Program, to help analyze the data. Collaboration among disciplines and departments is “a requirement, at this point,” says Montgomery. “We have the technology to create giant datasets. And, to make sense of them—to interpret them for relevance to our health questions—we need to have computational colleagues.”

Once investigators learn its capabilities, Montgomery sees CyTOF IMC moving far beyond its initial uses, and becoming an essential tool for labs across the School of Medicine. “Now that we can really make use of it, we can advance into many different areas,” she says. “A lot of people come in here to see me with their great ideas about what they want to do, and I tell them to go ahead and use the machine.”
Grants and contracts awarded to Yale School of Medicine  
September 2016 – November 2016

Federal
• Claire Hsia, DoD, Modulation of Host Responses to Microbial Products, 3 years, $2,025,803; Frederick Altic, DoN, Integrating Antipathogen Host Responses to Pseudomonas Hostile Effects on Primary Care Clinics in Ukraine, 4 years, $4,736,847; Anne Irving, DoD, Identification of a Cauterization Mechanism and Inhibition of HIV Reverse Transcriptase, 5 years, $2,396,165; Morris Bell, NIH, CNS, The Role of Sleep in the Development and Maintenance of Tumor-Centric Metabolites, 2 years, $518,984; Chirag Parikh, NIH, Novel Kidney Injury Tools, in Diseased Organ Donor and to Predict Graft Outcome, 4.9 years, $2,074,178; Abhijit Patil, DoD, Early Detection of Lung Cancer through CT, 3 years, $165,628; Godfrey Pearlson, DOT, A Bamechevical Analysis of the Protective Effect of Anti-SMAD4 Antibody on Shoulder Injury in Men’s Lacrosse, 3 years, $62,978; Douglas Brash, Leo Pharma A/S, Cholesterol Homeostasis and Its Role in COPD, 3 years, $1,317,761; Christopher Pittenger, NIH, Histamine Regulation of Basal Ganglia Function, 19 years, $348,607; John Hwa, NIH, Nano-Particles for Site-specific Genome Editing in Utero, 1.9 years, $35,800; Marie Egan, NIH, Identification of a Meaningful Cocaine Delivery of Radiosensitizer-Encapsulating Peptides in Cigarette Smoke-related COPD and Inflammation, 2 years, $469,707.

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• Claire Hsia, DoD, Modulation of Host Responses to Microbial Products, 3 years, $2,025,803; Frederick Altic, DoN, Integrating Antipathogen Host Responses to Pseudomonas Hostile Effects on Primary Care Clinics in Ukraine, 4 years, $4,736,847; Anne Irving, DoD, Identification of a Cauterization Mechanism and Inhibition of HIV Reverse Transcriptase, 5 years, $2,396,165; Morris Bell, NIH, CNS, The Role of Sleep in the Development and Maintenance of Tumor-Centric Metabolites, 2 years, $518,984; Chirag Parikh, NIH, Novel Kidney Injury Tools, in Diseased Organ Donor and to Predict Graft Outcome, 4.9 years, $2,074,178; Abhijit Patil, DoD, Early Detection of Lung Cancer through CT, 3 years, $165,628; Godfrey Pearlson, DOT, A Bamechevical Analysis of the Protective Effect of Anti-SMAD4 Antibody on Shoulder Injury in Men’s Lacrosse, 3 years, $62,978; Douglas Brash, Leo Pharma A/S, Cholesterol Homeostasis and Its Role in COPD, 3 years, $1,317,761; Christopher Pittenger, NIH, Histamine Regulation of Basal Ganglia Function, 19 years, $348,607; John Hwa, NIH, Nano-Particles for Site-specific Genome Editing in Utero, 1.9 years, $35,800; Marie Egan, NIH, Identification of a Meaningful Cocaine Delivery of Radiosensitizer-Encapsulating Peptides in Cigarette Smoke-related COPD and Inflammation, 2 years, $469,707.

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Grants and contracts awarded to Yale School of Medicine  
September 2016 – November 2016

Federal
• Claire Hsia, DoD, Modulation of Host Responses to Microbial Products, 3 years, $2,025,803; Frederick Altic, DoN, Integrating Antipathogen Host Responses to Pseudomonas Hostile Effects on Primary Care Clinics in Ukraine, 4 years, $4,736,847; Anne Irving, DoD, Identification of a Cauterization Mechanism and Inhibition of HIV Reverse Transcriptase, 5 years, $2,396,165; Morris Bell, NIH, CNS, The Role of Sleep in the Development and Maintenance of Tumor-Centric Metabolites, 2 years, $518,984; Chirag Parikh, NIH, Novel Kidney Injury Tools, in Diseased Organ Donor and to Predict Graft Outcome, 4.9 years, $2,074,178; Abhijit Patil, DoD, Early Detection of Lung Cancer through CT, 3 years, $165,628; Godfrey Pearlson, DOT, A Bamechevical Analysis of the Protective Effect of Anti-SMAD4 Antibody on Shoulder Injury in Men’s Lacrosse, 3 years, $62,978; Douglas Brash, Leo Pharma A/S, Cholesterol Homeostasis and Its Role in COPD, 3 years, $1,317,761; Christopher Pittenger, NIH, Histamine Regulation of Basal Ganglia Function, 19 years, $348,607; John Hwa, NIH, Nano-Particles for Site-specific Genome Editing in Utero, 1.9 years, $35,800; Marie Egan, NIH, Identification of a Meaningful Cocaine Delivery of Radiosensitizer-Encapsulating Peptides in Cigarette Smoke-related COPD and Inflammation, 2 years, $469,707.
Grant renewed for infectious disease surveillance

School of Public Health

joins with state to track flu, Lyme, HPV, other threats

The Connecticut Emerging Infectious Diseases Program (EIP), a collaboration between Yale School of Public Health (YSPH) and the state’s Department of Public Health, has been awarded $20.9 million to continue research and surveillance of infectious diseases in Connecticut for another five-year cycle, $14 million of which is being provided from the federal centers for Disease Control and Prevention (CDC) is earmarked to support the efforts of the YSPH office of EIP.

The Yale EIP tracks a wide range of infectious diseases that affect state residents. According to John Meek, M.P.H., EIP’s associate director, staffs annually monitor and investigate approximately 1,400 cases of food-borne illness, 1,900 cases of Clostridium difficile infection, 1,000 flu hospitalizations and 2,000 cases of high-grade cervical lesions caused by human papillomavirus infection.

In addition, EIP staff survey approximately 1,000 hospital or nursing home residents to estimate the burden of health-care-associated infections in these institutions and engage thousands of Connecticut residents in studies to assess the burden and evaluation prevention measures for tick-borne diseases.

Tracking these diseases allows EIP staff and state public health officials to better understand risk factors for contracting these diseases, identify targets for future public health interventions, and evaluate the effectiveness of current interventions.

“We are thrilled to be able to continue to build on the success of the past 20 years in conducting public health surveillance of the state of Connecticut and in the future,” John Meek, M.P.H., EIP’s associate director.

“Emerging infectious diseases are a reality for Connecticut and tackling these infections in partnership with the CDC and the Connecticut Department of Public Health has enabled a robust response to protect Connecticut residents for over 20 years,” says Sten H. Vermund, M.D., Ph.D., dean and Anna M.R. Lauder Professor of Public Health, and professor of pediatrics. “We are especially pleased with the role that YSPH students are playing in specific projects, both contributing substantially and learning about public health practice in the process.”

Yale is one of 10 sites that have received renewed funding as part of the CDC’s Emerging Infectious Programs, a national network that monitors disease outbreaks in order to inform policy surrounding methods of preventing and treating infectious diseases. Communities covered by the national EIP approximate the composition of total U.S. population in terms of age, race, gender, and other health indicators.

Yale was one of the first EIP sites funded in 1995, when the national program began.
Twenty years and counting for Women’s Health Research at Yale

The center funds research that illuminates specific health needs of women

BRCAl, a gene associated with increased risks of breast cancer, can be mutated in thousands of ways—but only some of those mutations are dangerous. The key question for oncologists, genetic counselors, and women with breast cancer is: which ones?

Ryan B. Jensen, Ph.D., associate professor of therapeutic radiology, is sorting through thousands of BRCAl mutations to spot the red flags. His work could greatly improve counseling and cancer treatment for breast cancer patients.

Jensen is moving his research forward in part thanks to a grant from Women’s Health Research at Yale (WHRY), a self-supporting center within Yale School of Medicine that will celebrate its 20th anniversary in February. With data developed through $5 million in WHRY grants to date, Yale scientists have gone on to secure $93 million in external grants to further their research into women’s health.

“Women continue to be under-supported in terms of research knowledge,” says Carolyn M. Mazure, Ph.D., the Norma Weinberg Spungen and Joan Lebon Bildner Professor of Psychiatry and Psychology, who founded the center in 1998 and has been executive director ever since.

The center focuses on the need to fully account for sex and gender in biomedical research. Women suffer higher rates of Alzheimer’s disease, for instance, and can present with different symptoms than men when experiencing heart attacks. But studies of these diseases traditionally pay inadequate attention to sex differences, Mazure says.

It was not until 1994 that the National Institutes of Health (NIH) required researchers to include women participants in clinical studies and to analyze data by sex or gender. It was not until last year that the NIH required female animals and tissue and cell samples in laboratory studies. To this day, many studies are still not designed to tease out sex differences.

WHRY-funded research, though, has already helped women and girls.

In 2002, for example, a landmark paper published in The Lancet led to better advice for breast cancer patients and those at higher risk for breast cancer. WHRY grant recipient Bruce G. Haffty, M.D., then of the Department of Therapeutic Radiology, showed that certain mutations in the genes BRCA1 and BRCA2 predisposed breast cancer patients to new tumors in either breast.

Girls with autism also stand to benefit from the center’s grants. Because boys outnumber girls in autism diagnoses, many studies include few if any girls.

“They’ve been orphaned from autism research,” says Pamela Ventola, Ph.D., assistant professor in the Yale Child Study Center.

With a 2015 WHRY grant, Ventola tested for the first time a behavioral intervention called Pivotal Response Therapy on girls with autism. The girls made bigger gains in social engagement and functioning than boys in the study—despite having started with more severe impairments.

“Without these pilot data, girls would still be under-studied,” Ventola says. “We are extremely grateful for the funding from WHRY. Without the work supported through this grant, we wouldn’t know the value of this therapy in girls.”

Jensen, too, says the funds were crucial to his work. When he arrived at Yale as a junior faculty member, he had recently made a crucial breakthrough, becoming the first in the world to purify the BRCA2 protein. But there was no way to follow up without seed money that would let him establish the preliminary data necessary for the larger NIH grants he later received and that continue to fund his work today.

“The pilot grants are great for young investigators—I got this within a year of when I came to Yale,” he says. “It gives you practice writing grants at this level, and then you get some feedback. It really helps you start preparing for the big NIH grants. And it keeps your lab going.”

WHRY-funded researchers at Yale study colon cancer and autoimmune disease in women, as well as ovarian cancer, infections during pregnancy, intimate partner violence, and other topics to advance women’s health or discover sex differences to benefit women and men.

Mazure advocates for women’s health research in Washington, D.C., and has frequently spoken at other universities about how they might build programs similar to Yale’s and fully integrate a focus on sex and gender into a medical school curriculum.

“We have been enthusiastic about helping others to build these centers,” says Mazure. “We want more people focusing on the importance of studying women and investigating sex and gender differences. It is vital to women’s health, and it can also help men. Because in studying differences, we learn things that are very important for the care and treatment of disorders that affect us all.”

Looking back over nearly 20 years, Mazure is quick to turn her attention toward the road that lies ahead. “We have made great progress,” she says. “But there is an enormous amount left to do.”

James S. Duncan, Ph.D., professor of medicine (immunology and infectious diseases) and editor of the Section of Allergy and Clinical Immunology from 1995 through 2011, will receive the 2018 Distinguished Scientist Award from the American Academy of Allergy, Asthma & Immunology.

Rosemarie L. Fisher, M.D., professor of medicine (digestive diseases) and of pediatrics, and, until last year, associate dean of graduate medical education, is honored with the Distinguished Service Membership from the American Association of Medical Colleges.

Peter M. Glazer, M.D., Ph.D., chair and Robert E. Hunter Professor of Therapeutic Radiology and professor of genetics, has received the National Cancer Institute’s Outstanding Investigator Award.

Chirag R. Parikh, M.D., Ph.D., professor of medicine (nephrology) and director of the Program of Applied Translational Research (PATR), receives the American Society of Nephrology’s Young Investigator Award.

Philip W. Askenase, M.D., professor of medicine (immunology) and chief of the Section of Allergy and Clinical Immunology from 1995 through 2011, will receive the 2018 Distinguished Scientist Award from the American Academy of Allergy, Asthma & Immunology.

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