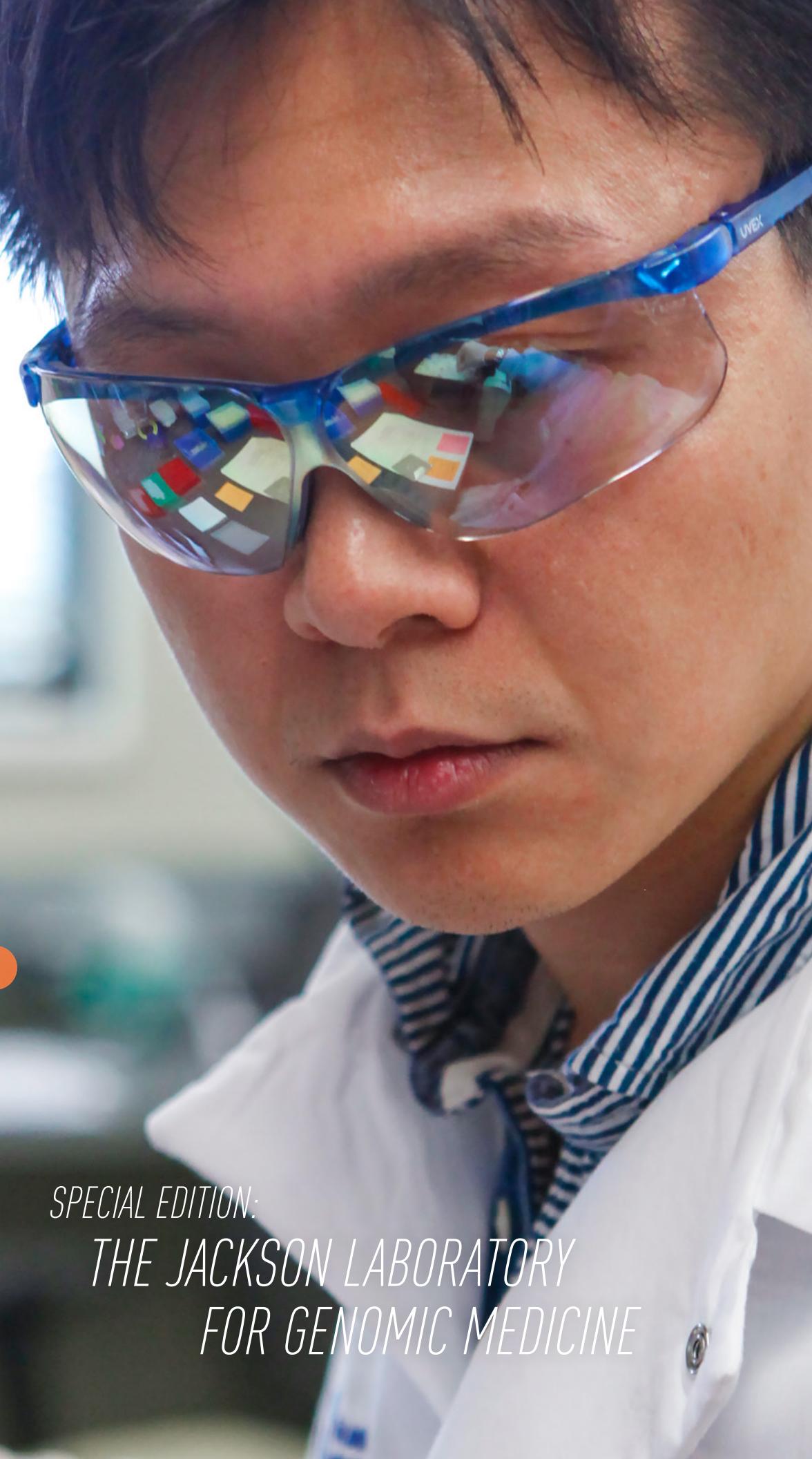


# THE SEARCH

- Toward genomic medicine
- On time, on budget
- Tipping the balance  
Karolina Palucka
- Kathleen Corbet  
A giving profession
- Recruiting top scientists
- Teaching the genome generation  
in Connecticut

SUMMER 2014 • VOL.7 • NO.2 • THE JACKSON LABORATORY

*SPECIAL EDITION:*  
**THE JACKSON LABORATORY  
FOR GENOMIC MEDICINE**





# THE SEARCH

A PUBLICATION OF THE JACKSON LABORATORY

**ON THE COVER** Research Assistant Cheng-Han Chung working in the laboratory of Professor Karolina Palucka, Ph.D., and Professor Jacques Banchereau, Ph.D., at JAX Genomic Medicine in Farmington, Conn.  
*Photograph by Jennifer Torrance*

**LEFT** Tubes containing RNA probes slowly thaw in a bucket of ice. Magalie Collet, a research assistant in Banchereau's laboratory, will use the probes in FlowRNA, an assay designed to detect RNA transcripts using flow cytometry.  
*Photograph by Jennifer Torrance*

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in Connecticut



## Kathleen Corbet

A giving profession

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## President's message

### THE DAWN OF A NEW ERA

This year marks a pivotal moment in the history of The Jackson Laboratory. Not only are we marking JAX's 85th anniversary, but we are also witnessing the dawn of a new era at the Laboratory, and indeed in biomedical science: an era in which our understanding of genomics, coupled with powerful new technologies, will enable us to transform human health.

At our annual Discovery Days event in Bar Harbor in July, alumni, friends and supporters of the Laboratory reflected on our past, learned about our current research and looked ahead to our exciting future. Participants heard from JAX faculty whose research focuses on areas ranging from immunology and the genomics of the microbiome to diabetes, cancer and addiction. They also had the opportunity to meet with our 2014 summer students. Working with their JAX mentors, these incredibly bright and creative high school and college students are already doing original research. I look forward to following their careers as they develop into the next generation of scientific leaders.

Our enthusiasm for what lies ahead for JAX spans all our geographic locations and our research and educational programs, but without a doubt the event we are all most anticipating is the grand opening of The Jackson Laboratory for Genomic Medicine, the focus of this issue of *The Search*. With the rapid growth of our Connecticut-based staff, JAX Genomic Medicine is already making significant contributions to biomedical research.

New JAX Genomic Medicine faculty member Karolina Palucka, for example, focuses on cancer immunology, looking for ways to engage the body's own natural defense system to fight cancer. [Read more about Dr. Palucka's work on page 22.] As more faculty and scientists join us, we will be able to accelerate even more rapidly the pace of discovery and the application of our discoveries to the clinical setting.

When we officially open the doors to the new JAX Genomic Medicine building in October, it will be with our proud history and our promise for tomorrow in mind. Building on the foundation of 85 years of leadership in mammalian genetics, we are ready to apply our understanding of complex genetics much more directly to develop precise solutions to preventing, diagnosing and treating disease. Illuminated by the power of genomics, the future looks bright indeed.

A handwritten signature in black ink that reads "Edison L." followed by a stylized "iu".

Edison Liu, M.D.

## The Jackson Laboratory

**President and Chief Executive Officer**  
Edison Liu, M.D.

**Vice President, Development and Communications**  
Kristen Rozansky

**Director of Communications**  
Barry Teater

**Mission**  
We discover precise genomic solutions for disease and empower the global biomedical community in our shared quest to improve human health.

**Locations**  
Bar Harbor, Maine  
Farmington, Conn.  
Sacramento, Calif.

**Printed August 2014**

 **The Jackson Laboratory**  
*Leading the search for tomorrow's cures*

President and CEO, The Jackson Laboratory

### 'YES' VOTE ON QUESTION 4 WOULD FUND NEW RESEARCH CENTER

Maine voters will have the opportunity this fall to accelerate research in cancer and other genetic diseases and create high-paying jobs for Maine residents.

Although The Jackson Laboratory is not specifically named in the Nov. 4 referendum, Question 4 on the ballot would provide \$10 million in construction funds to enable the Laboratory to build a state-of-the-art Center for Biometric Analysis.

If the bond issue passes, the \$10 million will be awarded through a competitive application process administered by the Maine Department of Economic and Community Development. The Laboratory is considered a top contender for the award because it has the required scientific and technical expertise, and also is prepared to contribute \$11 million of its own money toward the research center.

The Center for Biometric Analysis would detect and measure at the cellular level extremely subtle signs of disease in experimental mice using high-powered imaging and analytical devices. These analyses, coupled with gene sequencing and computational biology techniques, would help pinpoint the genetic roots of disease and contribute to better diagnosis, prevention and treatment of human cancers, neurodegenerative diseases and other afflictions.

### ROSSI FOUNDATION PLEDGES \$1M TO BIOMETRY CENTER

The Laboratory has received a pledge of \$1 million from the Cornelia Cogswell Rossi Foundation to support and name the Laboratory's Neurobehavioral Biometry Center.

The newly established Connie Cogswell Rossi Neurobehavioral Biometry Center will enable the Laboratory to develop a greater breadth and depth of knowledge of neurobehavioral testing. It will help the Laboratory and its external partners in understanding, and developing treatments for, a wide range of neurological and neurobehavioral disorders, including Alzheimer's, autism and addiction.

The Center will either continue as a stand-alone resource or become part of a larger and more comprehensive Center for Biometric Analysis that the Laboratory will propose to build in Maine, pending voter approval of Question 4, a \$10 million cancer research bond referendum, this fall.



### JAX COMMUNITY MEMORIALIZES DOUG COLEMAN

"Vanished, but not gone," is how Tom Coleman described his late father, Jackson Laboratory Professor Emeritus Douglas Coleman, Ph.D., at a memorial ceremony on the Bar Harbor campus on Aug. 4. Coleman said his father's lasting legacy encompassed his science, his children, his philanthropy, his environmental work and the many friendships he and his wife, Beverly, cultivated over their lifetimes.

The elder Coleman, 82, whose elegantly simple approach to addressing complex biological problems earned him scientific renown and almost every major science award except the Nobel Prize, died at his home in Lamoine, Maine, on April 16.

After Coleman's death, Jackson Laboratory President and CEO Edison Liu, M.D., said, "I've heard Doug Coleman say on several occasions that in all things scientific as well as environmental, he tried to leave things better than he found them. I would add a third category: He left an indelible and profoundly beneficial mark on The Jackson Laboratory community. Doug was a unique combination of brilliant, honest, funny and modest, and he was unbeatable company. He leaves an inspiring legacy at the Lab and a giant void in our hearts."

Coleman's work established the first clues to a genetic component in obesity. In the 1970s, he conducted a series of experiments that led him to propose the existence of a "satiety factor" that would account for obesity and type 2 diabetes among certain laboratory mice. That factor was later identified as leptin, a hormone that regulates food intake and body weight.

A native of Stratford, Ontario, Canada, Coleman came to the then-Roscoe B. Jackson Memorial Laboratory in 1958 as an associate staff scientist. He rose through the ranks, eventually becoming assistant director of research and then interim director of the Laboratory, before retiring in 1991.

*Read Tom Coleman's eulogy of his father online at [www.jax.org/theseach/coleman](http://www.jax.org/theseach/coleman).*



JAX's Edison Liu, Tom Litwin and Charles Lee with ASHG's Joseph McInerney

## RESEARCHERS FIND NEW MECHANISM FOR NEURODEGENERATION

A research team led by Jackson Laboratory Professor and Howard Hughes Medical Institute Investigator Susan Ackerman, Ph.D., has pinpointed a surprising mechanism behind neurodegeneration in mice, one that involves a defect in a key component of the cellular machinery that makes proteins, known as transfer RNA or tRNA.

The researchers report in the journal *Science* that a mutation in a gene that produces tRNAs operating only in the central nervous system results in a "stalling" or pausing of the protein production process in the neuronal ribosomes. When another protein the researchers identified, GTPBP2, is also missing, neurodegeneration results.

Neurodegeneration — the process through which mature neurons decay and ultimately die — is poorly understood, yet it underlies major human diseases, such as Alzheimer's, Parkinson's, Huntington's and amyotrophic lateral sclerosis (ALS).

## POTENTIAL THERAPEUTIC TARGET FOR WOUND HEALING, CANCER IDENTIFIED

A Jackson Laboratory research team led by Professor Lenny Shultz, Ph.D., reports that a protein involved in wound healing and tumor growth could be a potential therapeutic target.

In one of nature's mixed blessings, the mechanisms that work to heal cuts and wounds, rebuilding damaged cells, can also go out of control and cause cancer. But understanding those mechanisms could lead to new ways of stimulating healing in wound patients and dialing back cancerous proliferation.

A protein called iRhom2 is normally a short-lived protein that controls a cascade of events involved in wound healing as well as tumor growth. By introducing mutations in Rhbd2, the gene that encodes the iRhom2 protein, the researchers extended the protein's duration and wound-healing power.

## TROWBRIDGE, DAI AWARDED NCI GRANTS

Assistant Professors Jennifer Trowbridge, Ph.D., and Chengkai Dai, M.D., Ph.D., have each received new federal research grants through a funding mechanism designed to address "provocative questions" about cancer set out by the National Cancer Institute (NCI).

Trowbridge will receive \$426,426 over two years for her investigations in acute myeloid leukemia (AML). Several acquired mutations are associated with this disease, and Trowbridge is exploring whether the sequence in which the mutations occur has an effect on the severity of the cancer or the effectiveness of treatments.

Dai's two-year, \$478,688 grant will support his studies of metformin, a widely prescribed anti-diabetic drug that appears to have anti-cancer effects. He hypothesizes that metformin suppresses the proteotoxic stress response — a mechanism that helps normal cells survive various stresses but also protects cancer cells.

## NCI CANCER CENTER DESIGNATION RENEWED

The Laboratory's Cancer Center has once again earned the renewal of its Cancer Center Support Grant from the National Cancer Institute (NCI), which recognizes research institutions that meet "rigorous criteria for world-class, state-of-the-art programs in multidisciplinary cancer research."

The 50 JAX Cancer Center members include faculty, research scientists and adjunct members across JAX's three campuses who collectively hold more than 100 research grants totaling over \$40 million. Their overall research goal is to develop precise interventions to prevent cancer from progressing to an untreatable state.

The renewed grant funding will support innovative projects, the sharing of scientific services and resources among Cancer Centers, and the salaries of new cancer research investigators.

## RESEARCHERS REVEAL NATURE OF VITAL EYE STRUCTURE

A Jackson Laboratory-based research team has conducted an exhaustive exploration of an eye structure known as Schlemm's canal (SC), a key gatekeeper for the proper flow of eye fluid, presenting a number of insights relevant to glaucoma and other diseases.

For the study published July 22 in the journal *PLOS Biology*, the researchers at JAX and Tufts University School of Medicine in Boston used mouse models hosting fluorescent proteins to determine how SC forms in the eye and in relation to neighboring tissues.

The report, according to first author Krishnakumar Kizhatil, Ph.D., an associate research scientist in the laboratory of JAX Professor and Howard Hughes Medical Institute Investigator Simon W.M. John, Ph.D., "provides new understanding and tools that will facilitate molecular understanding of SC and its critical — but poorly understood — roles in ocular physiology, immunity and health."

## NCI AWARDS \$2.2 MILLION GRANT TO PROFESSOR YIJUN RUAN

The National Cancer Institute has awarded a three-year grant totaling \$2,168,535 to Professor Yijun Ruan, Ph.D., of The Jackson Laboratory for Genomic Medicine, for his research into the role of noncoding RNAs in cancer and other diseases.

The best-known RNAs are those that manufacture proteins from the "blueprint" provided by DNA. But there

are many kinds of non-coding RNAs (ncRNAs) that carry out other vital roles. In fact, there may be thousands of different kinds of ncRNAs yet to be discovered in the genome, each of which may have a specific role in healthy function or disease.

Using new technologies, Ruan and his lab will identify novel ncRNAs and the interactions between



Stay up to date with the latest JAX news. Visit [www.jax.org/news](http://www.jax.org/news)

## JAX EARNS TOP RATING FROM CHARITY NAVIGATOR

The Laboratory's sound fiscal management practices and commitment to accountability and transparency have earned the nonprofit organization a 4-star rating from Charity Navigator, America's largest independent charity evaluator.

*"The Jackson Laboratory's coveted 4-star rating puts it in a very select group of high-performing charities."*

— Ken Berger, president and CEO of Charity Navigator

This is the fourth consecutive year that the Laboratory has earned this top distinction. Only 7 percent of charities evaluated by Charity Navigator have received this highest possible rating on four or more consecutive evaluations, placing the Laboratory among the nation's most highly rated charities for good governance and responsible stewardship of philanthropic support.

*"The Jackson Laboratory's coveted 4-star rating puts it in a very select group of high-performing charities," says Ken Berger, president and CEO of Charity Navigator.*

*"The Jackson Laboratory's supporters should feel much more confident that their hard-earned dollars are being used efficiently and responsibly when it acquires such a high rating."*



An architectural model depicts the JAX Genomic Medicine building.

# Toward genomic medicine

STORY BY MARK WANNER  
PHOTOGRAPHY BY JENNIFER TORRANCE

What made this partnership possible?

## *In one word: genomics.*

### A NEW APPROACH TO MEDICINE

Genomics involves the study of all of an organism's genetic material as a whole system. It is a step beyond traditional genetics — which uses reductionist, gene-by-gene methods — and has only recently been made possible by rapid advancements in DNA-sequencing technology. Genomics research provides crucial insights into the workings of complex genetic diseases such as cancer, diabetes and neurodegeneration.

Eighty-five years ago this summer, a scientist with foresight established a research laboratory in Bar Harbor, Maine, on the Atlantic coast. The mission of The Jackson Laboratory was at the vanguard of science at the time: to reveal the genetic causes of cancer — then thought to be an infectious disease — and to find better therapies for patients.

Since its founding in 1929 the Laboratory's award-winning mammalian genetics research has made vital contributions to human disease research and medical progress. Its mouse models of human disease have supported biomedical research around the world. And its education programs have trained thousands of young and established scientists and physicians and nurtured the early careers of three future Nobel laureates.

Along the way, the tiny laboratory that first employed a dozen staff members in 1929 has grown to more than 1,500 employees. And with the October opening of its new research center, The Jackson Laboratory for Genomic Medicine, in Farmington, Conn., the Laboratory will launch into a major new realm.

"JAX Genomic Medicine represents a very powerful scientific, medical and economic partnership between the Laboratory, the state of Connecticut, the University of Connecticut, the UConn Health Center and Connecticut hospitals," says JAX President and CEO Edison Liu, M.D. "Together we will contribute to better health for people everywhere while growing Connecticut's bioscience economy."

But while genomics research is now possible, it is far from easy. As we learn more about how genomes work, we are also beginning to appreciate how much more there is left to learn. We still know relatively little about how multiple genes interact, how gene expression and protein production are regulated, what the consequences are when something goes slightly wrong in this vast and nuanced system, and so on.

It follows then that leveraging genomics research for medical progress offers both formidable challenges and vast potential benefits. Clinical genomics is a young and quickly growing field, but actual medical implementation has lagged behind early expectations. There needs to be a catalyst to accelerate progress, and JAX Genomic Medicine — primed with a \$291 million investment from the Connecticut legislature and governor — is poised to fill that role.



**ABOVE** Two months before the opening of JAX Genomic Medicine, staff members visit the construction site.

**LEFT** Workers install light fixtures in the lobby of JAX Genomic Medicine.

**LOWER LEFT** Charles Lee, Ph.D., scientific director of JAX Genomic Medicine, tours the new facility.



"Over our 85-year history, The Jackson Laboratory has emerged as a world leader in mammalian genetics, and our discoveries have paved the way for the major medical advances of our lifetime," says Liu. "Now, building on that foundation, our expanded focus on human genomics places us at the forefront of applying that genetic experience to human health. Our goal is to transform medicine through our integrated approach by moving basic science to clinical impact."

### INTRAMURAL POWER

On its own, JAX Genomic Medicine is an important institution off to a great start. Early recruiting has been extraordinarily successful, with several well-known and highly regarded senior scientists joining the faculty, led by Scientific Director Charles Lee, Ph.D., a pioneer in genomic structural variation research. Junior faculty members are doing exciting work in their own right, and two assistant professors at JAX Genomic Medicine, Zhengqing Ouyang, Ph.D., and Michael Stitzel, Ph.D., were selected by *GenomeWeb* for its 2013 list of up-and-coming genomics researchers.

A burgeoning research program with exciting new collaborations is gaining momentum even as the scientists perch in temporary laboratories in several different buildings around the UConn Health Center (UCHC) campus. The workforce has already grown to about 115 scientists and staff, ahead of initial employment goals.

On Oct. 7, the permanent facility will open, further accelerating faculty and staff growth that will culminate with about 300 employees within a decade. Both computational and bench research faculty will enjoy the latest in laboratory design and equipment, and a dedicated clinical genomics laboratory will provide sequencing and patient data analysis to physicians next door at UCHC and around the country.

As impressive as all this is, however, a crucial part of JAX Genomic Medicine's ultimate success depends on its being part of the larger Laboratory. Human data and clinical collaborations are essential for translational medicine, but so is an effective experimental system in which it is possible to test findings from patients. The patients themselves are off-limits due to ethical limitations for investigating the underlying biology and developing candidate therapies for diseases and disorders. For that work, researchers turn to model organisms, mice being prominent among them, for a variety of reasons. And no institution in the world compares to JAX for having more or better mice for modeling human diseases, or the expertise to work with them effectively.

Professor Jacques Banchereau, Ph.D., who leads JAX's immunology research program on both the Connecticut and Maine campuses, describes JAX's disease research as forming a triangle. Clinical collaborators, patient access and patient data are on one side, the best technology and capability to leverage it on another, with the mouse resources

and expertise completing the triangle, all within the same organization. To date there has been a significant gap between the worlds of genomics research and clinical care. JAX's research prowess and ability to move seamlessly between patients and experimental disease models creates an exciting opportunity to accelerate both the pace of biomedical discoveries and the speed with which they can be brought to the clinic.

### 'A PRIVILEGE'

Charles Lee left a number of prestigious appointments, including one at Harvard Medical School, to lead the scientific program at JAX Genomic Medicine. In an interview he did soon after his arrival in Farmington for a previous issue of *The Search*, his enthusiasm was palpable. As he said at the time, "Every day when I come to work I feel the positive energy from everyone around me, working hard together to make a difference, and it's all worth it. It's a privilege to have the opportunity to do something that goes far beyond ourselves, to make breakthroughs that will benefit mankind."

Now, with research projects well under way and the opening of the permanent facility fast approaching, Lee relishes both the challenges and vast potential of his opportunity. "JAX Genomic Medicine has already been making amazing strides forward, and this is just the beginning," he says. "Through our own research, as well as partnerships being developed with other Connecticut institutions including the University of Connecticut, Connecticut Children's Hospital and others, we are well poised to dramatically transform how we treat disease, develop new cures and keep people healthy."

# ON TIME, ON BUDGET

## JAX Genomic Medicine 'Collaboratorium' readies for grand opening

For the last 900 or so days, an electronic clock mounted on the wall of The Jackson Laboratory's engineering office in Bar Harbor has counted down the days, hours, minutes and seconds.

It's been a constant reminder of the most important deadline of John "Fitz" Fitzpatrick's 28-year engineering career: the day, Sept. 30, 2014, when JAX must finish construction of its new \$135 million research center, The Jackson Laboratory for Genomic Medicine, in Farmington, Conn., and have its occupancy permit in hand.

As the clock nears zero, "we're going to be done on time, on budget — all the things we said we'd do when we signed our agreement with the state of Connecticut," says Fitzpatrick, the Laboratory's senior director of facilities services.

### SOPHISTICATED BUT PRACTICAL

Rising on a 16-acre site on the University of Connecticut Health Center campus is a 183,500-square-foot building with state-of-the-art laboratories where JAX scientists will probe the human genome for new solutions to cancer, Alzheimer's, diabetes and other daunting diseases.

The design team, Centerbrook Architects & Planners and Tsoi/Kobus & Associates, was charged with creating a building sophisticated enough to entice internationally acclaimed scientists, bold enough to symbolize the state of Connecticut's new aspirations in the biosciences, yet practical enough for a no-frills, nonprofit organization serious about its research.

STORY BY BARRY TEATER  
PHOTOGRAPHY BY MARIE CHAO  
AND MICHAEL GARNER

16+  
ACRES

330  
EMPLOYEE CAPACITY

183,500  
SQUARE FEET

590,000  
HOURS OF LABOR FOR DESIGN AND CONSTRUCTION

\$135,000,000  
DESIGN & CONSTRUCTION COST



PHOTOGRAPHY BY MICHAEL GARNER

## "FITZ WAS RIGHT. HE SAID, 'LET'S SPEND THE MONEY ON SCIENCE, NOT ON MAKING THE ARCHITECTS LOOK GOOD.'"

— Jim Childress of Centerbrook Architects & Planners quoting John Fitzpatrick, senior director of facilities services.

"The architects did a fantastic job," Fitzpatrick says. "The building aesthetics had to reflect our status as a leader in the biomedical research industry without the appearance of being opulent. And I think the team hit it. It's a high-end facility, but it's not a building that is filled with superfluous amenities."

Says Centerbrook architect Jim Childress: "Fitz was right. He said, 'Let's spend the money on science, not on making the architects look good.'"

The four-story facility, faced with Canadian limestone and pre-weathered zinc panels and glass, is built in a graceful arc to fit the constraints of the site. A distinctive oval structure that Fitzpatrick calls "the snow globe" juts from one end, punctuating the main building like a comma. In time, as JAX Genomic Medicine grows, another wing will connect to it, forming a U-shaped campus.

JAX Genomic Medicine will include 17 "wet" biology labs and another 17 "dry" computational science labs, along with scientific service areas. The labs will be clustered in large, open suites to encourage collaboration among scientists and technicians, and to enable spaces to be reconfigured quickly and easily as research programs grow or shrink.

"That was the real soul-searching part," says Childress. "Science is changing so fast and so much."

At the building's entrance on Discovery Drive — a road named by JAX employees in a contest — visitors will walk into a light-filled, double-

story vaulted reception area leading to a 200-seat auditorium, two large conference/seminar rooms, and a 200-seat dining area that opens into an outdoor courtyard. On the second floor will be core service labs, a data center, offices, conference rooms, an employee fitness center and an informal seating area referred to as the "pub" for casual networking and formal pre-conference gatherings. Research labs and faculty offices will predominate on the third and fourth floors.

"The architects' interior design takes a very clean and minimalistic approach," Fitzpatrick says. "There's a lot of glass in the building. In many work spaces, if not most, you can stand in the building and have access to daylight in at least two different directions and in some places three."

### BUILT FOR COLLABORATION

The design team took seriously the advice of JAX scientists who insisted that the building foster collaboration. "We started calling it the Collaboratorium," says architect Rick Kobus of Tsoi/Kobus. "We were really trying to get people sharing ideas, brainstorming, working together in novel ways to unlock the secrets of the genome."

"The concepts of making the building very transparent, of putting science on display, of creating a collaborative corridor between the private offices, were really an exciting set of challenges."

The building is on track to earn LEED Gold status, a certification by the nonprofit U.S. Green Building Council for structures that incorporate low-impact materials, environmentally sensitive operating principles, and energy-conservation practices. The LEED designation — an acronym for Leadership in Energy and Environmental Design — will mean, for example, that employees will have to forego energy-wasting personal printers or coffee makers in their offices.

Despite these small sacrifices, "I'm confident this building is going to be received very well after our employees move in and get acclimated to their new space," Fitzpatrick says.

The facility already has become a strong recruiting tool for attracting top faculty. "Scientists are finding that it's very responsive to their needs," Kobus says. "It's a novel, new environment. I don't think there's another scientific environment like it."

The building can accommodate up to 330 employees, starting with the 115 or so who will move in this fall after working in 21,000 square feet of temporary space scattered across the UConn Health Center and in leased offices off campus.

### A 'SCHEDULE-DRIVEN PROJECT'

JAX Genomic Medicine will be formally dedicated on Oct. 7. The grand opening will cap 669 days of construction since ground was broken in December 2012.

"It was a pretty challenging schedule," Fitzpatrick says, especially during a time when, in addition to assisting with



## 17 "WET" BIOLOGY LABS

## 17 "DRY" COMPUTATIONAL BIOLOGY LABS



the programming and design of JAX Genomic Medicine, his seven-member engineering and technical services staff was also managing more than \$20 million in construction projects at JAX's Sacramento, Calif., facility and another \$15 million at the Bar Harbor campus.

"Nobody on the JAX team had ever designed or constructed a genomics facility before," he confesses. "That was a little challenging, but both our internal Facilities Engineering team and our external designers developed a very flexible and functional facility."

Initially Fitzpatrick devoted nearly all of his time to organizing the project, assembling the design and construction team, acquiring and renovating temporary space, achieving key design and early construction milestones, tracking budget projections, lining up vendors and coordinating with the UConn Health Center. "It was all-consuming," he says. This year his involvement has tapered off, thanks to the vendors JAX entrusted to oversee and build the facility: program manager Gilbane Inc. and construction manager Whiting-Turner Contracting Co.

"Whiting-Turner and Gilbane have been great to work with," he says. "And I can't say enough about how helpful my peers have been at UConn. If they were going to come on our campus and build here, I would hope that I would be half as gracious as they have been to us."

The JAX project began at an inauspicious time when more than \$600 million in construction



projects funded by the state's ambitious Bioscience Connecticut initiative were about to begin within a half-mile radius on the UConn Health Center campus. The impending building boom threatened to raise construction prices and thin the ranks of qualified contractors, so Fitzpatrick and his team acted quickly.

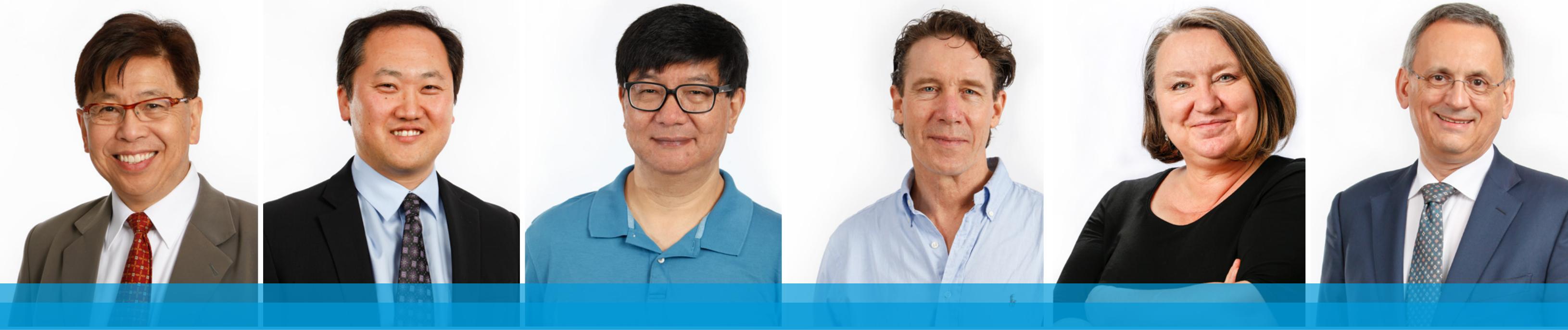
"We got the entire team together, we put a line in the sand and said we are going to be the first project out to bid . . . And we were the first ones on the street. I'm confident the project outcome benefitted immensely from that."

The team had only 31 months to take the project from an idea to a design to a finished building. A freakish 44-inch snowstorm in 2013 delayed construction for several days, and a long, cold winter this year further slowed productivity.

"Every project has its challenges, and this one has had its own unique issues to overcome, but it's the nature of the beast," Fitzpatrick shrugs. "You try to anticipate and minimize adverse impacts. You roll with the changes."

"This has been a schedule-driven project. I'm pretty happy that despite a few hiccups we've stayed on schedule from day one."





**Edison T. Liu, M.D.**

**President and CEO, The Jackson Laboratory**  
B.S. from Stanford University  
M.D. from Stanford University  
Internship and residency at Washington University, St. Louis  
Postdoctoral studies at the University of California, San Francisco  
Served two elected terms as president of the international Human Genome Organization

Dr. Liu came to JAX after founding and leading the Genome Institute of Singapore. His scientific research focuses on the functional genomics of human cancers, investigating gene regulation on a genomic scale that modulates cancer biology. His laboratory investigates the expression signatures in breast cancers that define biochemical and genetic perturbations as well as the transcriptional regulation of estrogen receptors. Dr. Liu's work spans cancer biology, genomics, human genetics and molecular epidemiology.

**Charles Lee, Ph.D., FACMG**

**Scientific Director, JAX Genomic Medicine**  
B.S., M.S. and Ph.D. from University of Alberta  
Research fellowships at Cambridge University and Harvard Medical School  
Research and faculty appointments at Harvard Medical School and Brigham and Women's Hospital  
Winner of the 2008 Ho-Am Prize in Medicine

Dr. Lee joined JAX Genomic Medicine from Harvard Medical School and Brigham and Women's Hospital. He is best known for his discovery that copy-number variation — a state in which cells have an abnormal number of DNA sections, sometimes associated with susceptibility or resistance to disease — is widespread and significant in the human genome. This discovery, and his subsequent research, have provided tools that clinicians use to make accurate diagnoses for genetic testing of conditions such as autism, birth defects and cancer. Dr. Lee is responsible for the scientific direction and coordination of JAX Genomic Medicine.

**Yijun Ruan, Ph.D.**

**Professor and Director of JAX Genomic Sciences**  
B.S. and M.S. from Huazhong Agricultural University  
Ph.D. from the University of Maryland, College Park  
Postdoctoral studies at the University of Maryland, College Park

Dr. Ruan's primary interest is to elucidate the structures and dynamics of all functional DNA elements in complex genomes. Using concepts and computational tools developed for social networks, researchers in his laboratory have recently visualized how the genome appears to organize genes with related functions into certain communities within a large-scale, three-dimensional network. Dr. Ruan's lab also is applying genome sequencing-based measurements to address complex biological questions such as how cancer cells progress and how stem cells maintain their unique properties.

**Frank McKeon, Ph.D.**

**Professor and Director of JAX Quantitative Cell Biology**  
B.A. from Pomona College  
Ph.D. from the University of California, San Francisco  
Postdoctoral studies at the University of California, San Francisco

Dr. McKeon is building a technology platform to address human disease at the level of adult or tissue-specific stem cells. Using this platform together with mouse genetics and human genomics, he has identified the stem cells that underlie lung regeneration following influenza infection, the cell-of-origin of highly lethal gastrointestinal cancers, and the regional specificity of stem cells in human organs.

**Karolina Palucka, M.D., Ph.D.**

**Professor and Associate Director of Cancer Immunology**  
M.D. from Warsaw Medical Academy, Poland  
Ph.D. from Karolinska Institute, Sweden  
Postdoctoral fellowship at Pitié-Salpêtrière Hospital, France

Clinical oncologist and cancer immunologist Karolina Palucka joined JAX Genomic Medicine as professor and associate director of cancer immunology. Her research exploits dendritic cells, which control the body's immune response to tumors, as the basis for new vaccines against melanomas and other human cancers. Prior to joining JAX, Palucka was the Michael A.E. Ramsay Chair for Cancer Immunology Research and director of the Ralph M. Steinman Center for Cancer Vaccines at the Baylor Institute for Immunology Research in Dallas.

**Jacques Banchereau, Ph.D.**

**Professor and Director of Immunological Sciences**  
B.S. from the University of Angers, France  
Ph.D. from the University of Paris, France  
Postdoctoral work at Schering-Plough, France

Dr. Banchereau was founding director of the Baylor Institute for Immunology Research in Dallas and more recently held top scientific positions at Hoffmann-La Roche. At JAX Genomic Medicine, he is building on the Laboratory's historical base of immunological research led by Nobel Laureate George Snell and is expanding the program across all three JAX campuses. He is leading the recruitment of new immunological investigators and his research lab is investigating cancer immunobiology, autoimmunity and host response to infectious diseases.

The Jackson Laboratory for Genomic Medicine has attracted a stellar cast of 14 junior and senior scientists from around the world, and more recruitments are under way.

These principal investigators are the first to join the faculty in Farmington, Conn.

# JAX GENOMIC MEDICINE RECRUITS TOP SCIENTISTS



**George Weinstock, Ph.D.**

**Professor and Associate Director  
for Microbial Genomics**

B.S. from University of Michigan  
Ph.D. from Massachusetts Institute of Technology  
Postdoctoral studies at Stanford University Medical School

A pioneer in the sequencing and genomic analysis of humans, model organisms and microbes, Dr. Weinstock joined the faculty of JAX Genomic Medicine as professor and associate director for microbial genomics. Dr. Weinstock is a leader of the Human Microbiome Project, an international effort to characterize the large and genetically varied population of microorganisms that inhabit the human body and impact human health. He comes to JAX Genomic Medicine from Washington University in St. Louis, where he was associate director of the university's Genome Institute.

**Reinhard Laubenbacher, Ph.D.**

**Professor of Computational Biology**

Vordiplom from University of Munich  
M.A. from Indiana University, Bloomington  
Ph.D. from Northwestern University

A mathematician and systems biologist, Dr. Laubenbacher holds the first joint academic appointment with the University of Connecticut Health Center and JAX Genomic Medicine. As the co-director of the health center's new Center for Quantitative Medicine, his focus is on implementing mathematical algorithms and related software to support research connected to biomedical problems, including genomic and other approaches to personalized medicine.

**Jeffrey Chuang, Ph.D.**

**Associate Professor of Computational Biology**

B.S. from Harvard University  
Ph.D. from Massachusetts Institute of Technology  
Postdoctoral studies at the University of California, San Francisco

Dr. Chuang is interested in computational and mathematical approaches to analyzing large DNA sequencing data sources in order to understand how genomes function and to make these findings clinically relevant to human health. His lab is developing projects in human and mouse genetics, cancer, epigenetics and RNA biology. Some of Dr. Chuang's more specific interests include evolutionary processes in cancer, regulatory sequences within RNA and developmental enhancers.

**Wa Xian, Ph.D.**

**Assistant Professor**

B.S. from Nankai University  
Ph.D. from University of Texas, Houston  
Postdoctoral studies at Baylor College of Medicine

Dr. Xian has investigated the cellular origins and progression of high-grade ovarian cancers and is advancing her research on adult stem cells. Her lab has identified the stem cells that underlie lung regeneration following influenza infection, the cell-of-origin of gastrointestinal cancers, and the region-specific pattern of stem cells in human organs. Her aim is to identify new therapeutic approaches for acute and chronic airway diseases and to target precursor lesions of highly lethal cancers.

**Zhengqing Ouyang, Ph.D.**

**Assistant Professor**

B.S. from Peking University  
Ph.D. from Stanford University  
Postdoctoral studies at Stanford University

Dr. Ouyang's research program focuses on using computational and statistical methods to investigate genome regulatory mechanisms in both normal and disease states. He is also developing bioinformatics software for genome data analysis and modeling.

**Duygu Ucar, Ph.D.**

**Assistant Professor**

B.S. from Bilkent University, Ankara, Turkey  
Ph.D. from Ohio State University  
Postdoctoral studies at the University of Iowa and Stanford University

Dr. Ucar is a computational scientist who studies the dynamic regulation of gene expression. She is particularly interested in the interaction between epigenetic chromatin states and gene regulatory elements for the control of gene expression. She develops algorithms to integrate and mine genetic and epigenetic datasets.

**Michael L. Stitzel, Ph.D.**

**Assistant Professor**

B.S. from Pennsylvania State University  
Ph.D. from The Johns Hopkins University  
Postdoctoral studies at the National Human Genome Research Institute

Dr. Stitzel came to JAX Genomic Medicine from the lab of Dr. Francis Collins, director of the National Institutes of Health. He studies the genetics and epigenetics of islet dysfunction and type 2 diabetes. His work has suggested that DNA changes associated with genetic susceptibility to type 2 diabetes are located in molecular switches that turn islet genes on or off.

**Adam Williams, Ph.D.**

**Assistant Professor**

B.S. from Cardiff University  
Ph.D. from University College London and the London-based MRC National Institute for Medical Research

Dr. Williams studies immune cell function with respect to treating asthma. He investigates the role of molecules known as non-coding RNAs in regulating gene expression relating to immune cell function — in particular, a category of immune cells known as CD4+ T cells.

# Tipping the balance

Cancer immunologist and former physician Karolina Palucka is pioneering ways to rev up the body's natural defenses to fight cancer

STORY BY NICOLE DAVIS  
PHOTOGRAPHY BY MARIE CHAO,  
JANINE GELINEAU AND JENNIFER TORRANCE

Cancer scars the body and touches the soul. For patients, of course, these imprints are everlasting. For doctors, the caregivers who slay the slipperiest of enemies while healing the wounds it leaves behind, who celebrate the victories and mourn the losses, the impact of the illness can be just as enduring.

These deep connections to cancer and cancer patients are what led Karolina Palucka, M.D., Ph.D., to join The Jackson Laboratory for Genomic Medicine in Farmington, Conn., in March as a professor and associate director of cancer immunology. Throughout her career, she has blended basic science and medicine, cancer and immunology, all with the goal of finding better, more precise ways to treat cancer.

"The diagnostic aspect of genomic medicine is very important, but so is the therapy component," says Charles Lee, Ph.D., scientific director of JAX Genomic Medicine. "We need to keep coming up with creative ways to develop novel and effective therapies to human diseases. Dr. Palucka has had amazing success in this area, and I am absolutely delighted to have her join our team here in Connecticut."

The roots of that success began in the clinic. As a young cancer doctor in Warsaw, Poland, in the 1980s, Palucka remembers the highs and lows of caring for her patients, many of them dying.

She felt frustrated. The tools at her disposal seemed limited, blunted, too often ineffective. "I was using different combinations of chemotherapy and all the standard treatments, but, in fact, I was not seeing progress. I was not seeing solutions," she says.

One patient, a young woman in her thirties with advanced breast cancer — not much older than Palucka herself — sparked a major transformation. "She really tipped the balance because I couldn't do much for her," says Palucka. "I loved the patients and I think they loved me, but I just could not continue doing that."

## *So Palucka made a bold move.*

Knowing little of the world of laboratory-based research, she accepted a scholarship to pursue a graduate degree in biomedical research, landing her at the Karolinska Institute in Sweden, one of the world's premier research institutions. Although Palucka traded her white doctor's coat for a lab coat, she didn't let go of her passions. Her commitment and care for patients remain as deep as they were 25 years ago.

### LEADING THE WAY

Through her graduate work, Palucka probed the inner workings of blood cells, immune cells and the cancers that arise within them. She was particularly intrigued by the immune system — an elaborate network of organs, tissues and cells that work together to defend the body against foreign threats, such as bacteria and viruses — and she began to explore how it might be mobilized to fight cancer.

It is easy to grasp the importance of such a defense when invaders, such as influenza or Salmonella, gain entry. Indeed, one of the key elements of immunity is the ability to distinguish normal tissues from foreign, "non-self" intruders. But how does this surveillance system respond to cancer? And more importantly, how can it be revved up to fight the disease?

Palucka became fascinated by a certain type of immune cell, known as a dendritic cell — named after the Greek word dendron, for tree, because of the cells' branch-like projections. Unlike some other types of immune cells, which are relatively abundant in the body and can be readily isolated for study, dendritic cells are exceedingly rare. Despite this scarcity, they play a critical role, connecting and coordinating the two main branches of the immune system.

A key advance in dendritic cell biology came in the early 1990s when three independent groups succeeded in growing human dendritic cells in the laboratory. Jacques Bachereau, Ph.D., who joined JAX in 2013 as a professor and director of immunological sciences, led one of these pioneering studies.

"It was a major breakthrough," says Palucka. "The field could now generate large numbers of these cells, which tremendously facilitated their study, but also opened doors to clinical applications."

She recalls seeing some of the data from these early studies. Compelled by them and the possibilities they inspired, Palucka began her own work on dendritic cells, isolating them from patients and growing them in the lab. Her ultimate goal: to design approaches that could be translated to the clinic.



To see a related video clip and photo gallery of Radu Marches, Ph.D., an associate research scientist working in the lab of Jacques Banchereau, visit [www.jax.org/thesearch/balance](http://www.jax.org/thesearch/balance)

## UNIFIED

Shortly after Palucka's work on dendritic cells began, she traveled to Venice, Italy, where a major scientific meeting was convened to discuss and highlight progress in dendritic cell biology. There she met Banchereau, then at the Schering-Plough Institute for Immunology Research in France, who mentioned plans to launch a new institute in Texas dedicated to translational medicine and with a specific focus on dendritic cells.

Palucka was intrigued. The organization would bring together not only Ph.D. researchers but also clinicians treating patients as well as clinician researchers—a place quite similar in spirit to JAX Genomic Medicine.

"For me, it was like the unification of my life," says Palucka. "I started in the clinic and then I was in the lab, and when I met Jacques, I told him this was my dream—these two things together."

That meeting sparked a long and fruitful collaboration. Two years later, Banchereau recruited Palucka to join the institute he founded, the Baylor Institute for Immunology Research (BIIR), in Dallas. The pair worked together there for over 15 years, publishing more than 100 scientific papers.

"Everything she has touched has been very successful," says Banchereau. "She has had an absolutely amazing and broad range of responsibility, and I think she

has developed in an outstanding way." During her tenure at BIIR, Palucka rose from a senior postdoctoral fellow to an endowed professor of cancer immunology and director of the Ralph M. Steinman Center for Cancer Vaccines.

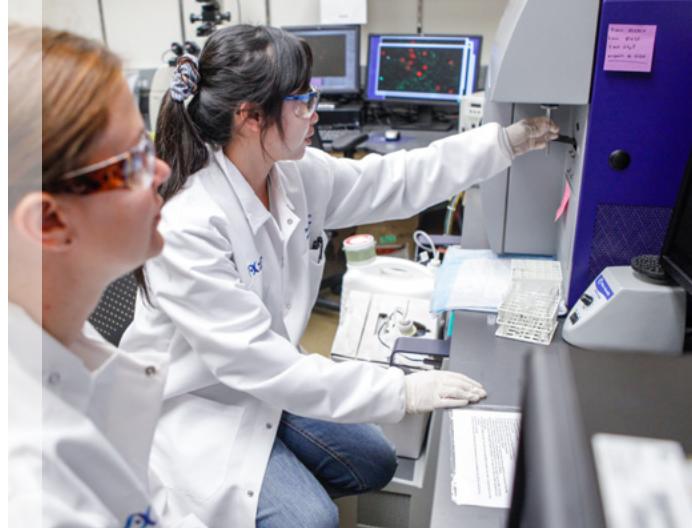
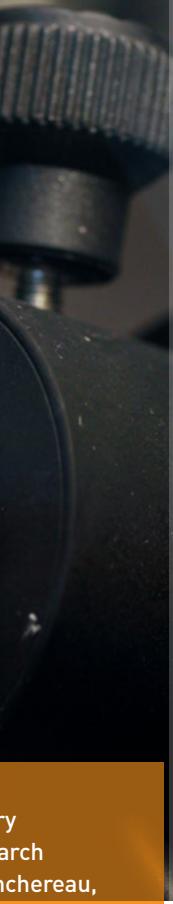
Banchereau holds deep respect not only for Palucka's professional accomplishments, but also her compassion. "She takes care of the patients. She takes care of her students, her postdocs," he says. "She takes care of people."

During his own recruitment to JAX, Banchereau recognized how essential his longtime colleague was to the program he aspired to build, which seeks to bring genomic solutions to various diseases, including cancer, that are impacted by the immune system.

For Palucka, the match again seemed ideal.

"I started with humans, then I went to cells, and it was time to go to genes—to really understand and put the genome to work, particularly its regulatory components. That for me was an extremely important thing," she says. "JAX Genomic Medicine is a very forward-looking place, and I really like its pioneering spirit."

She also cites JAX's expertise in the development and application of so-called "humanized mice." These highly specialized mice can receive an implanted human tumor—and even a human immune system—allowing scientists to study human cancers in a living system. Such capabilities are crucial for investigating immune-based therapies against cancer.



## A NEW WORLD

The last year has seen a groundswell of interest in leveraging the immune system against tumors—a field known as cancer immunotherapy. (See Beyond the News on page 34.) The human immunology program now beginning at JAX, co-led by Palucka and Banchereau, aims to be at the leading edge of this revolution.

Within her own laboratory, Palucka plans to pursue three major areas: cancer vaccines, dendritic cell "editing" and personalized cell-based therapies.

## IMPROVING CANCER VACCINES

Vaccines, whether designed to target measles, HIV or cancer, all share the same fundamental principle—to boost the immune system's activity so that it can seek out and destroy the necessary intruder. In the design of cancer vaccines, dendritic cells are a central component. Palucka has developed several experimental dendritic cell-based vaccines. These vaccines as well as those developed by others have been tested in clinical trials, yielding some early successes and disappointments. "This is just to show that it is very complex, and we still have to learn how to do it," says Palucka.

## DENDRITIC CELL 'EDITING'

Tumors naturally suppress dendritic cells—poisoning them, in effect—which hampers the cells' ability to function. It is not yet known how tumors do this dendritic cell dirty work. Together with JAX Professor Yijun Ruan, Ph.D., Palucka aims to scour the genome for clues. She hopes that these hints will uncover key genomic regulators that control the activities of dendritic cells. Once identified, these regulators can then be removed or "edited" out altogether—essentially eliminating what makes dendritic cells susceptible to tumor poisons.

## PERSONALIZING CELL-BASED THERAPIES

Tumors produce a range of substances that normal cells do not. Some of these so-called "tumor antigens" are shared across many cancer patients, but others are rare—even unique to an individual patient. Now, because of stunning leaps in the ability to decode and analyze tumor genomes, scientists can home in on these personalized cancer mutations as well as the immune cells that target them. These single-minded immune cells can then be grown up in the laboratory, boosting their numbers well beyond what is otherwise found in the body, and then injected back into the patient. Such treatment, although still in its infancy, has shown promise in early-stage studies across multiple cancers.

Palucka's optimism and enthusiasm for what lies ahead are obvious. The group she is building now at JAX will span both the Bar Harbor and Farmington campuses. Most members of her Dallas lab, 11 altogether, relocated to JAX along with her. "It's a soccer team," she jokes. Each lab member is a trained expert in human immunology.

As she looks ahead, Palucka envisions recruiting new members, particularly postdocs, and becoming an integral part of the fabric of JAX. Although she has already witnessed some amazing leaps, she sees more groundbreaking work yet to come.

"What a tremendous jump the field has made," says Palucka. "I think the next decade is really going to see some [therapies] getting into the clinic for everyday use. It is really a terrific time."

*Nicole Davis, Ph.D., is a freelance writer and communications consultant specializing in biomedicine and biotechnology. She has worked as a science communications professional for nearly a decade and earned her doctorate in genetics at Harvard University.*



**FAR LEFT** The super-steady hands of Jan Martinek cut ultra-thin sections of frozen tissue using a cryostat. Later on, the sections will be gently placed onto a glass slide and stained with fluorescently tagged antibodies and then imaged using confocal microscopy.

**TOP LEFT** Magalie Collet, left, and Postdoctoral Fellow Tina Wu run patient blood samples on a flow cytometer.

**BOTTOM LEFT** Karolina Palucka confers with Jacques Banchereau.

**ABOVE** Magalie Collet carefully pipets reagents into a microfuge tube.

# TEACHING THE GENOME GENERATION IN CONNECTICUT

Walt Nakonechny watches intently as Ingrid Burke manipulates a pipette between a rack of tiny vials and a petri dish, then ejects the tip with a click. Burke is new to this task but already has a crisp rhythm — vial, petri, click; vial petri, click.

Burke is not a lab technician but a science teacher at Northwestern Regional High School in Winsted, Conn. And Nakonechny, a former Connecticut high school teacher and bench researcher himself, is now the associate program director for genomic education at The Jackson Laboratory for Genomic Medicine, the first educator hired for the new facility in Farmington, Conn.

On this summer morning in the Laboratory's Bar Harbor training lab, Nakonechny and Burke are with 15 other northern New England science teachers attending a weeklong professional development program, "Teaching the Genome Generation," funded by Jane's Trust.

"The healthcare jobs of the future will be genome-based," explains Charles Wray, Ph.D., associate director for JAX Courses and Conferences. "So we need to prepare young people for careers in this growing field, as well as for being knowledgeable healthcare consumers."

The "teach the teachers" approach, adds Nakonechny, is an efficient way to bring greater understanding of the basics of genomics — molecular biology techniques, use of genome databases, and social, ethical and legal issues — to public schools. "These teachers can bring their knowledge back to their colleagues in Maine and Connecticut as well as their students," he says.

## NEW EDUCATIONAL OPPORTUNITIES IN CONNECTICUT

The workshop title, "Teaching the Genome Generation," sums up much of Tom Litwin's grand plan for JAX Genomic Medicine's educational programs. Litwin, Ph.D., the Laboratory's vice president for education, and his team are seeking out new ways to bring genomics into the public-school classroom, the university curriculum, the workforce and even physician education.

STORY BY JOYCE PETERSON  
PHOTOGRAPHY BY DANIELLE MEIER  
AND JENNIFER TORRANCE



*"...it's been very impressive how well Anu, as young as she is, has grasped the concepts of our work and really understood them."*

— Michael Stitzel, Ph.D., assistant professor



Postdoctoral Associate Ina Kycia at work in the lab of Assistant Professor Michael Stitzel.

"Genomics is driving personalized medicine, and personalized medicine is shaping the future of healthcare," Litwin says. "The Jackson Laboratory is taking on the responsibility of providing genomics education and training at every level."

With the opening of JAX Genomic Medicine in Farmington, the Laboratory will expand its educational offerings, ranging from STEM (short for science, technology, engineering and mathematics) programs for pre-college students to pre- and postdoctoral training to courses, conferences and workshops for mid-career scientists.

A grand opening scientific symposium on Oct. 8 will inaugurate the facility's new, fully equipped, TED-Talk-quality auditorium. A panel of international scientific leaders, including three Nobel laureates, will present what's new and what's coming in clinical genomics, modeling human diseases and genomic technologies.

Connecticut-area researchers can already sign up for a symposium on the new field of immunogenomics and a course on new, 3-D genome mapping technology (charmingly known as ChIA-PET, for Chromatin Interaction Analysis by Paired-End Tag Sequencing).

For physicians, JAX has launched an online training program, "Family History for Cancer Risk Assessment, Testing and Management." Designed in partnership with the University of Connecticut School of Medicine and with the support of Maine Cancer Foundation, the course provides participating physicians with continuing medical education (CME) training in identifying patients at increased risk of a genetic syndrome, such as hereditary breast and ovarian cancer, who would benefit from earlier or more frequent cancer screening.

## EDUCATION COLLABORATION

Some of the most innovative JAX Genomic Medicine education initiatives — some in the planning stages, some already in progress — involve close collaborations with Connecticut educational institutions.

"We're working with Farmington High School to integrate genomics education into their biology curriculum," Litwin says. "This includes offering a genomics track for senior capstone projects. We're also in the planning stages of a possible genomics workforce initiative for community colleges, with training, hands-on research opportunities and a possible career path to technical and administrative jobs at JAX Genomic Medicine."

But naturally, JAX Genomic Medicine's key educational partner is the University of Connecticut. Since February 2012, when Yijun Ruan, Ph.D., became the first researcher to join the JAX Genomic Medicine faculty, the institution has operated temporarily in leased space on the UConn Health Center campus in Farmington, and the permanent JAX Genomic Medicine facility will open in October next to the Health Center itself. In the meantime, close working relationships have blossomed among JAX and UConn researchers.

At UConn's main campus in Storrs, a master's in science program now integrates JAX expertise and research opportunities. New professional science master's-degree programs in applied genomics and microbial systems analysis are designed for people interested in finding technical work in either of the two fields.

What differentiates the UConn program from a standard master's in science is a substantive workplace lab management component. "We try and educate these people as to what it would be like, for example, to be hired to be the lab manager of a research program, working for a principal investigator," says Michael Lynes, Ph.D., professor and head of the department of molecular and cell biology.

The program also offers training in new technologies, such as next-generation genome sequencing, for



To see a video clip and a photo gallery of Anu Mathur and Michael Stitzel, visit [www.jax.org/theseearch/genomed](http://www.jax.org/theseearch/genomed)

which expertise is a requirement for many jobs at JAX Genomic Medicine and at other academic research institutions and pharmaceutical and biotech companies.

"Working with JAX Genomic Medicine works out quite nicely for us," Lynes says, "because we have a growing need for internships, so that our students get workplace experience. And when the match is right between student and employer, many of these internships turn into professional jobs."

## THE LABORATORY CLASSROOM

Y

lunes has a connection to JAX that goes all the way back to his high school days, when he was a 1972 participant in the Summer Student Program in Bar Harbor, and he credits his JAX mentors with guiding him through graduate school and professional decisions throughout his career.

In 2013 the Laboratory offered the first Summer Student Program opportunities for high school and college students in the Farmington labs of JAX Genomic Medicine. This year UConn senior Haley Strassner of Avon,

Conn., is in the laboratory of Assistant Professor Duygu Ucar, Ph.D., and Glastonbury High School senior Anu Mathur of Glastonbury, Conn., is in Assistant Professor Michael Stitzel's lab.

Stitzel's lab had identified certain regulatory regions of DNA called stretch enhancers. Mathur says, "They most likely play a very important role in gene regulation and expression. This summer I'm studying a stretch enhancer in a particular gene that's associated with risk factors for type 2 diabetes, trying to determine what kind of transcriptional activity it has and what exactly it's doing to alter gene expression."

Because the program runs only 12 weeks, "Anu's project has to be small and finite," Stitzel says, "but it's actually an important piece in the overall work of our lab."

"For me it's been very impressive how well Anu, as young as she is, has grasped the concepts of our work and really understood them."

Mathur says she had learned in her high school classes about some of the technologies used in genetics research laboratories, such as DNA-amplifying PCR (polymerase chain reaction), but getting to use them was "ridiculously cool."

She adds, "After this summer, I know I want to study biology or biochemistry. This is definitely contributing to what I want to do in the future."

# Kathleen Corbet

## A giving profession



STORY BY BARRY TEATER  
PHOTOGRAPHY BY MARIE CHAO

As a teen growing up in Connecticut, Kathleen Corbet assumed she would pursue a career in one of “the giving professions,” just as her father, an educator, and her mother, a nurse, had done.

As college approached, she began eyeing a career in social work.

“But my father would have nothing of it,” Corbet recalls. “You have to go into business,” he insisted.

What profoundly good advice that would turn out to be, for Corbet and her family, and later for The Jackson Laboratory and other philanthropic causes she would support.

Corbet ended up studying marketing and computer science at Boston College and then earning a master’s degree in finance at New York University. She parlayed that business education into a globe-trotting career in finance, culminating with her appointment — at the relatively young age of 44 — as the first female president of the financial services company Standard & Poor’s, where she was responsible for 8,000 employees in 25 countries.

Today, at 54, Corbet is retired from the corporate life and runs her own consulting and investment firm, Cross Ridge Capital, which has invested in 10 different businesses. She works from her home in New Canaan, Conn., where she lives with her husband, Randy, and their two sons, Dylan, 19, and Ian, 18.

She spends much of her time these days giving back to the institutions and people who contributed to her successful career, and to other business, civic and philanthropic endeavors.

“I am so grateful for so many things that I have been able to achieve in my life,” Corbet says, “but I know it’s because of my connection to people. I feel so lucky that I’ve been blessed by family, by friends, by colleagues, and I’m just thrilled to continue my commitment to people.”

She has given to Crosby High School in her native Waterbury, Conn., where her late father, John Fruin, a former chemistry and physics teacher, was principal.

She helped Boston College close on a \$400 million capital campaign and launch another seven-year \$1.5 billion campaign as a member of the Board of Trustees.

She has served on the Board of Directors for Pro Mujer International, a nonprofit organization that provides healthcare support, business training, and micro-lending opportunities for Latin American women trying to escape poverty.

She serves on the Board of Directors of MassMutual Financial Group, chairing its Audit Committee.

Last fall she was elected to a four-year term on the Town Council in New Canaan, Conn., a town of 20,000 people in Fairfield County.

And she has served on The Jackson Laboratory’s Board of Trustees since 2009.

“The Jackson Laboratory is extraordinarily fortunate to have Kathleen on our Board of Trustees,” says Edison Liu, M.D., president and CEO of the Laboratory. “Her expertise in business and finance, her willingness to ask tough questions and to embrace innovative approaches, and her unwavering belief in the Laboratory’s potential to transform human health make her an outstanding trustee and champion for our mission. On top of that, she is an absolutely wonderful person and a good personal friend.”

Corbet chairs the Board’s Advancement Committee, responsible for guiding the Laboratory’s fundraising and communications.

“Kathleen brings a powerful combination of thoughtfulness, insight and passion to her leadership of the Advancement Committee,” says Kristen Rozansky, the Laboratory’s vice president for development and communications. “Her commitment to our mission, coupled with her deep understanding of the importance of philanthropy, has been vital to our success in building support.”

Corbet was recruited to the Laboratory’s Board by one of her mentors, Brian Wruble, who chaired the Board from 2007 to 2011 after his own successful career on Wall Street. Corbet met Wruble when she was only 25 and worked for the company he led, Equitable Capital Management Corp. She quickly impressed him not only with her analytical prowess but her warm personality and ability to lead, develop and nurture employees.

“I’ve had probably 2,000 employees over the years, and I’ve always identified her as the single most talented person who ever worked for me,” Wruble says. “She’s really that good. She’s smart, she’s optimistic, she’s relentlessly logical, and she’s nice to everybody. People who worked for her absolutely loved her. They were more productive than they would have been working for anybody else.”

Corbet’s business, political and people skills have not only proven invaluable for the Laboratory’s fundraising, but for its expansion into her home state with the recent establishment of The Jackson Laboratory for Genomic Medicine in Farmington.

When Gov. Dannel Malloy began courting the research facility in 2011 as a centerpiece of his economic development plan for biomedical research, Corbet helped assess the Laboratory’s opportunities and challenges in Connecticut.

“Kathleen was a supportive voice for this project,” says Mike Hyde, the Laboratory’s vice president for external affairs and strategic partnerships. “She knows the state well, and she has the confidence of the Malloy administration. She is an astute observer of the political scene in Connecticut. She was a big help.”

Corbet says having the opportunity to help JAX Genomic Medicine partner with the state of Connecticut, the University of Connecticut, Yale University and various hospitals is gratifying.

“I love when I can help match the interests of one group with the needs of another,” she says. “I am thrilled to play a small part in that. I couldn’t be prouder.”

**“I love when I can help match the interests of one group with the needs of another.”**

As JAX Genomic Medicine prepares for its grand opening on Oct. 7, Corbet is bullish on its prospects for success, for the same reason she committed to the Laboratory in the first place: its people.

“I’m very proud of the leadership of the Lab,” she says. “Attracting Ed Liu from Singapore, that really got us started. There’s no question that we are recruiting among the top research scientists not only in the U.S. but from throughout the world, and that’s what makes me confident.”

# 5 questions



**Joshy George, Ph.D.**

**Computational Scientist**

The Jackson Laboratory for Genomic Medicine

**Q** *What was your career path to JAX?*

**A** I did my undergraduate and master's degree in electronics and communication engineering in India, and worked in signal processing and machine learning algorithms in several research organizations in India and Singapore. In 2003 I learned that several of the methods used in speech and image processing have applications in biology and was lucky to get an opportunity to work at the then newly started Genome Institute of Singapore [founded by JAX President and CEO Edison Liu, M.D.]. I found the field fascinating and moved to the Peter MacCallum Cancer Center in Australia to do my Ph.D. in ovarian cancer genomics. I worked in the research division there for seven years before I joined JAX Genomic Medicine in August 2013.

**Q** *Why did you want to work at JAX?*

**A** I believe that The Jackson Laboratory is uniquely placed to play a major role in personalized medicine, and I consider myself very lucky to be a part of this team.

**Q** *What is computational biology, and why is it important?*

**A** Computational biology is the application of computer science, mathematics and statistics to solve problems in biology. On a practical level a computational biologist is someone who makes use of techniques from different fields like machine learning and algorithm design to solve problems in biology.

Experiments to understand biological processes generate vast amounts of data. Computational biologists help to transform these raw data into biologically meaningful information and ideally should be involved in all aspects of the study, starting from the design of experiments.

**Q** *What projects are you working on right now?*

**A** I work as a computational scientist in the Computational Sciences – Statistics & Analytics group and do research in collaboration with several faculty members. My current projects include computational methods to estimate the genetic, epigenetic and transcriptional profiles of cells involved in diabetes, cancer and autoimmune diseases.

I also coordinate the efforts to characterize the genome of patient-derived xenograft (PDX) models developed at JAX. PDX models are essentially human tumors engrafted in immunodeficient mice and are excellent models to study therapeutic response to cancer. We assess the genomic mutations and gene-expression profiles of these tumors using next-generation DNA sequencing technology.

**Q** *What do you like most about your job?*

**A** The most interesting point about my job is its great variety. Every project involves the study of a new aspect of biology, and that is intellectually very stimulating. It is really fun to be part of a group of scientists who are very enthusiastic about their research.

# beyond the news

## CANCER IMMUNOTHERAPY TAKES CENTER STAGE



"It is really great to be in this field right now," JAX Professor Karolina Palucka, M.D., Ph.D., says, her excitement almost palpable.

Certainly, others at The Jackson Laboratory and beyond share her enthusiasm.

As a symbol of the turning tides in cancer immunotherapy, Palucka recalls the annual meeting of the American Society of Clinical Oncology, held each year to review and discuss progress in cancer treatment and research. As recently as a few years ago, cancer immunotherapy made a relatively minor showing. But last year and especially this year, the topic took center stage, with a number of talks featured in the meeting's plenary sessions.

"Cancer immunotherapy has really undergone a revolution in the past couple of years because finally, after so many years of hard work from many scientists, many talented people all over the world, we have a couple of drugs that interfere with T-cell function and that bring spectacular clinical responses," says Palucka.

She is referring to a new generation of drugs in particular that unleash the immune system, essentially freeing it to destroy cancer cells.

The exquisite design of the human immune system includes a number of internal checkpoints — safeguards that prevent it from running amok and attacking healthy tissues. Tumors can exploit these checkpoints, so immune cells, such as

dendritic cells and another type known as T-cells, are unable to rally against the disease. Newly developed drugs disable these checkpoints and are yielding some remarkable results in patients.

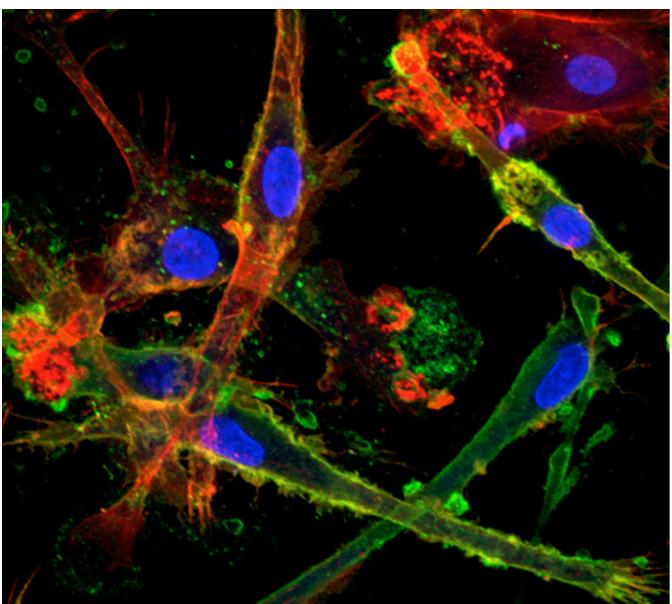
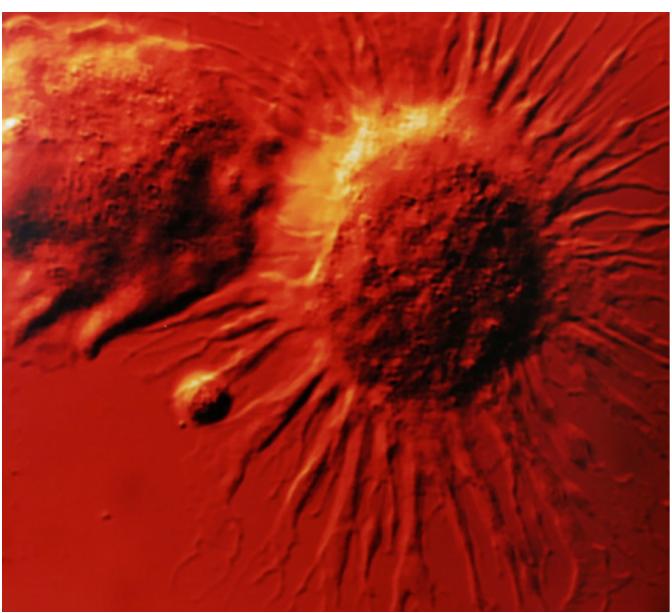
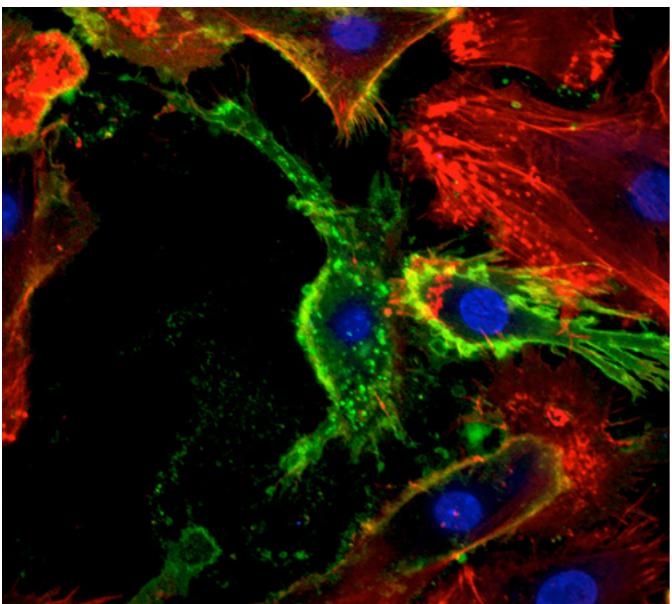
Ipilimumab (marketed as Yervoy®) targets a protein called CTLA-4, and was approved in 2011 for use in metastatic melanoma. The good news is that in some cases, the drug is able to blot out cancer for years — so far, up to 13. The bad news is that only a small percentage of patients see such lasting effects and the drug's side effects can be quite severe.

Just as these results were coming to light, another type of drug, with takes aim at a different checkpoint protein called PD-1, was also emerging. Such PD-1 inhibitors (which include nivolumab and MK3475) could be approved for use later this year. Early results are encouraging, and it appears the drugs can benefit not just patients with melanoma, which is known to rouse the immune system, but also other hard-to-treat cancers, such as lung.

"I think this is really what turned the tide because people said, 'Wow, nobody ever imagined lung cancer would be a tumor for immunotherapy,'" says Palucka.

While much more work remains to understand why some patients benefit and others do not, these new checkpoint drugs signal a real coming of age for the field of cancer immunotherapy. Remarkably, there have been other recent signs of progress.

Dendritic cells, like the one shown here, play a crucial role in the immune system. They are named after the Greek word, *dendron*, for tree, because of their branch-like projections. JAX researchers are uncovering ways to harness dendritic cells' power to treat a range of diseases, including cancer.



### STAINS



**YELLOW** — highlights key immune molecules that are involved in recognizing and presenting foreign substances to other immune cells



**GREEN** — marks key immune molecules, called MHC class II that recognize and present foreign substances to other immune cells



**RED** — marks a structural protein found in many different cells



**BLUE** — denotes nuclei, the cellular compartment that houses the genome



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Window overhangs at JAX Genomic  
Medicine filter light and cast  
complex geometric shadows.

*Photograph by Marie Chao*