SEARCH

HIDDEN IN THE SKIN

CLOSING THE GAP • A NEW SMA DRUG

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SEARCH

ON THE COVER

Assistant Professor Julia Oh, Ph.D., believes the possible role of the microbiome in cancer is an intriguing area for research. The microbiome consists of the fungi, viruses and bacteria (such as Staphylococcus, shown above) living on and in us.

The Jackson Laboratory
Leading the search for tomorrow's cures

FEATURES

DEPARTMENTS

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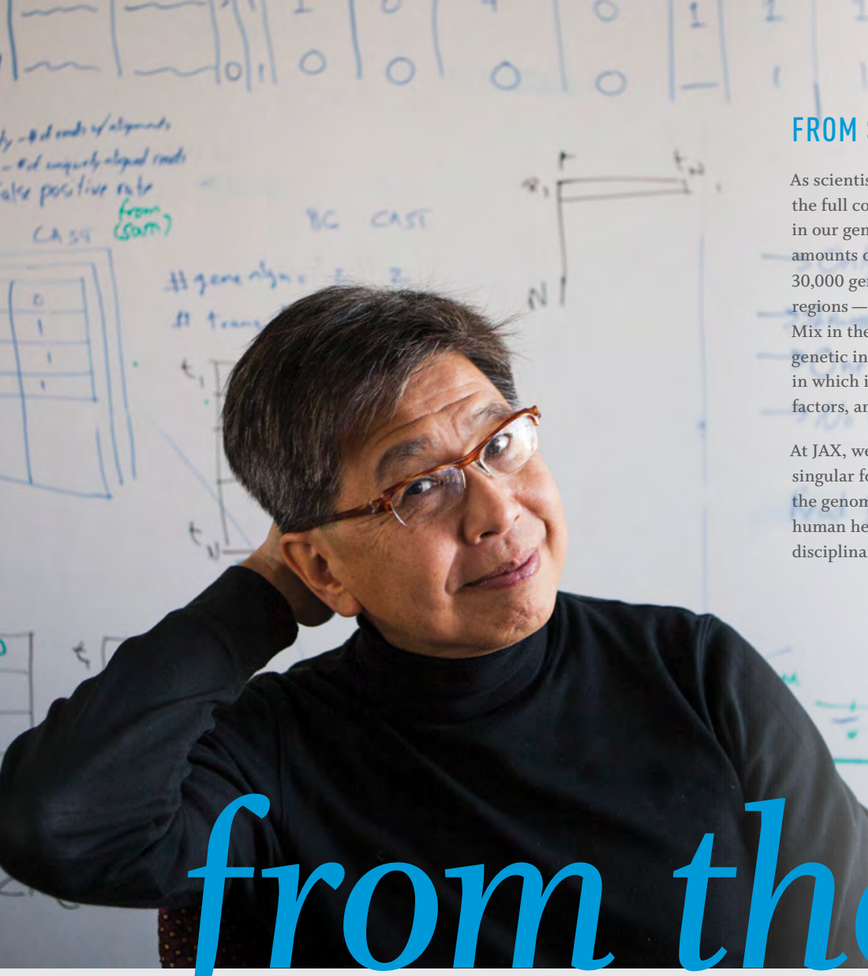

from the President

FROM SEQUENCES TO SOLUTIONS

As scientists, we are still in the process of discovering the full complexity of the information contained in our genetic material. The genome contains vast amounts of data, not just in our approximately 30,000 genes but also in the non-coding regions — the so-called "dark matter" — of our DNA. Mix in the added dimensions of variability in how genetic information is expressed and the many ways in which it interacts dynamically with external factors, and the picture becomes even more complex.

At JAX, we are the masters of complexity. With a singular focus on understanding the workings of the genome and using that knowledge to improve human health, our scientists bring a wide array of disciplinary focuses to bear upon that challenge.

From identifying variations in how genes are coded and expressed, to creating powerful computational tools and mouse models of disease, to looking beyond the human genome to focus on our microbiome, we are leading the search for cures on many genomic frontiers. As this issue of *Search* highlights, JAX science is playing a vital role in the progress on many rare and orphan diseases — and also generating promising breakthroughs for common conditions like glaucoma, the leading cause of blindness.

Our capacity to collect, analyze and interpret genomic data on a large scale — coupled with the ability to employ that same information to refine models of disease and then use those models for clinical testing — is what will ultimately enable us to develop genomic solutions for disease.

The story of Spinraza, a promising new therapy for spinal muscular atrophy (SMA), highlights the potential of JAX science to lead to cures.

JAX's role in identifying a possible treatment for a devastating disease like SMA is not an isolated case. It is just one example of what we can accomplish as we accelerate discovery with the support of those who share our vision.

In fact, you could say it's just the beginning.

Edison Liu, M.D.
President and CEO, The Jackson Laboratory

did you know?

More than 350 million people worldwide are affected by rare diseases. By definition, a rare disease is one that affects fewer than 200,000 individuals in the United States, and many of these diseases have devastating outcomes for patients and their families. Few drug companies invest in rare disease research, which slows the discovery of potential therapies.

Through its Rare and Orphan Disease Center, JAX works closely with foundations and scientists from around the world to facilitate research.

This research includes developing and sharing new mouse models that carry genetic mutations analogous to those of patients, enabling clinicians to study disease processes and test new, targeted therapeutics. On page 20, you can read about how one such mouse laid the foundation for the successful clinical trials of a new spinal muscular atrophy drug, Spinraza.

connect with us

PHOTOGRAPHY BY GRETA RYBUS

EMPOWERING YOUNG SCIENTISTS AND ENGINEERS

More than 200 students from 26 Maine high schools competed for coveted state titles and approximately $840,000 in scholarships March 25 at the 71st annual Maine State Science Fair.

The top prize went to Seung Heon Song of Gould Academy for his project, "Smart road signs." Finishing second and third, respectively, from Bangor High School were Sydney McDonald and Lily Waddell. These winners went on to represent Maine at the prestigious Intel International Science and Engineering Fair in Los Angeles in May.

The event, which was organized by The Jackson Laboratory and the Reach Center of the Maine Mathematics and Science Alliance, and held at Colby College, enabled Maine high school students to demonstrate their original science research and engineering projects.

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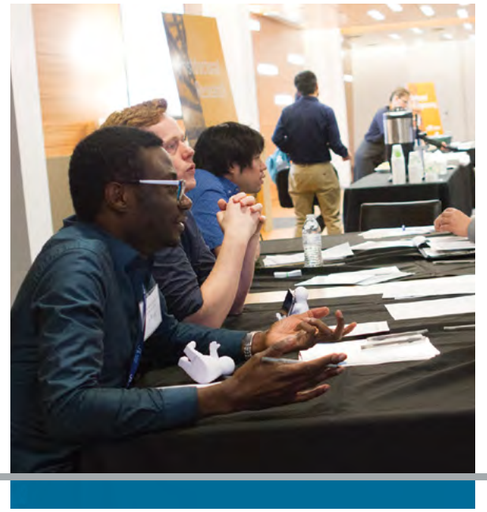


ON A MISSION TO HIRE

The drive to advance precision medicine at JAX Genomic Medicine in Farmington, Conn., began in 2014. To continue the momentum, JAX is hiring more than 60 genomic researchers, computer scientists, engineers and administrators to join the team.

On March 28, hundreds of people attended a career forum and open house for scientists and professionals interested in opportunities at JAX. Within the next few years, discoveries at JAX will not only advance personalized medicine, but will continue to grow Connecticut's bioscience industry.

FOSTERING STEM EDUCATION

On March 29, JAX Genomic Medicine opened its doors so parents, educators and students from grades 6 to 12 could learn about the exciting research happening there. JAX scientists gave engaging presentations about the newest breakthroughs in genomics research and precision medicine. They also shared with students how they can best prepare themselves to pursue careers in science and technology. The talks covered the following topics:

- Microbiome: The hidden world inside our bodies
- Cancer: Your genes and cancer progression
- Genome editing technologies: CRISPR is the Photoshop for DNA
- Computational biology: Decoding the human genome
- 4-D genomics: How do chromosomes interact in space and time?

PHOTOGRAPHY BY AARON BOOTHROYD & JARED SKOLNICK

Pete Williams

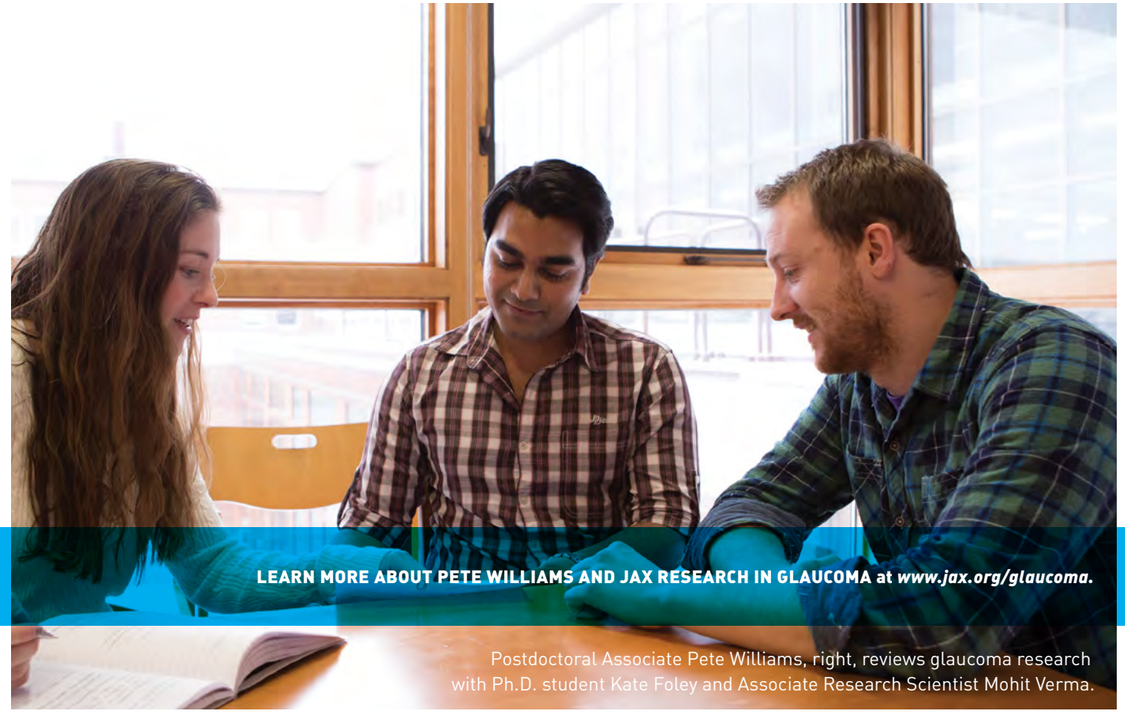
BY CARRIE COWAN, PH.D. | PHOTOGRAPHY BY TIFFANY LAUFER

Protecting the optic nerve from damage caused by glaucoma would offer hope to patients suffering from gradual, irreversible vision loss.

As the optic nerve passes from the eye to the brain, its individual axons run through a meshwork made out of semi-flexible fibers. Normally, when the meshwork isn't under stress, the axons pass cleanly through its pores. But pressure, such as the increased ocular pressure that is a hallmark of glaucoma, bows this network, causing the pores to deform and pinch the axons within the optic nerve. Once the nerve is damaged, it's impossible to repair.

Pete Williams, Ph.D., wants to change that. Working as a postdoctoral associate in the research lab of JAX Professor and Howard Hughes Medical Institute Investigator Simon W.M. John, Ph.D., Williams is focused on identifying the genetic processes that contribute to optic nerve degeneration.

New research from Williams and John, published in the journal *Science*, found that simply adding vitamin B3 to the drinking water of mice that are genetically predisposed to glaucoma proved to be effective at preventing the disease. This research offers promise for developing inexpensive and safe treatments for glaucoma patients.



LEARN MORE ABOUT PETE WILLIAMS AND JAX RESEARCH IN GLAUCOMA at *www.jax.org/glaucoma*.

Postdoctoral Associate Pete Williams, right, reviews glaucoma research with Ph.D. student Kate Foley and Associate Research Scientist Mohit Verma.

HIDDEN IN THE SKIN

BY NICOLE DAVIS | PHOTOGRAPHY BY TIFFANY LAUFER | ILLUSTRATION BY KAREN DAVIS & DANIELLE MEIER

Julia Oh, Ph.D., probes the depths of human skin to characterize the microbial communities that contribute to health and disease.

Did you shower this morning? Wash your hands before lunch? If so, chances are you effectively rinsed away the dirt and microbes clinging to your skin's surface. But before you breathe a sigh of germ-free relief, consider this: even the most vigorous washing is unlikely to hinder — much less remove — the assortment of bacteria, viruses, fungi and other microscopic organisms that reside deep within your skin. This microbial menagerie, often referred to as the skin microbiome, is increasingly recognized both for its resilience as well as for its abilities to maintain health and, sometimes, incite disease.

"The skin microbiome is really remarkable," says Julia Oh, an assistant professor at The Jackson Laboratory (JAX). "It is constantly being repopulated and yet, across different body sites, we see that healthy individuals' skin microbiomes are quite stable in composition. That's surprising considering how exposed the skin is — to the environment and to other people."

Although it is tempting to imagine it as one uniform system, the skin is actually a patchwork of many varied environments, each with distinct conditions. Facial skin is typically oily, while the forearms are dry. Feet, tucked inside socks and shoes for most of the day, are often damp and sweaty. Such differing ecologies attract and support the growth of unique microbial communities.

One of the first detailed views of these communities emerged as part of the Human Microbiome Project, a sweeping, five-year effort to catalog the microbes living throughout the human body. In June 2012, the consortium published a flurry of papers that described the results of a broad microbial census involving nearly 250 healthy volunteers. It spanned various body sites, including the skin behind the ears and along the inner crease of the elbows. Oh sees great potential in these types of studies, not only for enabling scientists to understand more about the tiny passengers that reside in skin, but also to lay the groundwork for deep, mechanistic studies that will guide the development of innovative microbial-based treatments for a variety of skin conditions, including psoriasis, eczema and cancer.

Though she started her laboratory at JAX less than two years ago, her team has already blazed bold new trails in microbiome research. Recently, Oh and her colleagues took a careful look at the dynamics of the skin microbiome. As published in *Cell*, they examined how the number and diversity of skin microbes change over time, both short periods (months) and long periods (years). Called a tour de force by experts in the field, the work helps illuminate the astonishing stability of the skin's bacterial, viral and fungal inhabitants. Moreover, it suggests that the unique makeup of skin microbiomes in healthy individuals can be regulated by biological factors, such as genetics, immune health, skin physiology and skin health, as well as environmental factors like hygiene.

Communities and collaboration

Oh remembers the precise moment when her interest in the microbiome emerged. She was roughly midway through her graduate work in Ronald Davis' lab at Stanford, when a colleague presented the results of a recent research paper about the microbes in soil. "That paper just blew my mind," she recalls. "I didn't really think of microbes as living in complex communities. E. coli, Saccharomyces cerevisiae, those were the model organisms I worked with — and naively, how I thought they existed in the world."

Indeed, some of the early tools for exploring microbial communities were first honed through studies of soil and seawater. Perhaps the most critical tool is genomic sequencing. "The application of sequencing technology to this problem was just so elegant. I was utterly captivated," says Oh. With rapidly falling costs and increasing throughput, examinations of other microbial worlds soon became feasible.

Now, in her lab at JAX, Oh is leveraging these tools and many others to their full capacities in order to reveal the biology of the microbiome. One question that particularly intrigues her: How do microbes interact with and help shape the immune system? To answer it, she has launched several collaborations with fellow scientists, including Derya Unutmaz, a JAX professor and immunologist. Together, they are exploring how and when different microbes signal the immune system, and vice versa. By listening to these conversations, Oh, Unutmaz and their colleagues may uncover ways to interrupt or possibly even mimic them, with the goal of thwarting disease.

The researchers recently completed one of their first projects and are already preparing the results for publication. They also expanded their work by recruiting another key collaborator, Bruce Strober, who leads the department of dermatology at UConn Health.

"It's a fantastic collaboration," says Unutmaz. "Julia is one of the best collaborators I've ever had."

> *"Although we might think we know all the species that are present in the skin microbiome, we really don't."*
>
> – Julia Oh

In addition, Oh is turning her attention to another facet of the microbiome, but this time her focus is on the gut. Like the skin, the gut has many meters of surface area, each inch having an intimate interaction with its local microbiota. The gut microbiome is well known for its role in digestion, allowing the body to extract nutrients from substances that it otherwise could not. "What hasn't been fully appreciated is that the microbiome can also have very profound, indirect effects on how quickly our body can develop diseases like cancer, but also on how powerfully we respond to different therapeutics that act through the immune system," explains Oh. "What we want to know is, does that also include the checkpoint inhibitors?"

Checkpoint inhibitors target the immune system's internal safeguards (or "checkpoints") that help prevent immune cells from running off the rails and attacking healthy tissues. Cancer cells can hijack these checkpoints, enabling tumors to grow without restraint. In the last few years, it has become clear that checkpoint inhibitors can bring about dramatic remissions in some cancer patients, but for others, the drugs are ineffective, particularly in certain forms of breast cancer. Oh and her colleagues want to figure out why, and whether or not some of the blame lies with the gut's microbes. If true, the idea could spark new approaches to help augment or boost the effectiveness of checkpoint inhibitors and possibly other types of drugs.

Microbial dark matter

Although the picture of the skin microbiome that Oh and others are painting is vivid and compelling, the view is far from complete. "Although we might think we know all the species that are present in the skin microbiome, we really don't," says Oh. "We have a relatively limited understanding of the skin's biodiversity."

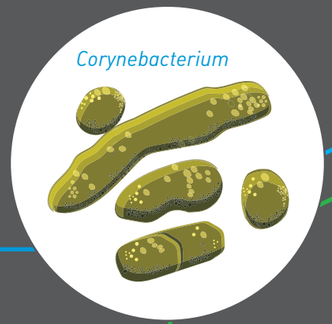
Oh's recent study published in *mBio* helps illustrate this point. She and her colleagues harnessed a sequencing technology known as single-molecule sequencing. Unlike other methods for decoding the genomes of diverse microbial communities, this approach reads DNA as one long thread, instead of thousands of short fragments. The advantage is that previously unidentified microbes can be more readily found. "This is the microbial dark matter — the microbes living in and on us that go undetected."

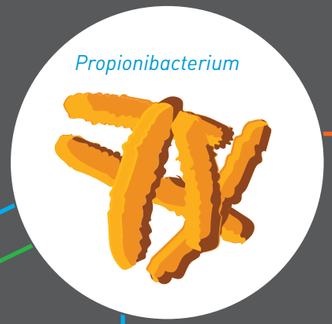
Using single-molecule sequencing to probe the skin microbiome of just one person, the researchers identified a species of bacteria that had not been previously characterized. Remarkably, the bacteria, known as *Corynebacterium simulans*, appear to be restricted to the skin on the foot, including the toe web, toenail and heel. Moreover, in this particular individual, *C. simulans* accounted for the majority of the microbial dark matter within the foot microbiome — roughly two-thirds, all told. By developing additional computational approaches to help identify microbial dark matter, Oh and her lab believe that other types of *Corynebacterium* may also account for a significant portion of the undetected microbes living on the foot and other skin sites across different individuals.

She envisions many similar advances in microbiome research yet to come, stemming from innovations in technology and computational methods, as well as experimental approaches. "There are just tremendous opportunities," Oh says. "I'm excited about the work we and others are doing."

the skin microbiome

"Germs," the invisible carriers of disease and infection, have long had a bad reputation. But we now know that we coexist with trillions of them in relative harmony. The relationship is largely mutually beneficial. Bacteria in our gut help us absorb vitamin K and break down otherwise indigestible carbohydrates. Bacteria in our skin and nose block pathogenic species from colonizing us and speed up the healing process when the skin barrier is breached. In return, we provide them a safe haven, with adequate food and a temperature-controlled environment.

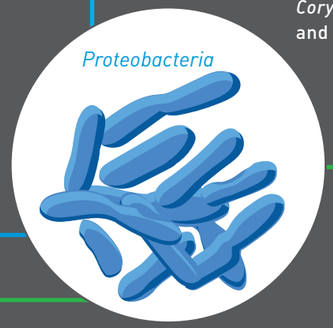


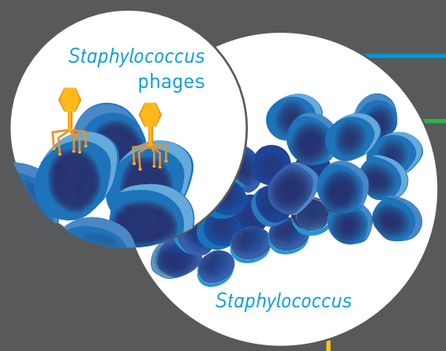


Oily sites such as the forehead, back, etc., are home to *Propionibacterium*, one of the most common bacteria found at any skin site on adults.

Dry sites like the forearms and palms contain a mixture of *Propionibacterium*, *Corynebacterium*, *Streptococcus*, *Proteobacteria* and *Staphylococcus*.

Moist sites, including creases of elbows and knees, groin and feet have a mixture of *Propionibacterium*, *Corynebacterium*, *Proteobacteria* and *Staphylococcus*.





In a class by itself, the toenail is dominated by *Staphylococcus* and *Staphylococcus* phages.

LEARN MORE ABOUT THE MICROBIOME at *www.jax.org/microbiome*.

CLOSING

Zhengqing Ouyang

Assistant Professor Zhengqing Ouyang, Ph.D., is pioneering new ways to sort through the "big data" in genomics, casting light on some of the most important — and previously overlooked — aspects of the human genome.

THE GAP

BY NICOLE DAVIS | PHOTOGRAPHY BY MARIE CHAO

With mind-blowing speed, it is now possible to read the information that lies embedded within the human genome. Yet translating this information into meaningful knowledge, lending insight into how cells develop and how the human body is made vulnerable to disease, requires statistical and computational methods that are just as powerful as the genome sequencing technologies themselves. This is the challenge of the emerging field of genomic data for scientists like Ouyang — to make sense of the genome's "big data" and to blow open the bottleneck that separates technological speed from analytical might.

"The speed of data generation has increased tremendously in the past 15 years, but the way we process and analyze these data has not kept pace. There is a real gap."

– Zhengqing Ouyang

Ouyang aims to close this gap. Based at the JAX Genomic Medicine facility in Farmington, Conn., his laboratory is developing statistical and computational methods that help interpret the data flowing from genome sequencing as well as other genome-scale technologies.

One of the strengths of Ouyang's quantitative approach is the ability to co-opt tools and methods that have been successfully applied to other problems, even those outside of biomedicine.

By developing and applying these models, and many others, to big questions in genomics, Ouyang hopes to realize a bold vision: to unlock the biological basis of how cells in the body work and what predisposes them to disease. And, just as meteorologists collect measurements of different variables in the atmosphere to develop climate models and forecast the weather, Ouyang and his colleagues gather various measurements from thousands of locations within the genome to create models that help predict how key parts of the genome function.

Visit ***www.jax.org/closethegap*** to learn more about how Ouyang and his colleagues are attacking some of the thorniest questions in genomics.

BARCELONA, SPAIN

SEOUL, SOUTH KOREA

> "Supporting the growth of human genomics research internationally is a core piece of HUGO's mission, and there's far more to be done in this area."
>
> – Charles Lee

Moving forward with human genomics

BY MARK WANNER | ILLUSTRATION & PHOTOGRAPHY BY JANE CHA

Charles Lee, Ph.D., FACMG, professor and scientific director at The Jackson Laboratory for Genomic Medicine, began his term as president of the Human Genome Organisation (HUGO) at the annual Human Genome Meeting in early February in Barcelona, Spain.

He assumes the presidency at a time when genomic data is piling up and clinical implementation of genomics is becoming a reality. As a result, it is important to address many issues associated with genomics and precision medicine now rather than someday in the future. After a meeting packed with impressive science and compelling presentations, Lee contemplated HUGO's place in global research and clinical communities and its value moving forward.

"I would like to expand our outreach and support to more regions around the globe," Lee says. "Supporting the growth of human genomics research internationally is a core piece of HUGO's mission, and there's far more to be done in this area."

Lee says it's of particular importance to expand the populations represented in genomic databases. Today the data are mostly from populations of European origin, and acquiring large amounts of data from patients and healthy people in Africa, Asia and the Middle East is becoming increasingly vital to correctly assess and annotate disease variants.

"We've seen several examples of a rare genetic variant being incorrectly correlated with disease in one population, only to find out later that it's relatively common in healthy individuals from another population," Lee says. "Having better representation from a wide range of people will increase the effectiveness and expand the value of clinical genomics worldwide."

Lee believes that bringing genomics researchers together from all corners of the globe could foster collaborative projects and build an environment to encourage data sharing and access.

"The sequencing of the first human genome was a huge achievement, but a single genome tells us relatively little about human genome diversity, which has long been my personal area of research interest," Lee says. "To get at the difficult questions regarding disease variants, complex diseases and more, we need to gather many thousands or even millions of genomes for analysis. There are efforts under way to do just that, but it will certainly take more than a village to make it happen."

Our mouse model paved the way for a new SMA drug

BY JOYCE DALL'ACQUA PETERSON | PHOTOGRAPHY BY AARON BOOTHROYD

Picture a tiny baby in his crib. You'd expect him to be waving his arms and kicking his legs at the sight of his mother, but his arms are flopped by his side, and even turning his head to look at her is too much effort for him.

The leading genetic cause of death in infants and toddlers is a disease you may never have heard of: spinal muscular atrophy or SMA, a neuromuscular disease characterized by muscle weakness and atrophy.

In type 1 SMA, the most severe form of the disease, babies show symptoms by six months of age, and rarely survive past their second birthday. Onset of milder forms of the disease is much later, even in adulthood. In all, up to 25,000 Americans have SMA, making it one of the least rare of rare diseases.

But now there's hope for even the tiniest, most vulnerable SMA patients.

In December, following successful clinical trials, the U.S. Food and Drug Administration approved the first drug to treat children — even newborns — and adults with SMA: nusinersen, produced by the Biogen pharmaceutical company as Spinraza. The FDA approval came after a successful clinical trial, demonstrating improved motor function in infants who were diagnosed with SMA before 6 months of age and who received their first injection of Spinraza when they were less than 7 months old. Remarkably, children who normally would have succumbed to their disease were not only alive but reaching major developmental milestones.

And before the drug trials in patients, research using mouse models provided the essential foundation of knowledge of the mechanisms of SMA.

Thirteen years ago, the SMA Foundation asked The Jackson Laboratory (JAX) to distribute mouse models of the disease to the biomedical research community. And over the past decade, work by JAX researchers in SMA has led to a new approach to modeling genetic diseases that could pave the way to many other breakthrough treatments.

"My lab started focusing on SMA research," says Cat Lutz, Ph.D., director of the JAX Rare and Orphan Disease Center, "to find out what was needed to understand the disease in all its forms, from the lethal, early-onset type 1 to the less severe types 2 and 3, which are more common in the population because the patients survive longer."

SMA is caused by defects in the SMN1 gene, which encodes the SMN protein. The SMN protein is critical to the health and survival of the nerve cells, known as motor neurons. Loss of motor neurons in the spinal cord and lower brain stem results in progressive muscular atrophy, in the most severe cases resulting in paralysis and loss of the ability to breathe or swallow.

IMAGE BY TONGRO IMAGES INC. VIA THINKSTOCK BY GETTY IMAGES

Senior Research Scientist Cat Lutz and her team primarily focus on developing preclinical mouse models of neurodegeneration to test therapeutics and inform clinical trials.

LEARN MORE ABOUT THE RARE AND ORPHAN DISEASE CENTER AT THE JACKSON LABORATORY at *www.jax.org/raredisease*.

SMA patients do not produce enough SMN protein, and the less SMN protein they produce, the more severe the disease. Moreover, disease severity also depends on the patient's level of a second gene, SMN2, which somewhat compensates for faulty SMN1 function. As a result, SMA disease prognosis depends on how many copies of SMN2 are present. Two or fewer copies of SMN2 leads to earlier onset, more severe disease, while three or more copies provide enough function to result in a later-onset, milder form of SMA.

"It was clear that if we could restore levels of SMN protein in patients with SMA," Lutz says, "we could reduce the severity of the disease, but it was not clear exactly when SMN should be administered."

In 2011, Lutz, working with Umrao R. Monani, Ph.D., and colleagues at Columbia University, researchers at Regeneron Pharmaceuticals Inc., and the SMA Foundation, reported in the *Journal of Clinical Investigation* on a new mouse model that opened up a therapeutic path for the disease.

"Our special model of SMA allowed us to investigate the effects of turning on SMN expression at different time points during the course of the disease," Lutz explained at the time the paper was published. "We found that restoring the SMN protein even after disease symptoms appeared increased the survival of the mice and slowed down disease progression."

The researchers had also discovered that for the best effect, early administration of the SMN protein works best. "There was a therapeutic 'window of opportunity' during which the type 1 mice responded best to the SMN treatment," Lutz says. Mice treated later, after symptoms appeared, showed some improvement, but those treated after substantial neurodegeneration had already occurred failed to show therapeutic benefit. The Lutz lab went on to develop another model of SMA; in this case the mouse was representative of a type 2 patient. Encouragingly, the mice again showed benefit in response to treatment and again, the earlier the intervention, the better the outcome.

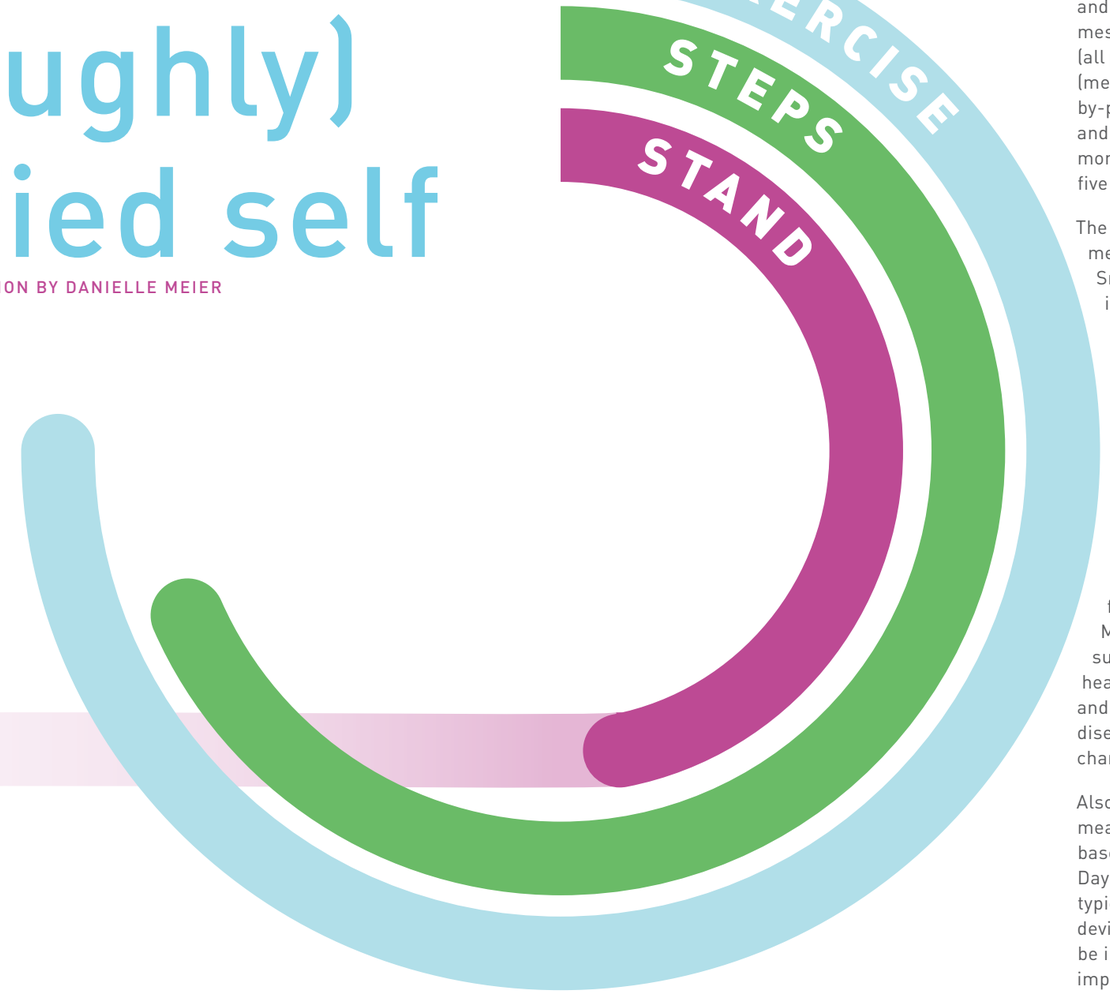
This work with a mouse model of SMA by Lutz and her colleagues laid the foundation for the successful clinical trials of Spinraza.

"A colleague once asked me why I was working so hard on a rare disease like SMA to benefit so few patients," Lutz recounts. "The fact is, all the things we learn from these rare and orphan diseases will be applicable to Parkinson's, Alzheimer's and other diseases with bigger patient populations.

"And when you see kids with SMA actually walking and playing, who without treatment probably would not even be alive, that's why we work so hard," she says.

The (thoroughly) quantified self

BY MARK WANNER | ILLUSTRATION BY DANIELLE MEIER



On the path to precision medicine, mice make great experimental subjects, in part because researchers can work with them in, well, very precise ways. They can measure everything about them, even monitoring them 24/7 in special cages. They can choose the variables between mice, or mouse populations, including genetics and environment. The biological insights gained provide the foundation for tailoring therapeutics to individuals.

But how do we translate that insight to humans? How can we be precise about our medicine when everything — genetics, environment, behavior — varies between each person all the time? How can we get our arms around the messiness of our own environments, behaviors and conditions so we can use data from our genomes to best effect?

Stanford University's Michael Snyder, Ph.D., thinks he may have the answer. Snyder made waves several years ago when he took the "quantified self" concept to new frontiers, measuring close to as much about himself as possible at that time. Metabolism, blood chemistry, activity — hundreds and hundreds of data points a day tracked the minutiae of his life and yielded some interesting findings. Now he is widening the scope of the research.

Snyder's lab is working with 100 healthy volunteers who agreed to provide even more measurements, including a deep dive into their genome sequences. They also gather data continually with wearables and smart phones, including activity and metabolism. In addition, Snyder and his team are looking at as many molecules as they can in blood and urine: the transcriptome (all messenger RNA), the proteome (all proteins), the metabolome (metabolic compounds and by-products), antibody profiles and so on. Finally, they're monitoring the microbiome at five sites in and on the body.

The healthy volunteer measurements add up to what Snyder calls the iPOP, or individual personal 'omics profile. In all, the project will amass billions of measurements over time. The early returns are intriguing. So far almost 70 subjects have had their genomes thoroughly analyzed, and 11 had gene mutations or variants that merited an even closer look, a much higher frequency than anticipated. Most involve higher susceptibilities to cancer, heart disease, type 2 diabetes and other common, complex diseases, and have led to some changes in their medical care.

Also of note, the constant measurements add up to a baseline of normal function. Day by day people learn what is typical for them, which means deviations from the norm can be informative and, at times, important. For example, Snyder can tell who took a trip in a plane just by their blood oxygen levels, which dip during flights before recovering to normal after. He himself once flew to a conference and felt abnormally fatigued after. His oxygen remained very low and his heart rate elevated, so instead of chalking it up to bad jet lag, he went to a doctor and found he had Lyme disease. With constant measuring it was unmissable, but without the data he would have likely tried to soldier through, at least at first.

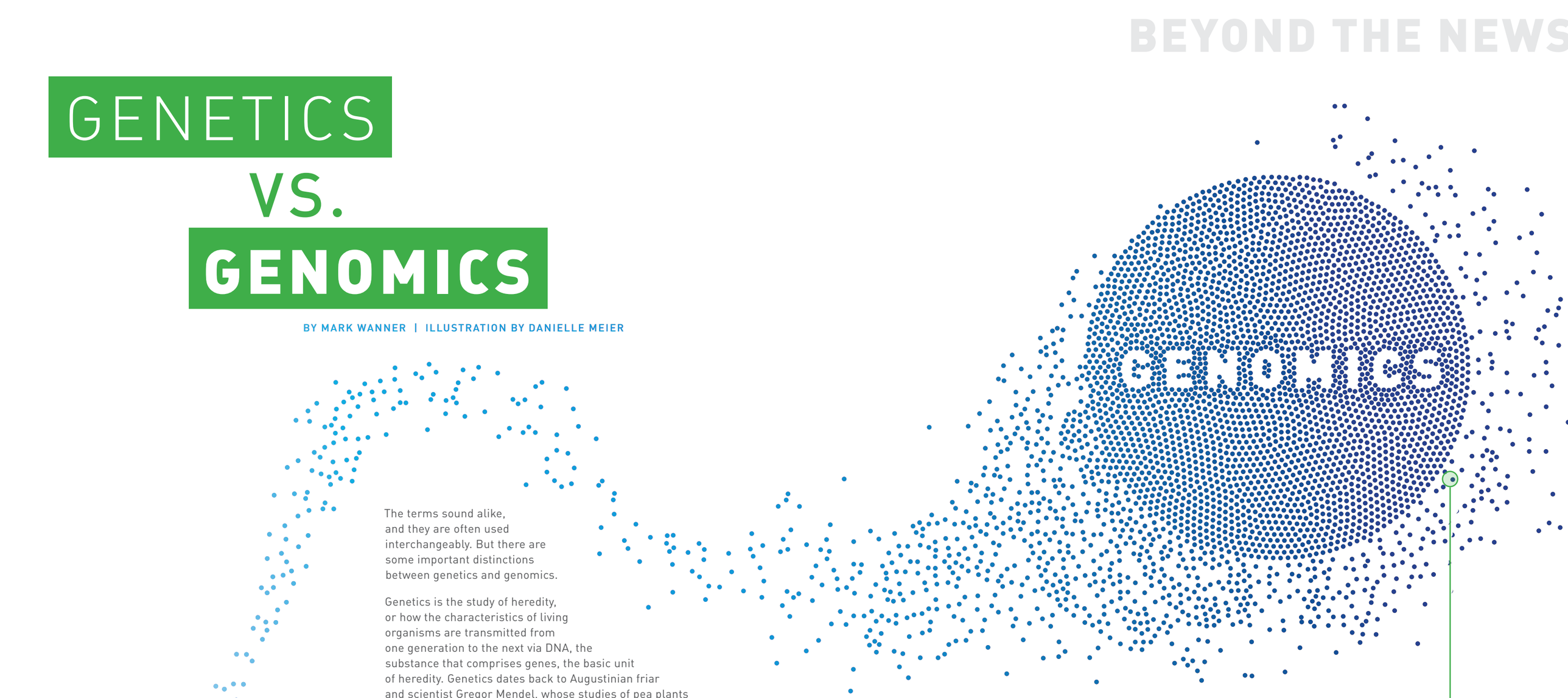
There are also related, but more focused research projects under way. In one, Snyder is collaborating with JAX Professor George Weinstock, Ph.D., to investigate type 2 diabetes. As in the iPOP project, they are gathering large amounts of host and microbiome data from 80 subjects, half of whom are pre-diabetic, for three years. The resulting physiology and 'omics data sets will be massive, and Weinstock and Snyder are hoping to tease out patterns that reveal when someone is about to become diabetic before they actually do.

It is a new frontier, but combining baseline biological data, such as our genome sequences, with real-time physiological data could create truly precision medicine. Knowing more about our susceptibilities from our biology is a good start. Establishing true physiological baselines makes possible the detection of even small perturbations in them, providing the ability to respond faster and more proactively. It's not yet feasible to do this on a wide scale, of course, but the work provides a fascinating look at what may be our data-rich medical future.

UNDERSTAND HOW GENETICS RESEARCH IMPACTS HUMAN MEDICINE at *www.jax.org/precision.*

GENETICS VS. GENOMICS

BY MARK WANNER | ILLUSTRATION BY DANIELLE MEIER



The terms sound alike, and they are often used interchangeably. But there are some important distinctions between genetics and genomics.

Genetics is the study of heredity, or how the characteristics of living organisms are transmitted from one generation to the next via DNA, the substance that comprises genes, the basic unit of heredity. Genetics dates back to Augustinian friar and scientist Gregor Mendel, whose studies of pea plants in the mid-1800s established many of the rules of heredity.

More specifically, genetics involves the study of a limited numbers of genes, or parts of genes, that have a known function. In biomedical research, scientists try to understand how genes guide the body's development, cause disease or affect response to drugs.

The term genomics was first coined in 1986 by the late Jackson Laboratory scientist Tom Roderick, Ph.D.

Genomics, in contrast, is the study of the entirety of an organism's genes — called the genome. Using high-performance computing and math techniques known as bioinformatics, genomics researchers analyze enormous amounts of DNA-sequence data to find variations that affect health, disease or drug response. In humans that means searching through about 3 billion units of DNA across 23,000 genes.

Genomics is a much newer field than genetics and became possible only in the last couple of decades due to technical advances in DNA sequencing and computational biology.

JAX has expertise in both genetics and genomics. Scientists at the Maine headquarters practice basic, experimental genetics using mice while scientists at The Jackson Laboratory in Connecticut study the human genome.

These scientists collaborate with one another, and their complementary approaches are essential to discovering precise genomic solutions for human disease.

LEARN MORE ABOUT GENETICS AND GENOMICS at *www.jax.org/genetics.*

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

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