A Juggler of Quanta

Wearing jeans and an old Who t-shirt, **Jeremy Metz, Ph.D.,** looks more like a high-school student than a postdoctoral research fellow. But when he begins talking about stochastic simulations and mitotic spindles, it becomes clear that he really does belong at Einstein.

Dr. Metz is a research associate in the laboratory of Ao Ma, Ph.D., assistant professor of physiology & biophysics. He specializes in quantum information, quantum computing, quantum optics—new fields all based on the bizarre behaviors of particles at the atomic (quantum) level. There, for instance, a single particle can act as if it were in more than one place at the same time. Scientists are harnessing these strange properties to develop all sorts of new technologies, some of them proving highly useful in biomedical research.

Born in Germany and raised in Wales, Dr. Metz developed a taste for physics at an early age. "I always liked the way physics allows you to explain things from the bottom up—that is, the way you can start with a few basic principles and then build complicated models," he says. "But I also had an interest in biology, and I wanted to try applying physics principles to biological systems, which is what I am doing here at Einstein," he says.

Dr. Metz is developing mathematical models of the assembly and function of the cell's mitotic spindle, a self-organizing "machine" composed of microtubules, that segregates chromosomes into two identical groups in preparation for cell division.

This line of inquiry (a collaborative effort with Dr. Ma and David James Sharp, Ph.D., associate professor of physiology & biophysics) exemplifies basic research with tremendous clinical potential. "A number of diseases, including cancer and many birth defects, are believed to result from dysfunctions of the microtubules," he explains.

This fertile mix of science, math and computing seems to come naturally to Dr. Metz, who is at the leading edge of the first generation to come of age after the Internet was created. Still, he doesn't take it for granted. Most of all, he prizes the instant accessibility of the scientific literature. "If you have a hunch about something, you can just check it out online, instead of spending hours in the library," he says.

Just a few years ago, Dr. Metz was working as a bartender and then as a machine operator—temporary jobs during his "gap year" (the lengthy holiday that many British students take between high school and college). He's now conversant in four languages, thanks to his travels and his multicultural childhood.

Dr. Metz enrolled in 2000 at Imperial College in London, where he earned a master's degree in physics, followed by a doctorate in theoretical quantum optics and quantum computing—credentials that, in 2008, landed him his first academic post,

at Einstein. "In terms of academics, the US is a central hub," he says. "Back in Britain, scientists are encouraged to come here at some point in their careers, and I decided to do that first."

In his spare time, Dr. Metz enjoys swimming, running, juggling, sampling the city's multicultural cuisine, reading (especially books by Haruki Murakami and Stephen King) and—no surprise—"playing around with three-D computer graphics modeling."

Visitors to the Price Center/Block Research Pavilion should take note: That "kid" who looks as if he's playing video games is actually working toward a cure for cancer.

Daily's News

Earlier in her career, **Johanna Daily, M.D.,** found herself at a crossroads. While she loved clinical care, she also had a flair for research. But doing justice to her lab work would sharply curtail her time in the clinic.

To sort things out, she did the sensible thing: took a long vacation from her post as an infectious disease specialist at Boston's Brigham and Women's Hospital. But instead of heading for the nearest beach, she journeyed to Malawi, Africa, to participate in a study investigating why some children die of malaria and others don't.

The experience affected her profoundly but didn't solve her conundrum. "I came back and thought, 'research is too much for me—let me just stay in the clinic,'" she recalls. Not until a few years later, in 1999, did she finally shift her emphasis from patients to test tubes. "I was a little bit of a ping-pong ball," she admits.

After a few strategic bounces—including graduate studies in epidemiology at Harvard and field work in Senegal—Dr. Daily landed at Einstein in January 2009 as an associate professor of medicine. She is working to define the molecular mechanisms responsible for the variable outcomes in people with malaria. "It was not a direct route to a career as an investigator, but the journey has enriched the research questions I ask," says the new recruit. "We have had some interesting results."

"Groundbreaking" would be a better description of the results that she and her Boston colleagues published in *Nature* in 2007. Using blood samples from more than 40 malaria patients in Senegal, they determined which of the nearly 6,000 genes in *Plasmodium falciparum*—the most virulent species of the malaria parasite—switch on or off during human infection. Her team identified three distinct biological states of the parasite never before observed, including one in which the microbe seems to sense what is happening within its human host and adjust its biology accordingly.

The research not only revealed novel targets for anti-malarial drugs and vaccines but fundamentally shifted the way scientists view this ancient disease. For decades, our understanding of *P. falciparum* was based on studies carried out in cultured cells, not in the parasite's natural environment. Thanks to Dr. Daily, it is now apparent that we've overlooked key parts of the malaria parasite's biological repertoire.

Dr. Daily also studies drug resistance, a never-ending concern with this wily and resilient parasite. Humans have the upper hand for now, with combination therapies based on artemisinin (a drug derived from the wormwood plant), but that advantage may be short-lived. In one field project, she has been teaching Senegalese researchers molecular techniques for detecting drug resistance, a key step in guiding changes in therapy and staying one step ahead of the disease.

The Bronx sees only a handful of cases of malaria a year, so Dr. Daily must travel thousands of miles to conduct research and find scientific partners. She must also navigate institutional review boards in both local and foreign institutions. "These are tremendous challenges," she says, "but I am compelled by the questions and the partnerships."

Dr. Daily hopes to offer research opportunities in global health to students here at Einstein. "If you have a chance to see this as a possible career, then your imagination takes over," she says. "That is what happened to me."

10,000 Steps to Good Health

Fresh out of engineering school, **Irwin J. Kurland, M.D., Ph.D.,** had a dream job designing satellites, lasers and other high-tech wonders at Hughes Aircraft in California. But after a few years, he began to worry that he'd end up like his supervisors—"all working on military contracts and figuring out how to blow things up more effectively," he recalls. "I decided I'd rather apply my engineering skills to medical research."

The idealistic young engineer would go on to earn an M.D. and then a Ph.D. in molecular physiology, a prelude to a high-profile career in endocrinology, diabetes research and—most recently—metabolomics. This emerging discipline assesses a person's health by looking at changes in the concentrations of nutrients, such as fats and carbohydrates, when they are metabolized by the body's chemical reactions.

While his career trajectory is unusual, Dr. Kurland's very existence borders on the miraculous, with both his parents survivors of the Holocaust in Poland. His mother and her family evaded the Nazis by living for years in a tiny "room" dug beneath the forest floor, and his father barely escaped execution

in a concentration camp. "The day before they were going to kill everyone, the Russians came," he says.

Earlier this year, a generation and a world away from those dark days, Dr. Kurland joined the Einstein faculty as an associate professor of medicine and director of the new Metabolomics and Stable Isotope Core Facility of the Einstein Diabetes Research Center. He is also studying metabolic flexibility—the body's ability to match fuel demand to fuel supply as it switches between using carbohydrates (right after meals) and fats (after fasting overnight). "Individuals who have a problem in fuel switching are commonly obese and predisposed to developing diabetes," he explains.

Another research focus is a symptomless condition called pre-diabetes, in which blood glucose levels are barely above normal but not yet in the diabetic range. Pre-diabetes is surprisingly common in the US: 57 million people are affected, according to the American Diabetes Association; those most at risk of developing it are overweight or have high blood-cholesterol levels. Detecting and treating pre-diabetes (mainly through weight loss, exercise and, when necessary, drugs) is crucially important: Not only does the condition often lead to full-blown diabetes, but researchers now know that pre-diabetes itself can contribute to long-term damage to the heart and circulatory system.

Diagnosing pre-diabetes has been notoriously difficult. But that may change now that Dr. Kurland has patented a test that will soon be evaluated in a clinical trial.

The standard glucose-tolerance test for diabetes involves drinking a glucose solution and then, two or more hours later, measuring blood sugar; a high level indicates insulin resistance (the body's failure to respond properly to the insulin it produces)—the hallmark of type 2 diabetes. But the test isn't sensitive enough to detect the subtle faltering of the normally rapid insulin response that occurs right after a carbohydrate-containing meal, indicating that the person has pre-diabetes.

Dr. Kurland's pre-diabetes test uses glucose tagged with stable, non-radioactive isotopes. By measuring the isotope pattern in the glucose response, the test spots subtle metabolic abnormalities that can occur within minutes of a meal.

Dr. Kurland notes that his test wouldn't be needed if people avoided becoming overweight, the main culprit underlying pre-diabetes and type 2 diabetes. The solution, he says, is a balanced diet and regular exercise. His suggestion: Buy a pedometer, and take 10,000 steps a day—equivalent to about five miles.

"Studies show that this level of activity works wonders at helping people control, or prevent, diabetes," he says. "And increased walking in general has been found to lower the death rate in adults with diabetes." E

Price Center/ Block Research Pavilion **Recognizing Our Donors**

The Price Center/Block Research Pavilion represents the shared vision of the Board of Overseers, deans past and present, Einstein faculty and, crucially, our donors. Their desire to make a difference led the LeFrak and Winter families to make major commitments to advance the research at the new facility. Both families were recognized for their generosity at receptions held in their honor.

Winter Family Attends Dedication

Benjamin and Susan Winter were honored on March 9 at a private dedication ceremony and reception at the Price Center/Block Research Pavilion. The event was hosted by Allen M. Spiegel, M.D., the Marilyn and Stanley M. Katz Dean. It was held to recognize the Winters for their recent major gift to Einstein in support of biomedical research at the new facility, whose main lobby has been named in their honor.

Following the dedication ceremony, Mr. and Mrs. Winter and their family were given a guided tour of the laboratories of Jeffrey E. Pessin, Ph.D., the Judy R. and Alfred A. Rosenberg Professor of Diabetes Research and director of the Diabetes Research Center, and Matthew Levy, Ph.D., assistant professor in the department of biochemistry. Dr. Pessin is spearheading the creation of a Metabolomic Core Facility in the Price Center/Block Research Pavilion. Dr. Levy's work focuses on the design of aptamers, nucleic acids that may be useful in the diagnosis and treatment of diabetes and other diseases.

Pictured above are Susan and Benjamin Winter (second and third from right) with (from left) daughter Alison, son David, grandson Charlie and daughter-in-law Liz.