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Young Investigators Honored

School of Medicine recognizes the talents of students and fellows

By Audrey Huang
Johns Hopkins Medicine

How we listen to ourselves when we talk, the underlying defect in a rare neurological disorder and a plan for identifying potential drugs faster and cheaper are a few of many research projects that will be honored this year at the 30th annual Young Investigators' Day at Johns Hopkins. Eleven students and seven fellows will be celebrated, along with all young investigators in the School of Medicine.

Curtis Chong, center, with advisers David Sullivan and Jun Liu. An MD/PhD candidate in pharmacology and molecular sciences, Chong has already identified potential new uses for three FDA-approved drugs.
Photo by Will Kirk / HIPS

"The trainees at Hopkins are the driving force behind our research here," said Chi V. Dang, vice dean for research in the School of Medicine. "We would be nowhere without them."

The Young Investigators' Day program will start at 4 p.m. on Thursday, April 19, in the School of Medicine's Mountcastle Auditorium, East Baltimore campus, where selected awardees will present their research and all will receive honors. A poster session and reception will follow.

"This really is a celebration of all of our students and fellows," said Randall Reed, a professor of molecular biology and genetics and chair of the selection committee. "Selecting the awardees is one of the most difficult tasks that the committee members face each year. The applicants all were outstanding."

Renee Domergue, a PhD candidate in the Cellular and Molecular Medicine Program, is the recipient of the Alicia Showalter Reynolds Award. "I've been attending Young Investigators' Day celebrations since I started at Hopkins and always have been impressed with the caliber of work," she said. "It's a tremendous honor to be considered in the same league as the other recipients past and present."

Domergue's research in Brendan Cormack's lab discovered that the culprit behind yeast infections adapts to hosts by sensing and adjusting to available nutrients it needs to survive.

Young Kwon, a PhD candidate in biological chemistry and recipient of one of four Paul Erlich Research Awards, said, "I am so honored to be recognized by this award. When I was a second-year student, a senior student in our lab received a Young Investigators' Award, and witnessing that inspired and encouraged me to be as successful."

While working with mentor Craig Montell, Kwon discovered that a fruit fly gene called Lazaro is required for a second biochemical pathway that controls the activity of a protein called the TRP channel, found in fruit fly neurons and responsible for sensing light. The fly TRP channel is the founding member of a family of related proteins in mammals that are essential for guiding certain nerves during development and for responding to stimuli including heat, taste and sound.

Also recognized for research relating to how we perceive light was another Paul Erlich awardee, postdoctoral fellow **Hsi-Wen "Rock" Liao,** who while working in King-Wai Yau's lab discovered a new pigment called melanopsin in the light-sensing cells of the retina.

Seyun Kim, a PhD candidate in biological chemistry, praises his thesis adviser, Pierre Coulombe, "who is always inspirational, creative, encouraging and supportive. Without Pierre I wouldn't have anything fruitful." Kim, who received the Martin and Carol Macht Award, discovered that a protein long thought to provide only mechanical support for keeping cells and tissues from literally falling apart turns out to have much wider utility. The protein, K17, also influences wound healing and maintains the structural integrity of hair follicles. Kim's work, published in *Nature* last year, may have implications for preventing or treating chronic wounds such as pressure or bedsores arising from long periods of immobility.

Medical student **Kaisorn Chaichana,** who received a Paul Erlich Award, said, "The greatest contributors to my project's success were my mentors." Working with Alfredo Quinones-Hinojosa and a collaborator in Mexico, Oscar Gonzalez-Perez, Chaichana teased apart the characteristics of cells that give rise to brain tumors and found that most of these cells share traits normally seen in neural stem cells.

The 14 Young Investigators' Day Awards are named for former Johns Hopkins students and well-respected former faculty members. They are accompanied by a cash prize funded by friends, family and the Johns Hopkins Medical and Surgical Society. Some recipients say they feel a special connection to their named award.

"Receiving the Hans J. Prochaska award is a great honor since Dr. Prochaska received his MD and PhD degrees here at Hopkins," said MD/PhD candidate **Justin Bailey**. "His career is an inspiration for me as a future scientist-clinician." Bailey, while working in the lab of Robert Siliciano, discovered that rare HIV-1-infected individuals known as elite suppressors maintain undetectable virus levels and are indeed infected with fully functional virus. They also discovered that this so-called viral suppression is not controlled by antibodies. "Understanding how elite suppressors keep their viral levels so low may guide development of vaccines and drugs," he said.

Working with Peter Esphenshade, **Adam Hughes,** a PhD candidate in the Biochemistry, Cellular and Molecular Biology program, discovered a long-sought protein that controls cholesterol production and potentially drug metabolism in humans. Recipient of the David Israel Macht Award, Hughes said he wonders "if Dr. Macht, who made major contributions to the field of pharmacology, would take interest in our research if he were here with us today. It's extremely humbling to

receive this honor as Dr. Macht was a tremendous scientist."

"Nupur Dinesh Thekdi was my floor mate when I first joined Randy Reed's lab," said **Cheuk Leung,** also a PhD candidate in the Biochemistry, Cellular and Molecular Biology program. "It is my honor to receive the award in memory of Nupur and his spirit for science." Leung's project uncovered a stem cell-like role for cells in the nose that repair severely damaged nerve cells that contribute to our ability to smell.

Curtis Chong, an MD/PhD candidate in pharmacology and molecular sciences, received the Michael A. Shanoff Award for his project "Two Approaches to Drug Discovery," through which he identified potential new uses for three FDA-approved drugs.

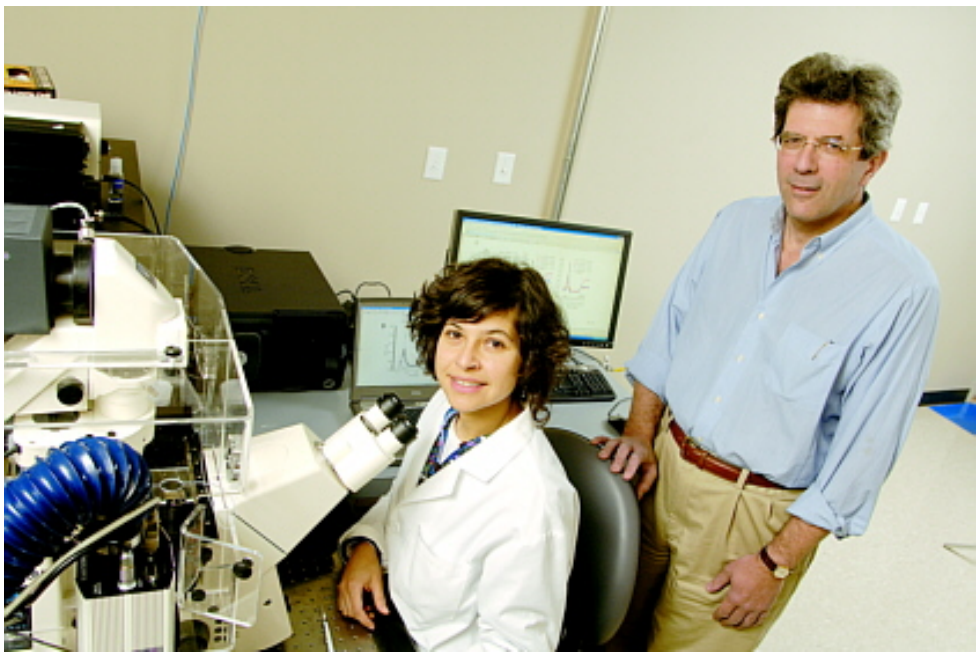
"Fast, affordable and broad-reaching drug development sharply contrasts with the current state of drug discovery," said Chong, who spent a summer working in Maputo, Mozambique, evaluating patients in an emergency room. Many of the patients had drug-resistant malaria, and Chong witnessed firsthand the fatal consequences of no available treatments. "At the current cost and rate of drug discovery, it will take more than 300 years for the number of available drugs in the world to double — and it's even worse in parts of the world where there is no financial incentive," he said.

Upon his return to Johns Hopkins, Chong helped establish the Johns Hopkins Clinical Compound Screening Initiative, a collection of more than 2,000 existing drugs that currently is being screened by many Johns Hopkins labs for diseases from HIV to cancer.

Chong and colleagues found two drugs — an immune suppressant and an antifungal — that block cancer-induced blood vessel growth in mice. Separately they have identified an antihistamine that shows promise for halting multidrug-resistant malaria in mice. Because these drugs already are FDA approved for other uses, "the path from lab to clinical trails hopefully will be much shorter than that of a newly derived drug," Chong said.

Grateful to his thesis advisers, Jun Liu and David Sullivan, Chong said the best thing about being a Johns Hopkins medical student "is working with such a talented group of people who hold such high standards — it motivates me to do my best each day."

Gabriela Caraveo Piso, a PhD candidate in the immunology graduate program, received the Mette Strand Award for her project "Action of TFII-I Outside the Nucleus as an Inhibitor of Agonist Induced Calcium Entry," where she discovered a new role — controlling calcium entry into cells — for the TFII-I, or TF "two-eye," protein previously known to control genes.



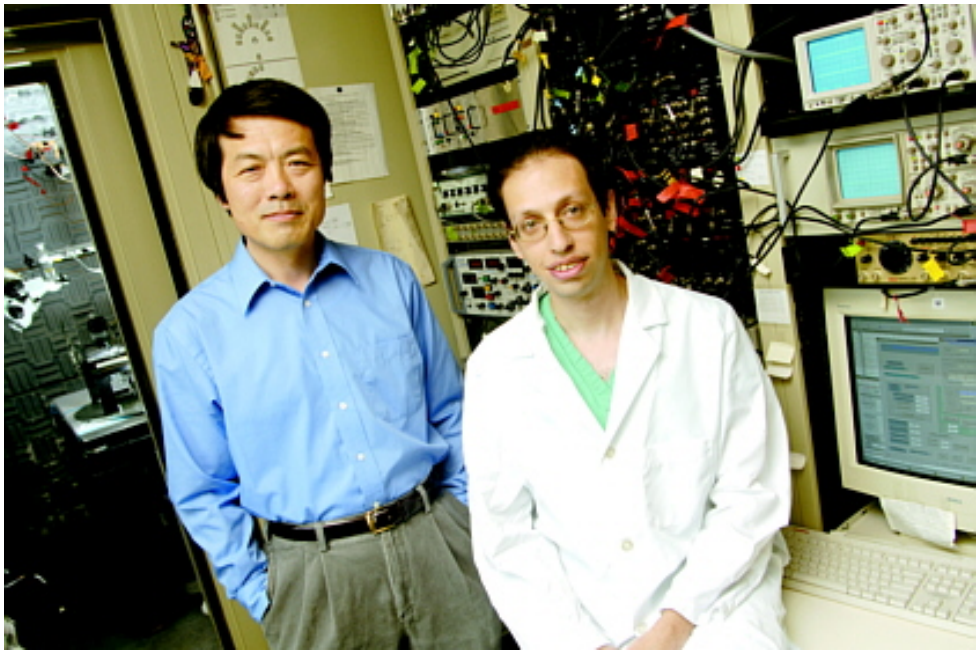
In addition to delineating a previously unknown mechanism by which calcium can enter cells, Caraveo's

Mette Strand Award winner Gabriela Caraveo Piso, with adviser Stephen Desiderio, discovered a new role — controlling calcium entry into cells — for the TFII-I protein. Caraveo is a PhD candidate in the immunology graduate program.
Photo by Will Kirk / HIPS

work may have teased out the function of a protein implicated in Williams-Beuren syndrome, a rare cognitive disorder associated with overly social behavior and lack of spatial awareness. Those affected are highly expressive, have exceptionally strong language abilities and "can talk up a storm," for example, but at the same time, they are poor at global organization, having problems re-creating patterns in drawings. The syndrome occurs in roughly one in 25,000 births and is caused by a deletion of a small section of chromosome 7 that contains several genes, including the gene that encodes the TFII-I protein. "We know that defects in a cell's ability to take in calcium can lead to other neurological and behavioral conditions," she said.

Caraveo, whose work was published last fall in *Science,* attributes her success to her adviser, Stephen Desiderio, who "profoundly shaped the way I approach science by showing me how to channel enthusiasm and passion into rigorous research design — he makes science such a thrill," she said.

Steven Eliades, an MD/PhD candidate in biomedical engineering, received a Paul Erlich Research Award for his project "Auditory-Vocal Interactions in the Primate Auditory Cortex."



Steven Eliades, right, with his adviser, Xiaoqin Wang. Eliades, an MD/PhD candidate in biomedical engineering, is studying how the brain processes many sound inputs. He received one of four Paul Erlich Research Awards.
Photo by Will Kirk / HIPS

Eliades examined "how we listen to ourselves when we talk" to figure out how the brain processes many sound inputs. "We have to be able to hear everyone else despite how loud our own voice is," Eliades said. "Otherwise, we wouldn't be able to communicate." Likewise, being able to hear ourselves as we talk allows the brain to correct any speech errors, he explained.

By studying nerve cell activity in monkeys while they vocalized, Eliades discovered two distinct groups of nerve cells in the part of the brain responsible for processing sound, the auditory cortex. One group of nerve cells was turned off during vocalization, while the other group was turned on, and both groups appeared to be controlled by vocalization itself. By changing external sounds, Eliades found that these two groups of nerve cells allow animals to both hear outside sounds and monitor their own voices during vocalization.

One major hurdle Eliades had to overcome was that monkeys restrained in a lab refuse to "speak" reliably. "For several years, this project seemed dead with failure after failure," he said. Only after he figured out a way to record free-roaming monkeys interacting with each other in their colony did he begin to make some progress.

"This award means a lot to me personally and professionally," said Eliades, adding that he is grateful to his adviser, Xiaoqin Wang, "for giving me a huge amount of freedom to come up with my own approach to the problem and being patient enough to allow things to play out."

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