

Columbia's Zuckerman Institute Awarded \$25.1M by BRAIN Initiative to Drive Neuroscience Discovery

~ Series of awards unites experts from different fields and universities; bolsters innovative, team approach to deciphering the complexities of the brain ~

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NEW YORK — Today, a team of Zuckerman Institute neuroscientists, data scientists and engineers together received a \$15.3 million BRAIN Initiative award to answer one of biology's most fundamental questions: How does the brain tell the body to move? The five-year award, administered by the National Institute of Neurological Disorders and Stroke, will support an unprecedented cross-disciplinary collaboration that brings together 10 labs and dozens of scientists. The team is charged with deciphering how the brain guides movement, a grand challenge in neuroscience with wide-reaching implications for science and medicine.

"Our ultimate goal is to create a functional blueprint, a map, of all the brain's connections that together drive movement," said Thomas M. Jessell, PhD, codirector of [Columbia's Zuckerman Institute](#) and the co-lead recipient of today's award. "With the BRAIN Initiative's enthusiastic support for this first-of-its-kind team approach, we have the means to gain insight into one of the most complex neuroscience questions of our time."

This new funding is one of just five awards to universities nationwide as part of the BRAIN Initiative's new [Team-Research BRAIN Circuit U19 program](#), which was created to fund exceptional teams to address major questions in neuroscience.

Teams from two other universities also include Zuckerman Institute researchers. Richard Mann, PhD, received \$3.2 million as part of a Caltech team to understand how the brain of a fruit fly sends information to the motor system to generate coordinated movements. Zuckerman Institute researcher Attila Losonczy, MD, PhD, also received \$2.4 million as part of a Stanford University collaboration to investigate the purpose of sharp-wave ripples — mysterious oscillations in the brain thought to be involved in the consolidation of long-term memories.

Columbia's U19 award is co-led by two Principal Investigators: Dr. Jessell and Zuckerman Institute scientist Rui Costa, DVM, PhD. The research will be performed almost entirely within

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the Greene Science Center, Columbia's new state-of-the-art facility designed by Renzo Piano and purpose-built to spark interaction and a collision of ideas.

There, these Zuckerman Institute researchers aim to first map the nerve cells in the spinal cord that, like strings on a marionette, direct the body to move. Using this knowledge, they will then work to decipher the precise choreography in the brain that governs aspects of movement, from a single step to a complex ballet.

Throughout the research, computational neuroscientists and data scientists will develop models behind the general principles of movement that can then be tested and refined in experiments. The teams will also leverage the latest imaging, instrumentation and analytical tools and data architectures — driven by the Zuckerman Institute's dedicated team members and innovation hubs.

“Creating a map of how the brain tells the body to move would be nothing short of revolutionary,” said Dr. Costa, “as it would serve as a critical reference for investigating disease.”

“Today, when someone suffers a stroke, critical connections between the brain and spinal cord are lost,” said Dr. Costa, who is also a professor of neuroscience and neurology at Columbia University Medical Center (CUMC). “We try to restore the connections, but we don't actually know how they formed in the first place. If we did, we would have a far better chance at finding ways to restore the connections with greater precision than is possible today.”

Additionally, this past July the BRAIN Initiative awarded a separate, \$4.2 million grant to Zuckerman Institute Principal Investigator Elizabeth Hillman, PhD, to improve the use and interpretation of human brain imaging methods. Dr. Hillman, who is also a lead investigator on the Columbia U19 award tasked with deciphering movement, is working to better understand the neural origins of resting-state functional magnetic resonance imaging (fMRI) by analyzing the real-time activity of neurons across the entire brain.

The July grant to Dr. Hillman, who is also a professor of biomedical engineering at Columbia's Fu Foundation School for Engineering and Applied Sciences, allows her to build upon discoveries made in late 2016, when she and her team used wide-field optical imaging in mice to uncover patterns of synchronized neural activity that could predict changing patterns of blood flow in the brain. This discovery provided strong support for the popular yet somewhat controversial fMRI method which infers functional connectivity of brain regions from changing fluctuations in brain-wide blood flow. With the new four-year grant, Dr. Hillman will investigate the cellular basis and drivers of these brain-wide patterns of neural activity.

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She will also collaborate with Columbia's department of neurosurgery, where data collected in human epilepsy patients and during brain surgery can be carefully compared to mouse experiments. This project will also include fMRI collaborators at the National Institute of Mental Health.

Taken together, these BRAIN Initiative projects represent a more than \$25 million investment in Columbia's Zuckerman Institute researchers in the last three months alone.

The Columbia teams believe that these grants will catalyze a new paradigm for neuroscience discovery at the Zuckerman Institute, noting that great science does not happen in a vacuum. Answering the most complex questions about the brain — such as how we think, act and behave — requires intensive collaboration of experts from diverse fields.

“Columbia's Zuckerman Institute was founded on the notion that true partnership among researchers — the dynamic back-and-forth, the sharing of technology and data, the developing, testing and revising of theories in real time — is at the heart of what drives science forward,” said Dr. Jessell, who is also Claire Tow Professor of Motor Neuron Disorders at CUMC and an Investigator at the Howard Hughes Medical Institute. “We hope that our work and our progress will serve to inspire others to do the same.”

The Brain Research through Advancing Innovative Neurotechnologies, or BRAIN Initiative, was established in 2014 by President Barack Obama to accelerate and revolutionize the understanding of the human brain. The BRAIN Initiative has supported scientists from across the United States to develop innovative tools and technologies that explore the brain's inner-workings.

Award details are as follows:

“Computational and circuit mechanisms underlying motor control” ([1U19NS104649-01](#))

Total award: \$15,250,530 over five years.

Principal Investigators: Rui Costa, DVM, PhD (contact PI) and Thomas M. Jessell, PhD.

Co-Investigators: Larry Abbott, PhD, Rajendra Bose, PhD, Randy Bruno, PhD, Mark Churchland, PhD, John Cunningham, PhD, Sean Escola, PhD, Elizabeth Hillman, PhD, Andreas Mueller, PhD, Liam Paninski, PhD, Darcy Peterka, PhD, Nathaniel Sawtell, PhD, Tanya Tabachnik, Tian Zheng PhD, and Jose Carmena PhD (UC Berkeley).

Other team members: Luke Hammond, Richard Hormigo, Gabriela Martins, PhD, and Arthur Uhimov.

“Decoding the neural basis of resting-state functional connectivity mapping” ([1RF1MH114276-01](#))

Total award: \$4,166,051 over four years.

Principal Investigator: Elizabeth Hillman, PhD

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"A Brain Circuit Program for Understanding the Sensorimotor Basis of Behavior" ([1U19NS104655-01](#))

Total award to Columbia University: \$3,236,316 over five years.

Columbia Principal Investigator: Richard Mann, PhD.

Other award Principal Investigators: Michael Dickinson, PhD (contact PI, Caltech), Thomas Clandinin, PhD, Shaul Druckman, PhD, Richard Murray, PhD, John Tuthill, PhD, and Rachel Wilson, PhD.

"Towards a Complete Description of the Circuitry Underlying Sharp Wave-Mediated Memory Replay" ([1U19NS104590](#))

Total award to Columbia University: \$2,399,129 over five years.

Columbia Principal Investigator: Attila Losonczy, MD, PhD.

Other award Principal Investigators: Ivan Soltesz, PhD, (contact PI, Stanford University), Gyorgy Buzsaki, PhD, John Lisman, PhD, and Mark Schnitzer, PhD.

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