UC SANTA BARBARA

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Andrew Masuda

More Than a Feeling

Much of what scientists know about how cells function is the result of directly observing their inner workings using fluorescent reporter proteins, originally discovered in jellyfish. A reporter protein is used as a marker and attached to another protein or gene of interest, allowing the function or location of the target to be tracked and monitored.

However, standard fluorescent proteins are limited because they depend on oxygen to emit light. And they cannot be used to study research animals, since light cannot penetrate opaque biological tissue. As a result, fluorescent reporters do not work deep in anaerobic systems, such as gut microbes, or inside living animals. This leaves two fascinating and medically important biological systems outside the purview of existing biomolecular imaging techniques.

Arnab Mukherjee, an assistant professor in UC Santa Barbara's Department of Chemical Engineering, has focused his research on developing new reporter proteins that tackle these challenges. He wants to illuminate what he refers to as the "invisible dark matter" of biology by engineering new genetic reporters that will fluoresce in anaerobic environments and can be seen in living animals using magnetic resonance imaging (MRI).

To create oxygen-independent fluorescent reporters, Mukherjee's research group is integrating molecular and metabolic engineering, modeling and directed evolution, which mimics the process of natural selection by steering proteins toward a user-defined goal. The team also is exploring how unusual biophysical properties such as

water diffusion and paramagnetism, a phenomenon in which some materials are weakly attracted by an externally applied magnetic field, could be engineered to build MRI-visible reporters for studying biology in live animals.

“There is only so much you can learn from observing neurons in a petri dish. The potential impact of tracking them as they’re going about their jobs inside a living, breathing animal is tremendous,” said Mukherjee, who runs the Molecular Bioimaging Lab at UCSB. “Cancer, gastrointestinal problems, neurobiology and immunotherapy are just some of the topics that can be studied further and understood better as a result.”

To help Mukherjee shed light on the matter, the National Institutes of Health, the principal medical research agency of the federal government, awarded him its Maximizing Investigators’ Research Award (MIRA). The $1.8 million grant, overseen by the National Institute of General Medical Sciences (NIGMS), is intended to enhance the chances of scientific discovery and important breakthroughs by providing scientists with five years of research funding.

“The award instills further confidence in my research vision, my mission and in my lab,” said Mukherjee, who received his Ph.D. in chemical engineering from the University of Illinois at Urbana-Champaign before starting as an associate professor at UCSB in 2017. “The NIH program funds my entire research program, not just a single research project. That stability means I won’t need to spend as much time writing proposals to fund students and my lab. I can dive deeper into my research.”

Mukherjee is especially interested in unraveling the mysteries surrounding gut biology. The mammalian gut is almost entirely anaerobic, supporting a microbial ecosystem that is critical for sustaining human health.

“Intestinal problems are shown to impact a person’s physical and mental wellbeing – and the molecular mechanisms behind this are just beginning to emerge. We can really move research surrounding this complex anaerobic ecosystem forward with new protein technologies that permit molecular imaging in anaerobic gut bacteria and directly inside the living gut,” explained Mukherjee, whose grandmother suffered from intestinal problems for many years. “I’m confident that over the next several years we will begin to understand more about the human gut and finally be able to provide a deeper scientific basis to the term ‘gut feeling,’ and make it more than a figure of speech.”

Neuroscience is another field that could benefit from Mukherjee’s molecular bioimaging research. He is member of UCSB’s Neuroscience Research Institute (NRI), a group of investigators from various departments whose collective goal is to work collaboratively toward scientific research breakthroughs.

“I’m not a neuroscientist, but the beauty of the institute is that faculty from other departments provide us with questions, and my group tries to develop the technology to answer those questions,” said Mukherjee. “New reporter proteins would allow us to analyze biomolecules inside a brain, allowing us to measure, at a molecular level, the impact factors, like stress, addiction and medication, have on the brain.”

About UC Santa Barbara

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