THE FRONT ROW
at Scripps Research

The gut-brain axis: A key to metabolism and longevity

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ABOUT THE LECTURE

The organs in our body are like a symphony, in which each instrument plays a vital role in maintaining harmony. In her lecture, Scripps Research neuroscience professor Supriya Srinivasan explored the intricate communication between two of these organs: the brain and gut. She discussed the pathways that regulate this connection, their impact on metabolism and longevity, and potential therapeutic strategies for disease treatment.

TOP TAKEAWAY POINTS

- Our organs are in constant communication. They send signals to each other using chemical messengers, or hormones, to achieve homeostasis throughout the body. But disruptions in this metabolic signaling can lead to diabetes, muscle loss, cancer, neurodegenerative diseases and countless other conditions.

- Srinivasan and her lab are investigating the complex crosstalk between the brain and gut. Using *C. elegans* as a model system—a microscopic nematode that shares 70% of its genes with humans—they study the specific molecules and genes involved in this communication.

- One of Srinivasan's first key discoveries was that serotonin is a principal driver of fat loss. They found that removing a neuronal enzyme that produces serotonin led to fat accumulation in the intestine, while increased serotonin in the synapse—the region between neurons—made the worms lean.

- Using a genetic screen, they pinpointed that the tachykinin peptide is the key signal regulating metabolism between the brain and the gut. They found that stimulating this pathway promoted fat loss, without having any negative effect on longevity.

- The researchers also wanted to understand how the nervous system knows to send this information to the gut. They identified an insulin peptide—different from the one that regulates glucose—that is secreted during fasting. Deleting this molecule shortened lifespan, suggesting it plays a vital role in the aging process.

- Now, the Srinivasan lab is investigating how gut bacteria influence this insulin peptide's activity, hoping to uncover the signals that regulate how an animal goes from a fasting to a feeding state. She is also collaborating with Calibr-Skaggs, Scripps Research's drug discovery arm, to translate her findings into small molecule medicines. They are identifying how the tachykinin receptor—called NKR2—can be targeted to treat metabolic diseases.

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