THE FRONT ROW
at Scripps Research

Sensing danger: How the nervous and immune systems coordinate inflammation

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ABOUT THE LECTURE

Inflammation often gets a bad reputation, but it's actually the body's essential process for restoring balance after an infection or injury. In this Front Row lecture, Scripps Research Assistant Professor Alejandra Mendoza shared how her work uncovered a novel way the nervous and immune systems work together to manage inflammation. By discovering that specialized immune cells called regulatory T cells produce enkephalins—natural opioid molecules that directly suppress pain in sensory neurons—Mendoza's work revealed that these immune cells prevent inflammation by decreasing pain first, not the other way around. This discovery shows how our bodies carefully balance protective and destructive inflammation, and it could provide new therapeutic possibilities for chronic diseases like psoriasis, pain syndromes or even cancer.

TOP TAKEAWAY POINTS

- The human body constantly senses and responds to stimuli in the environment to maintain homeostasis—the stable internal conditions necessary for survival. Homeostasis is essential for cells and organs to function properly. The body carefully manages specific ranges of temperature, blood sugar and other parameters, and deviations from these "set points" can impair cellular function and cause tissue damage.

- To maintain homeostasis, the body uses inflammation to restore normal functions after an infection or injury. Barrier tissues like the skin must carefully balance inflammation because of its protective and potentially destructive qualities. Too little inflammation leaves the body defenseless against pathogens and cancers, while too much inflammation drives chronic diseases like psoriasis and atopic dermatitis, making this balance critical for health.

- Mendoza and her lab identified the unique relationship between sensory neurons and regulatory T cells that helps maintain homeostasis. Contrary to prior thought, sensory neurons don't simply detect threats and trigger pain—they directly communicate with regulatory T cells via signaling molecules that dampen inflammatory responses. This regulation matters as the two-way communication between immune cells and sensory neurons can create dangerous feedback loops where immune activation triggers pain, which in turn amplifies inflammation, potentially spiraling into chronic inflammatory diseases. By dampening pain perception first, regulatory T cells prevent the feedback loop that would otherwise amplify inflammation, revealing that controlling pain is actually a mechanism to control inflammation, not just a consequence of it.

- The Mendoza Lab is uncovering new signaling molecules, beyond enkephalins, that mediate communication between sensory neurons and immune cells. They have found that distinct types of sensory neurons respond differently to specific forms of inflammation, revealing a finely tuned system of neuro-immune crosstalk. By identifying molecules that form feedback loops to amplify or dampen inflammation, the Mendoza Lab aims to modulate these pathways, reducing inflammation in chronic conditions while enhancing beneficial immune responses, such as those directed against tumor cells.

- Understanding how immune cells and neurons talk to each other opens therapeutic opportunities to break chronic pain-inflammation cycles in conditions like psoriasis and rheumatoid arthritis. The Mendoza lab aims to use this discovery to fuel further analysis of the neuro-immune relationship across the body and identify potential therapies to manage pain and inflammation.

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