Neurons play role in controlling innate immunity in presence of pathogens

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There is finally definitive proof in a preclinical study published in *Science* on April 7 about which sensory neurons control innate (inborn and immediate) immunity in a pathogen's presence.

"Our studies have implications for the understanding of the effect of anger or acute stress on immunity, because acute stress suppresses immunity," said senior author Alejandro Aballay, Ph.D. , Associate Professor in Molecular Genetics and Microbiology. "Our discovery -- that inactivation of a receptor for a noradrenaline-like molecule that is involved in the arousal response results in enhanced immunity -- suggests that there is a strong selective advantage to suppressing the immune response during stress."

The OCTR-1 receptor in the two neurons in question (ASH and ASI) is a catecholamine receptor (G-protein-coupled catecholamine receptor) similar to vertebrate adrenergic receptors, Aballay said. "OCTR-1 functions in sensory neurons that have the potential to sense pathogens or molecules related to inflammation, suggesting that host catecholamines regulate immune responses in response to changes in the surrounding environment."

In addition, the scientists found that the nervous system controls a family of genes that are part of a surprising unfolded protein response (UPR) pathway that is controlled by a different receptor, an apoptotic receptor that has the potential to sense the damage caused by infecting microorganisms. Aballay said that this work dovetails with the concept

of endurance – how a body learns to co-exist with a pathogen, by igniting not only immune pathways that keep the pathogen in check but also pathways that control the damage induced by the infection.

In this study, exposure to the dangerous bacterium Pseudomonas aeruginosa up-regulates genes to levels comparable to those induced by a well-known stressor of the endoplasmic reticulum (ER), a drug called tunicamycin. This study is the first direct demonstration that a bacterial infection can activate a non-canonical UPR pathway to alleviate the ER stress that occurs in the cells during innate immune response against bacterial infections, Aballay said. “We have been able to take advantage of the simple and well-studied nervous and immune systems of C. elegans to demonstrate that two neurons, which have the potential to sense disease, regulate conserved innate immunity pathways and control the organismal response to bacterial infections,” Aballay said.

Recent mouse studies show that the nervous system, through the animal organ that can detect pheromones, for example, has the potential to “smell” molecules related to disease or inflammation in the outside world. Given the complexity of the mammalian nervous and immune systems, the role that such a “smelling” mechanism may have on a host’s response to infections remains unknown, but will be a future area for study, Aballay said.

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