

## PROGRESS IN NEUROSCIENCE PINS

Seminar Series of the Brain & Mind Research Institute Weill Cornell Medical College (WCMC) &



The Graduate Program in Neuroscience of WCMC and Sloan Kettering Institute

Thursday, 3/27/14, 4 PM, coffee at 3:45 PM Weill Auditorium

## **Reflex Basis of Immunity**

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Neural reflexes modulate organ responses to maintain physiological homeostasis. Inflammation disrupts homeostasis because pathogen and damage-associated molecules mediate metabolic and transcriptional responses in target organs, including the brain. During the course of studying mechanisms to suppress inflammation-mediated organ injury, we discovered a reflex neural circuit that suppresses the innate immune response. Termed "the inflammatory reflex," action potentials arising in the efferent vagus nerve regulate acetylcholine release from a unique T cell subtype that expresses choline acetyltransferase (TCHaT). Acetylcholine nicotinic acetylcholine receptors expressed interacts with a7 on macrophage mitochondria to inhibit mitochondrial DNA release, and suppress inflammasome activation. This closed loop regulatory circuit is activated by action potentials arising in sensory neurons in response to TNF, IL-1, endotoxin, and other endogenous and exogenous inflammatory molecules. Recent clinical trials of stimulating the inflammatory reflex to treat rheumatoid arthritis have shown promise. Together, anatomic, functional, neurophysiological, and molecular evidence have revealed the neural basis of immunity.

## Recent relevant publications:

1: Olofsson PS, Kalb T, Roth J, Zou Y, Erlandsson-Harris H, Yang H, Ting JP, Wang H, Andersson U, Antoine DJ, Chavan SS, Hotamisligil GS, Tracey KJ. Novel role of PKR in inflammasome activation and HMGB1 release. **Nature**. 2012 Aug 30;488(7413):670-4. doi: 10.1038/nature11290. PubMed PMID: 22801494.

2: Andersson U, Tracey KJ. Neural reflexes in inflammation and immunity. **J Exp Med**. 2012 Jun 4;209(6):1057-68. doi: 10.1084/jem.20120571. Review. PubMed PMID: 22665702; PubMed Central PMCID: PMC3371736.



