CHINESE-AMERICAN LUNG ASSOCIATION

CALA Happy Friday Seminar

October 21st, 2022

Time: EST 10:30 am; PST: 7:30 am; Beijing time: 10:30pm

Zoom: 849 9682 9273 (Password: 654321)

Brainstem Dbh+ Neurons Control Chronic Allergen-Induced Airway Hyperreactivity

Yujuan Su, Ph.D
Postdoctoral Associate
Dr. Xin Sun lab
University of California at San Diego

Bio: Dr. Yujuan Su obtained her B.S. from Shandong University in China and completed Ph.D. training at the Institute of Neuroscience, Chinese Academy of Sciences in China. Currently, she is an assistant project scientist after completing postdoc research in Dr. Xin Sun's lab at the University of California at San Diego. Yujuan started her postdoc work with systematically whole-tissue mapping of the lung-innervating sensory neurons. This part of work has awarded her the American Heart Association (AHA) fellowship and a first author publication at AJP-lung. The bulk of her study on functional mapping of the allergen circuit is in review now. Yujuan presented this work at the Lung Gordon Research Conference in 2021, and it was enthusiastic received. She has also been selected to give an oral presentation at the Vertebrate Sensory Keystone Conference later this month. Yujuan's training in neuroscience and lung biology makes her well-suited to continue to study the interoception interface between the lung and the central nervous system.

Abstract: Chronic exposure of the lung to irritants such as allergen is a primary cause of asthma characterized by exaggerated airway constriction, also called hyperreactivity, which can be life-threatening. Aside from immune cells, vagal sensory neurons are important for airway hyperreactivity. However, the identity and signature of the downstream nodes of this adaptive circuit remains poorly understood. Here we show that a single population of Dbh+ neurons in the nucleus of the solitary tract (nTS) of the brainstem, and downstream neurons in the nucleus ambiguous (NA), are both necessary and sufficient for chronic allergen-induced airway hyperreactivity. We found that repeated exposures of mice to inhaled allergen activates nTS neurons in a mast cell-, interleukin 4 (IL-4)- and vagal nerve-dependent manner. Single-nucleus RNA-seq of the nTS at baseline and following allergen challenges reveals that a Dbh+ population is preferentially activated. Ablation or chemogenetic inactivation of Dbh+ nTS neurons blunted, while chemogenetic activation promoted hyperreactivity. Viral tracing indicates that Dbh+ nTS neurons, capable of producing norepinephrine, project to the NA, and NA neurons are necessary and sufficient to relay allergen signals to postganglionic neurons that then directly drive airway constriction. Focusing on transmitters, delivery of norepinephrine antagonists to the NA blunted allergen-induced hyperreactivity. Together, these findings provide molecular, anatomical and functional definitions of key nodes of a canonical allergen response circuit. The knowledge opens the possibility of targeted neural modulation as an approach to control refractory allergen-induced airway constriction.