therapy was completely protective in mice depleted of a single effector. While dual depletion resulted in diminished MAb efficacy in terms of survival, mice retaining neutrophils had marked improvements in survival with MAb therapy compared with other dual-depletion groups. The dissociation of bacterial density and survival suggested that inflammation was a primary driver of host outcome. Levels of IL-10 and TNFα and a reciprocal relationship in mice across effector depletion groups and were lower in mouse groups with higher survival when adjusted for bacterial density. IL-10 disruption completely abrogated the survival benefit of MAb therapy without altering bacterial clearance mediated by MAb. In contrast, TNFα disruption enhanced MAb efficacy for survival, and the presence of TNFα was antagonistic to MAb efficacy.

Conclusion. These results confirm that host outcomes from A. baumannii infection are driven by host inflammatory response rather than bacterial density alone. Furthermore, novel therapeutic approaches seeking to improve outcomes from such infections must seek to shift the balance of pro-/anti-inflammatory cytokines to favor a down-modulated inflammatory response.

Disclosures. All Authors: No reported Disclosures.

972. A Mycobacterium tuberculosis Secreted Lipid Triggers Cough Through a Neuronal Cough Receptor

Paxon Cruz, BSc;  Cody Buhl, BSc and Michael Shilooh, MD, PhD; 1University of Texas Southwestern Medical Center, Dallas, Texas; 2University of Texas Southwestern, Dallas, Texas

Session: 125. Pathogenesis and Inflammatory Response
Friday, October 4, 2019: 10:45 AM

Background. A hallmark symptom of active pulmonary tuberculosis vital for disease transmission is cough. The current paradigm for tuberculosis-related cough is that it results from airway damage or irritation. However, there is limited experimental data to support this theory, and whether Mycobacterium tuberculosis (MtB) induces cough to facilitate its own transmission has not been explored. The cough reflex is a complex and coordinated event involving both the nervous and musculoskeletal systems initiated by particulate or chemical molecules activating nociceptive neurons, which sense pain or irritation. This activation induces a signaling cascade ultimately resulting in a cough. Respiratory nociceptive neurons innervate the airways of humans and most mammals and thus are poised to respond to noxious molecules to help protect the lung from damage. Because MtB is a lung pathogen, cough is a primary mechanism of MtB transmission, and respiratory nociceptive neurons activate cough; we hypothesized that MtB produces molecules that stimulate cough thereby facilitating its spread from infected to uninfected individuals. We previously identified a cough molecule produced by MtB, and in this work characterize its neuronal receptor using genetics, biochemistry, and pharmacology.

Methods. We used an in vitro neuronal activation bioassay to study MtB-cough-inducing molecules. We also used a biochemical assay to identify the cough receptor. Finally, we used gene silencing, biochemistry, and pharmacologic inhibition to validate and characterize the activity of the newly discovered cough receptor.

Results. We isolated a complex lipid produced by MtB that activates nociceptive neurons. Both an organic MtB extract and the purified molecule alone were sufficient to induce cough in a conscious guinea pig cough model and guinea pigs infected with wild-type MtB cough much more frequently than guinea pigs infected with MtB strains unable to produce nociceptive molecules. Using genetics, biochemistry, and pharmacologic techniques, we identified and validated a cough receptor for the MtB lipid expressed on nociceptive neurons.

Conclusion. We conclude that MtB produces a molecule that activates nociceptive neurons and induces cough through a specific neuronal receptor. These findings have significant implications for our understanding of MtB transmission.

Disclosures. All Authors: No reported Disclosures.