and T-cell interactions between CD4 T cells and Mtb-infected cells presenting cognate antigen on MHCII. This suggested a local immune response in the lung, which we confirmed by finding high levels of IFNγ production in the Mtb-infected lung. IFNγ production by CD4 T cells has been thought to be critical for immunity against Mycobacterium tuberculosis (Mtb); however, recent studies show that IFNγ-producing CD4 T cells are more effective at preventing dissemination than controlling Mtb in the lung. Because optimal control of Mtb infection requires direct interactions between CD4 T cells and Mtb-infected cells presenting cognate antigen on MHCII, we sought to determine the location of CD4 T-cell antigen recognition and IFNγ production in the Mtb-infected lung.

Methods. We infected mice with an ultra-low dose (ULD) of Mtb (1–3 CFU), a mycobacterial load that recapitulates many features of human Mtb granulomas. Using immunohistochemistry and quantitative imaging, we examined their lungs 35 days later for phenotypic controls of Mtb infection and could guide new strategies for vaccine and immunotherapeutic development.

Disclosures. All authors: No reported disclosures.

166. TGF-β Restricts T-cell IFNg Production in Pulmonary Tuberculous Granulomas
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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 activates cough, we hypothesized that Mtb produces molecules that stimulate cough, thereby facilitating its spread from infected to uninfected individuals.

Methods. We used an in vitro neuronal activation bioassay to fractionate, identify, and characterize Mtb-cough inducing molecules. We also measured cough in vivo in response to pure Mtb-derived cough molecules and during Mtb infection using a guinea pig model.

Results. We found that an acellular organic extract of Mtb triggers and activates nociceptive neurons in vitro with a neuronal response that is as robust as the response to capsaicin, an established nociceptive and cough-inducing molecule. Using analytical chemistry and our neuronal bioassay, we then isolated 2 molecules produced by Mtb that activate nociceptive neurons. Both the organic Mtb extract and purified molecules alone were sufficient to induce cough in a conscious guinea pig cough model. Finally guinea pigs infected with wild-type Mtb cough much more frequently than guinea pigs infected with Mtb strains unable to produce nociceptive molecules.

Conclusion. We conclude that Mtb produces molecules that activate nociceptive neurons and induce cough. These findings have significant implications for our understanding of Mtb transmission.

Disclosures. All authors: No reported disclosures.

165. Mycobacterium tuberculosis Produces Molecules That Trigger Nociceptive Neurons to Activate Cough
Cody Ruhl, BS1, Lexy Kindt, BS, BS1, Haaris Khan, BS1; Chelsea E. Stamm, BS1; Breanna Pasko, BS1; Luis Franco, PhD2 and Michael U. Shilooh, MD, PhD2, 1Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas and 2Center for Autophagy Research, University of Texas Southwestern Medical Center, Dallas, Texas

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Background. IFNg production by CD4 T cells has been thought to be critical for immunity against Mycobacterium tuberculosis (Mtb); however, recent studies show that IFNγ-producing CD4 T cells are more effective at preventing dissemination than controlling Mtb in the lung. Because optimal control of Mtb infection requires direct interactions between CD4 T cells and Mtb-infected cells presenting cognate antigen on MHCII, we sought to determine the location of CD4 T-cell antigen recognition and IFNγ production in the Mtb-infected lung.

Methods. We infected mice with an ultra-low dose (ULD) of Mtb (1–3 CFU), a mycobacterial load that recapitulates many features of human Mtb granulomas. Using immunohistochemistry and quantitative imaging, we examined their lungs 35 days later for phenotypic controls of Mtb infection and could guide new strategies for vaccine and immunotherapeutic development.

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