[PS1.30]

Pseudomonas LPS enhances neutrophil influx and inflammation in the lungs of TREM-2 deficient mice and promotes bacterial clearance

O Sharif*[1,2], R Gawish[1,2], U Matt[1,2], K Stich[2], B Doninger[1,2], S Knapp[1,2]

[1]Center for Molecular Medicine (CeMM) of the Austrian Academy of Science, Austria, [2]Dept. of Medicine 1, Div. of Infectious Diseases and Tropical Medicine, Medical University of Vienna, Austria

Triggering receptor expressed on myeloid cell 2 (TREM-2) is a cell surface receptor that negatively regulates Toll like receptor 4 (TLR4) mediated inflammation in bone marrow derived macrophages in a poorly defined manner. Resident alveolar macrophages play an important role in respiratory tract infections, such as Pseudomonas infection, but the role of TREM-2 herein is unknown. Here, we show that TREM-2 is expressed on resident alveolar macrophages and that remarkably TREM-2 deficient mice display enhanced inflammation and consequently decreased bacterial burden in their lungs following intranasal infection with Pseudomonas aeruginosa. Pseudomonas LPS mediates these in-vivo effects as intranasal inoculation of mice with Pseudomonas LPS recapitulates the enhanced inflammation and neutrophil influx observed following infection with live bacteria in TREM-2-/- mice. Mechanistically, we demonstrate that TREM-2 is able to negatively regulate inflammation in response to both Pseudomonas and its LPS through its effects on the nuclear factor kappaB (NF-kB) pathway. These data show that TREM-2 modulates innate immune responses to Pseudomonas in vivo via recognition of its LPS in a TLR4 and NF-kB dependent manner.

Keywords: TREM-2, Pseudomonas, LPS, TLR4