The triggering receptor expressed on myeloid cells 2 inhibits complement component 1q effector mechanisms and exerts detrimental effects during pneumococcal pneumonia.

Phagocytosis and inflammation within the lungs is crucial for host defense during bacterial pneumonia. Triggering receptor expressed on myeloid cells (TREM)-2 was proposed to negatively regulate TLR-mediated responses and enhance phagocytosis by macrophages, but the role of TREM-2 in respiratory tract infections is unknown. Here, we established the presence of TREM-2 on alveolar macrophages (AM) and explored the function of TREM-2 in the innate immune response to pneumococcal infection in vivo. Unexpectedly, we found Trem-2-/- AM to display augmented bacterial phagocytosis in vitro and in vivo compared to WT AM. Mechanistically, we detected that in the absence of TREM-2, pulmonary macrophages selectively produced elevated complement component 1q (C1q) levels. We found that these increased C1q levels depended on peroxisome proliferator-activated receptor-? (PPAR-?) activity and were responsible for the enhanced phagocytosis of bacteria. Upon infection with S. pneumoniae, Trem-2-/- mice exhibited an augmented bacterial clearance from
lungs, decreased bacteremia and improved survival compared to their WT counterparts. This work is
the first to disclose a role for TREM-2 in clinically relevant respiratory tract infections and
demonstrates a previously unknown link between TREM-2 and opsonin production within the lungs.

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