

P027 Role of triggering receptors expressed on myeloid cells (TREM)-1 in Gram-negative sepsis (melioidosis)
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Background. TREM-1 amplifies Toll-like-receptor-initiated responses against pathogens. We aimed to characterize the TREM-1-expression and function in Gram-negative sepsis caused by *Burkholderia pseudomallei* (melioidosis).

Methods & Results. Patients with melioidosis demonstrated increased soluble-TREM-1 plasma levels and TREM-1 surface-expression on monocytes, but not granulocytes compared to healthy controls. High TREM-1 levels correlated with mortality. Mice inoculated with a lethal dose of *B.pseudomallei* displayed a gradual rise in soluble-TREM-1 and increase in blood monocyte but not granulocyte TREM-1 expression. At the primary infection-site, however, granulocyte TREM-1 expression was enhanced and the rise in soluble-TREM-1 occurred earlier. Additionally, purified human TREM-1⁺granulocytes showed reduced responsiveness to *B.pseudomallei* relative to TREM-1⁺granulocytes; a difference not detected for TREM-1⁻ and TREM-1⁺monocytes. Treatment with a peptide mimicking a conserved-domain of soluble-TREM-1 partially protected mice from *B.pseudomallei* induced lethality.

Conclusion. During melioidosis TREM-1 expression is differentially regulated on granulocytes and monocytes; measurements of TREM-1-expression on blood granulocytes may not provide adequate information on granulocyte TREM-1-expression at the infection site. TREM-1 may be a therapeutic target in melioidosis.