

Savva A and Roger T. (2013). Targeting Toll-like receptors: promising therapeutic strategies for the management of sepsis-associated pathology and infectious diseases. *Front. Immunol.* 4:387.

Toll-like receptors (TLRs) are pattern recognition receptors playing a fundamental role in sensing microbial invasion and initiating innate and adaptive immune responses. TLRs are also triggered by danger signals released by injured or stressed cells during sepsis. Here we focus on studies developing TLR agonists and antagonists for the treatment of infectious diseases and sepsis. Positioned at the cell surface, TLR4 is essential for sensing lipopolysaccharide of Gram-negative bacteria, TLR2 is involved in the recognition of a large panel of microbial ligands, while TLR5 recognizes flagellin. Endosomal TLR3, TLR7, TLR8, TLR9 are specialized in the sensing of nucleic acids produced notably during viral infections. TLR4 and TLR2 are favorite targets for developing anti-sepsis drugs, and antagonistic compounds have shown efficient protection from septic shock in pre-clinical models. Results from clinical trials evaluating anti-TLR4 and anti-TLR2 approaches are presented, discussing the challenges of study design in sepsis and future exploitation of these agents in infectious diseases. We also report results from studies suggesting that the TLR5 agonist flagellin may protect from infections of the gastrointestinal tract and that agonists of endosomal TLRs are very promising for treating chronic viral infections. Altogether, TLR-targeted therapies have a strong potential for prevention and intervention in infectious diseases, notably sepsis.