

Lima CX, Souza DG, Amaral FA, Fagundes CT, Rodrigues IP, Alves-Filho JC, Kosco-Vilbois M, Ferlin W, Shang L, Elson G, Teixeira MM. (2015). Therapeutic Effects of Treatment with Anti-TLR2 and Anti-TLR4 Monoclonal Antibodies in Polymicrobial Sepsis. *PLoS One*. 10(7):e0132336.

## **INTRODUCTION:**

Toll-like receptors (TLRs) play an important role in the recognition of microbial products and in host defense against infection. However, the massive release of inflammatory mediators into the bloodstream following TLR activation following sepsis is thought to contribute to disease pathogenesis.

## **METHODS:**

Here, we evaluated the effects of preventive or therapeutic administration of monoclonal antibodies (mAbs) targeting either TLR2 or TLR4 in a model of severe polymicrobial sepsis induced by cecal ligation and puncture in mice.

## **RESULTS:**

Pre-treatment with anti-TLR2 or anti-TLR4 mAb alone showed significant protection from sepsis-associated death. Protective effects were observed even when the administration of either anti-TLR2 or anti-TLR4 alone was delayed (i.e., 3 h after sepsis induction). Delayed administration of either mAb in combination with antibiotics resulted in additive protection.

## **CONCLUSION:**

Although attempts to translate preclinical findings to clinical sepsis have failed so far, our preclinical experiments strongly suggest that there is a sufficient therapeutic window within which patients with ongoing sepsis could benefit from combined antibiotic plus anti-TLR2 or anti-TLR4 mAb treatment.