



## LXR $\alpha$ REGULATES NEUTROPHIL AND MACROPHAGE MIGRATION DURING CLP-INDUCED SEPSIS

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Sepsis is a global public health problem, which is one of the main causes of mortality in intensive care unit patients. Sepsis consists is an exacerbated systemic inflammatory response triggered by an uncontrolled infection, in which the excessive production of inflammatory mediators drives to an immune suppression by increase leukocyte apoptosis and exhaustion, following to multiple organ failure and death. Liver X receptors (LXR) are nuclear receptors that regulate lipid homeostasis and plays a role in the regulation of immune cells response. LXR have two isoforms,  $\alpha$ , and  $\beta$ . LXR $\alpha$  has been described to be essential to leukocyte migration, while LXR $\beta$  is essential for thymocyte selection. In addition, LXR agonists induces the anti-inflammatory program in immune cells by increase lipid efflux molecules, such as ABCA1 and the inhibition of nuclear factor kappa beta translocation. Here we investigate the involvement of LXR $\alpha$  on the progression of sepsis. Thus, WT and LXR $\alpha$ -deficient (LXR $\alpha$ KO) animals were submitted to the sepsis model using cecal ligation and puncture (CLP), and the immune response was evaluated. Our results showed that LXR $\alpha$ KO mice are more susceptible to sepsis and also display higher temperature than WT mice in the presence of similar bacterial load in the peritoneal cavity. Also, we observed increased macrophage and neutrophils infiltration in the peritoneal cavity of LXR $\alpha$ KO compared to WT mice. However, the expression of LXR target genes *Abca1*, *ApoE* and *Aim*, as well the pro-inflammatory markers *Nos2*, *Il-6*, *Il-12*, *Il-1 $\beta$* , and *Tnf- $\alpha$*  is decreased in LXR $\alpha$ KO CLP-submitted mice. Similarly, the secretion of TNF- $\alpha$ , IL-12, and MPC-1 was significantly decreased. Together, our findings suggest that LXR $\alpha$  has an essential role in the immune response against pathogens and leucocyte migration, and, therefore, it is central in the development of sepsis and in its further outcomes.