FAILURE OF NEUTROPHIL MIGRATION TO INFECTION FOCUS IN SEVERE POLYMICROBIAL SEPSIS IS MEDIATED BY TLR2 AND TLR4 SIGNALING

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We demonstrated that failure of neutrophil migration into the infectious focus is observed in severe sepsis and the process is mediated by nitric oxide. The present study aimed to investigate the role of TLR2 and TLR4 on the failure of neutrophil migration to infection focus in mice subjected to polymicrobial sepsis. TLR2 deficient (TLR2-/-), wild type C57BL/6, wild type C3H/HePas and TLR4 mutated C3H/HeJ mice were subjected to sub-lethal or lethal polymicrobial sepsis induced by cecal ligation and puncture. After, survival rate, neutrophil migration to infection focus, bacteremia, lung neutrophil sequestration, cytokines and nitric oxide production were evaluated. It was observed that TLR2 and TLR4 signaling are crucial to establish the impairment of neutrophil migration in lethal CLP, since TLR2-/- and C3H/HeJ mice did not present significant increase of systemic NO production and, as consequence, they did not present failure of neutrophil migration to infection focus, constraining locally the infection. As consequence, it was observed low bacteremia, high survival and low systemic inflammation determined by levels of circulating cytokines and lung neutrophil sequestration. These results highlight the harmful role of TLR2 and TLR4 signaling in polymicrobial sepsis. (Financial support: FAPESP and CNPq) **Keywords: sepsis, Toll receptors, nitric oxide**