Inflammasome activation in platelets during sepsis

Ana Paula T Monteiro¹, Eugenio Hottz¹, Ligia Paiva¹, Fernando Bozza², Patrícia Bozza¹
¹Laboratório de Imunofarmacologia, IOC, Fiocruz/RJ; ²Laboratório de Medicina Intensiva, Instituto de Pesquisa Clínica Evandro Chagas (IPEC/RJ)

Infectious diseases are a world wide problem, and in this context bacteria and viruses have a significant role. Sepsis is a systemic inflammatory response syndrome with a confirmed infectious site. The platelet role in sepsis is mainly associated with disseminated intravascular coagulation. Platelets are anucleated cellular fragments originated in megakaryocytes, working primarily in coagulation. However a lot of attention has been given to the participation of platelets as inflammatory cells. The Nod like receptors (NLR) are a group of receptors associated with pathogens and cellular/tissue damage molecular patterns recognition. Several NLRs are implicated in inflammasome activation, a platform that culminates with caspase-1 activation. Caspase-1 activation leads up to IL-1β/IL-18 cleavage in its active forms and pyroptosis. Recently our group demonstrated that platelets from dengue patients can synthesize, process and release IL-1β through NLRP3 inflammasome. The aim of this study is to investigate the inflammasome proteins expression in platelets and its ability to assembly inflammasome during bacterial stimuli. In vitro and in vivo approaches were used, as did platelets from sepsis patient. Platelets were analyzed using flow cytometry and confocal microscopy. Platelets obtained from sepsis patients presented more NLRP3 and IL-1β expression and more caspase-1 activation, evaluated by FLICA assay. An in vivo model of sepsis, cecal ligation and puncture, presented the same pattern of expression. Confocal microscopy analysis of platelets from sepsis induced mice showed a co-localization of NLRP3 and ASC, an adapter protein. The in vitro stimulation of human platelets with E. coli e K. pneumoniae produced IL-1β, increased NLRP3 expression and caspase-1 activation. This data shows that platelets during sepsis can produce IL-1β and present an increase in NLRP3 expression. The in vitro data suggest that the bacterial stimulus is, at least partially, responsible for this activation.

Acknowledgements: CNPq, FAPERJ, Capes.

Key Words: Sepsis, platelets, inflammasome.