Role Of Adenosine Receptors And Glucose Concentration In Macrophages Response To *Staphylococcus Aureus* Antigens.

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Infectious diseases are among the majors causes of mortality around the world. The macrophages act in the phagocytosis of pathogenic agents and in the production of inflammatory mediators, like cytokines, matrix-metalloproteinases (MMP), reactive oxygen species (ROS) and nitric oxide (NO). Several studies has addressed the inflammatory response to gram-negative bacterial infections, however the gram-positive bacterial infections are poor studied, despite their prevalence and high mortality. Both adenosine and glucose are described to regulate inflammatory response in gram-negative bacterial infections models, but the role of these mediators in gram-positive bacterial infections is unknown. The objective of this work was investigate the role of adenosine receptors and increased glucose concentration in macrophages activation by *Staphylococcus aureus* antigens, considering that this bacteria is the main organism in hospital infections. The treatment of RAW 264.7 macrophages with *S. aureus* antigens lipoteichoic acid (LTA) and peptidoglycan (PEG) resulted in the production of pro-inflammatory mediators. LTA stimulated ROS, NO, TNF-α and MMP-9 production, meanwhile PEG increased TNF-α and MMP-9 production. Both LTA and PEG augmented A2A and A2B adenosine receptors expression and ATP degradation, resulting in increased adenosine accumulation. Pharmacological blockade of A2A and A2B adenosine receptors by antagonists resulted in exacerbated activation of macrophages by LTA. Similar results were obtained by the reduction of these receptors by RNA interference. In opposition, the stimulation of adenosine receptors by agonist treatment promoted reduced activation of macrophages by *S. aureus* antigens. The exposition of RAW 264.7 macrophages to increased glucose concentration resulted in augmented activation by LTA, with increased NO, TNF-α and MMP-9 production. Adenosine receptors seem to participate in an autocrine mechanism of inflammatory response regulation, suggesting a putative therapeutic target. The glucose modulation of macrophages inflammatory response could contribute to diabetes associated complications, like atherosclerosis and chronic inflammation.

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