POS-A23

PD en Biología Molecular y Biomedicina/Molecular Biology and Biomedicine

IDENTIFICATION OF BORRELIA BURGDORFERI PHAGOCYTIC RECEPTORS AND THEIR ROLE IN THE INFLAMMATORY RESPONSE

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Phagocytosis of Borrelia burgdorferi, the causative agent of Lyme disease, is a poorly understood process, despite its importance during the host immune response to infection. B. burgdorferi has been shown to bind to different receptors on the surface of phagocytic cells, including the β2 integrin, complement receptor 3 (CR3). In turn, phagocytosis is required for the full response of macrophages including the production of proinflammatory factors. In spite of its importance, little is known about the complement of receptors and signals that mediate the phagocytic internalization of B. burgdorferi. The identification of the full complement of phagocytic receptors and their pro/anti-inflammatory activity will allow us to define internalization alternatives associated to pro or anti-inflammatory routes and, in the future, devise novel strategies to increase phagocytosis without a consequent intensification of the inflammation. In order to identify signals that are involved in the early response of macrophages, my group performed a phosphoproteomic analysis (Phospho-Ser/Thr) of the murine macrophage-like cell line, RAW264.7, stimulated with live Bb. Analysis of the phosphoproteome identified the FcgRI-mediated phagocytosis pathway (KEGG pathway mmu04666) as a potential candidate. My thesis project aims to determine whether this pathway mediates the internalization of B. burgdorferi in macrophages and therefore modulates the inflammatory response to the spirochete. Furthermore, I aim to identify the ligand(s) present on the surface of B. burgdorferi that is/are recognized by these receptors We are also in the process of defining the role of other membrane receptors potentially involved in the phagocytosis of B. burgdorferi, with the aid of several 'omic' techniques, such as microarrays and high-throughput transcriptomics. The major objective is to identify the full complement of receptors that mediate the phagocytic internalization of the spirochete and their contribution to the inflammatory output of macrophages.