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Brucella virulence and pathogenesis, from bench to bedside

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Abstract

The complex immune system of mammals is the result of co-evolutionary forces that include battles against pathogens, as sensing and defeating intruders is a prerequisite to host survival. The various microorganisms have evolved multiple mechanisms to evade both arms of the immunity: the innate and the adaptive immune systems. The successful pathogenic intracellular bacterium Brucella is not an exception to the rule: Brucella displays mechanisms that allow evading immune surveillance in order to establish persistent infections in mammals leading to the brucellosis. Brucella is able to survive and replicate intracellularly in host cells by expressing several virulence factors, among them, the periplasmic cyclic glucan. This polysaccharide is built of a cyclic backbone of 17 to 25 glucose units in β-1,2 linkages (CβG). Brucella CβG was demonstrated to modulate lipid raft organization both at the plasma membrane of infected cells and intracellularly at the site of the Brucella-containing vacuole. CβG are expressed in large amounts, representing 1-5% of the bacteria dry weight.

Brucella glucans are agonists of the TLR4 signaling pathway, without contribution of CD14. Unlike LPS, they do not show endotoxicity both in vitro and in vivo. Brucella cyclic glucans are strong activators of human dendritic cells, promoting proinflammatory cytokine expression, antigen cross-priming, and cross-presentation to specific CD4+ and CD8+ T cells in physiological and pathological conditions. Thus cyclic glucans represent a new class of adjuvants. In addition, we will discuss about new ways to investigate human brucellosis.

Biography

Dr Jean-Pierre Gorvel has completed his PhD in 1986 from Aix-Marseille University and postdoctoral studies from the European Molecular Biology Laboratory (EMBL, Hedelberg, Germany). He is the Director of Research at CNRS, the largest Research organization in France and has directed several research entities in France and abroad. He has published more than 130 papers in reputed journals and serving as an editorial board member of several Journals and as Editor-in-Chief of Microbial Pathogenesis.