Intracellular Shigella remodels its LPS to dampen the innate immune recognition and evade inflammasome activation

Mon, 29/07/2013 - 13:13 — admin
Gruppo di Ricerca:
Ida Paciello

Lipopolysaccharide (LPS) is a potent bacterial effector triggering the activation of the innate immune system following binding with the complex CD14, MD-2 and TLR4. The LPS of the enteropathogen *Shigella flexneri* is a hexa-acylated isoform possessing an optimal inflammatory activity. Symptoms of shigellosis are produced by severe inflammation due to the invasion process of *Shigella* in colonic and rectal mucosa. Here we addressed the question of the role played by the *Shigella* LPS in eliciting a dysregulated inflammatory response of the host. We unveil that (i) *Shigella* is able to modify the LPS composition, e.g. the lipid A and core domains, during proliferation within epithelial cells; (ii) the LPS of intracellular bacteria (iLPS) and that of bacteria grown in laboratory medium (eLPS) differ in the number of acyl chains in lipid A, iLPS being the hypo-acylated; (iii) the immunopotential of iLPS is dramatically lower than that of eLPS; (iv) both LPS forms mainly signal through the TLR4/MyD88 pathway; (v) iLPS down-regulates the inflammasome-mediated release of IL-1β in *Shigella*-infected macrophages; and (vi) iLPS exhibits a reduced capacity to prime PMNs for an oxidative burst. We hypothesized that the two forms of LPS might govern different steps of the invasive process of *Shigella*. In the first phases the bacteria, decorated with hypo-acylated LPS, are able to lower the immune system surveillance, while in the late phases *Shigella* harboring immunopotent LPS are fully recognized by the immune system which can then successfully resolve the infection.

Anno del Convegno:
2013