Requirement for TLR9 in the immunomodulatory activity of Propionibacterium acnes.

Propionibacterium acnes (formerly Corynebacterium parvum) is part of the human flora and, as such, is associated with several human pathologies. It possesses strong immunomodulatory activities, which makes this bacterium interesting for prophylactic and therapeutic vaccination. The bacterial component(s) and the host receptor(s) involved in the induction of these activities are poorly understood. We show in this study that TLR9 is crucial in generating the characteristic effects of killed P. acnes priming in the spleen, such as extramedullary hemopoiesis and organ enlargement, and granuloma formation in the liver. Furthermore, the ability to overproduce TNF-alpha and IFN-gamma in response to LPS, lipid A, synthetic lipopeptide Pam(3)CysK(4), or whole killed bacteria was present in P. acnes-primed wild-type, but not TLR9(-/-), mice. Finally, P. acnes priming failed to induce enhanced resistance to murine typhoid fever in TLR9(-/-) mice. Thus, TLR9 plays an essential role in the induction of immunomodulatory effects by P. acnes. Because IFN-gamma is a key mediator of these effects, and enhanced IFN-gamma mRNA expression was absent in spleen and liver of P. acnes-primed TLR9(-/-) mice, we conclude that TLR9 is required for the induction of IFN-gamma by P. acnes.