Triacyl-lipopentapeptide adjuvants: TLR2-dependent activation of macrophages and modulation of receptor-mediated cell activation by altering acyl-moieties.

Abstract:
Synthetic lipopeptides derived from bacterial lipoprotein are efficient immunoadjuvants. In vitro they activate antigen presenting cells (APCs) to induce the translocation of nuclear factor kappa B (NF-kappaB) and the activation of further transcription factors. This results in the expression of genes encoding cytokines such as IL-1, IL-6, TNF-alpha and in the release of reactive oxygen/nitrogen intermediates. The molecular structure of microbial products determines TLR specificity and thus their activatory potential and immunoadjuvanticity. In the present study, we investigated the lipopeptide-induced activation of leukocytes at different cellular levels by applying derivatives of a synthetic lipopentapeptide-fatty acid library. Our results show that TLR2 plays a key role for the activation of bone marrow-derived macrophages (BMDMs) by lipopentapeptide derivatives and that the fatty acid composition of the lipopeptides determines their activation potential and TLR specificity.