LPS Peptide Mimics Induce NF-κB Translocation in Macrophages and are Specific for TLR-4

Adjuvants are considered as catalysts for activating the innate immune response directed against a particular antigen. The immune response is initiated when toll-like receptor (TLR) proteins on the cell surface recognize pathogen associated molecular patterns (PAMPs). One such PAMP, bacterial lipopolysaccharide (LPS), is known to cause septic shock when it binds TLR-4, initiating signal transduction that culminates with the translocation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) into the nucleus from the cytoplasm. NF-κB binds to its promoter, leading to the transcription of various cytokines, such as interleukin-1β (IL-1β), which are released into the extracellular matrix and result in inflammation. Controlling this inflammatory cascade via the TLR-4 pathway and the ability to regulate the immune response is an important characteristic of adjuvants. Use of synthetic peptides that functionally mimic LPS can cause localized inflammation necessary during an immune response, without the adverse effects of septic shock, and have the potential to be used as adjuvants in vaccines. PHAGE display technology was used to identify LPS peptide mimics by their reactivity with the LPS antibody and their ability to initiate this inflammatory cascade resulting in the translocation of NF-κB to the nucleus in the macrophage cell line RAW264.7. With the addition of inhibitor CLI-095, no translocation of NF-κB occurred, indicating that these peptides are specific to TLR-4. These TLR-4 agonists have the ability to be developed into a new class of adjuvants as they mimic LPS and can hence be considered as a PAMP or TLR-4 agonist.