

Adjuvants: Immunostimulatory

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Immune-potentiating adjuvants are thought to activate the **innate immune system** via **toll-like receptors (TLRs)** or **pattern recognition receptors (PRR)**. Cooperation between these two components is desirable in directing the balance of humoral and cell-mediated immunity associated with the acquired immune response.

Monophosphoryl lipid A (MPL)

MPL is a non-toxic component derived from **lipopolysaccharide (LPS)** of bacterial cell walls and interacts with **TLR-4** and **TLR-2**, inducing a **Th1-skewed response**. MPL is thought to directly **activate macrophages** resulting in the induction of **IFN- γ** and **IL-2**. However, it is not as potent at inducing antibody responses.

Unmethylated CpG dinucleotides

Unmethylated CpG dinucleotides are recognised by the innate immune system, as they are under-represented and methylated in vertebrate DNA. The immune response to unmethylated CpG has been linked in humans to the **activation of TLR-9**. Interactions result in the **maturation of dendritic cells**, **upregulation of MHC class II** to produce professional antigen presenting cells, **induction of Th1 cytokines** and triggering **B-cell proliferation**.

Saponins

Saponins are derived from the bark of a Chilean tree, *Quillaja saponaria*, so unlike other immunostimulatory adjuvants, is not pathogen derived. A highly purified fraction called **QS21** is a potent adjuvant for the induction of a **Th1-dominated response**, including CTLs. Saponins are thought to form pores in cell membranes that allow antigens to gain access to the **endogenous presentation pathway** resulting in presentation by MHC class I and hence CTL activation.

Cytokines

Cytokines can also be used directly to modify or redirect the immune response. However as they are proteins, they have a short half life and, are generally very expensive.