Overview of Part VI

- **Laser**
  - Laser vaccine adjuvant prior to vaccination
  - Laser enhances migration of dermal APCs
  - Patch vaccine delivery

- **Bacterial adjuvants**
  - From exo- and endotoxins
  - LPS-based adjuvants and lipid A analogons
  - Bacterial toxins for antigen delivery

- **Heat shock proteins**
  - Plants as biofactories
  - Self-adjuvanted antigens
  - Plant HSPs and their immune properties

- **Nanoparticles**
  - Liposome-based vaccines
  - Nanotechnology for pulmonary vaccine delivery
  - Nanoparticles as oral adjuvants

- **Alum and chitosan**
  - Formulation of aluminum-containing adjuvants
  - Molecular pathways and working mechanism
  - Chitosan, a carbohydrate polymer as adjuvant

- **Polymers**
  - From colloids to dendrimers
  - Favorable properties of nanoparticles
  - Controlled release strategies
A complete vaccine development does not stop at the antigen. Most antigens are poorly immunogenic and need the support of strong adjuvants. This counts for recombinant vaccines based on protein antigens but also for DNA vaccines. Neither pure protein nor naked DNA does really work. The essential pro-inflammatory response is triggered by adjuvants, activator and enhancer of the innate immune response. Adjuvant and antigen must form a perfect mix. Until now only two adjuvants are globally licensed for human vaccines. Unfortunately, research on vaccine adjuvants has so far received little attention. More efforts are necessary to develop innovative nontoxic adjuvants, especially for mucosal vaccine delivery.

Laser adjuvantation. Laser vaccine adjuvant (LVA) is based on a brief (2 min) laser illumination of the injection site prior to ID vaccination, which primes our body for a better response to the vaccine.

LPS adjuvants. The generation of new detoxified LPS species with higher adjuvant characteristics than alum and acceptable toxicity has opened new perspectives to the vaccination.

Bacterial toxins. Endotoxins as well as exotoxins have been exploited as adjuvants, mainly mutated toxins with ablated or reduced enzymatic activity or modified chemical structure to reduce their cytotoxic effects.

Plant heat shock proteins. The data evidence a general ability of plant HSPs of stimulating immune responses and shed light also on a more specific use of HSP-polypeptide complexes derived from plant tissues expressing recombinant antigens.

Functionalized nanoliposomes. It has become clear that the physicochemical properties of liposomal vaccines – method of antigen attachment, lipid composition, bilayer fluidity, particle charge, and other properties – exert strong effects on the resulting immune response.

Emerging nanotechnology. Development of dry powder-based vaccines can potentially reduce or may eliminate cold-chain requirements, promote sterility, and increase the overall stability of antigens and thus reduce the overall cost of the product.

Oral adjuvants. Concerning oral vaccination, a big challenge for the immune system is to reach the right equilibrium between tolerance and inflammatory response at mucosal level. The intestine is the largest lymphoid organ in mammals and contains more immune cells and the largest concentration of antibodies than any other organ including the spleen and liver.

Chitosan. In the search for new types of adjuvants, the carbohydrate polymer chitosan has gained increasing interest, due to its demonstrated immunostimulatory effect. Chitosan derives from the natural product chitin.

Aluminum-containing formulas. Currently, alum is still the only licensed vaccine adjuvant in the USA. In Europe, however, since the 1990s of the last century, MF59, an oil-in-water emulsion, MPL (monophospholipid A, an LPS analog) + alum, and AS03 are also approved for use.

New polymers. Nano-sized systems can be inorganic colloids, organic colloids (synthesized by emulsion polymerization or mini/nano-emulsion techniques), polymeric aggregates (micelles or polymersomes), core cross-linked aggregates (nanohydrogels, cross-linked micelles, or polyplexes), multifunctional polymer coils, dendritic polymers, or perfect dendrimers.