

Vaccine Developments

Alexander Badamchi & Adam Walters
Imperial College, London, UK



Whole Organism

One of the first reports of successful vaccination was by Edward Jenner in 1796. He noted that a crude isolate of cow pox virus prevented infection with potentially fatal and disfiguring smallpox. With this discovery the field of vaccinology was born and takes its name from *vacca*, the Latin for cow.



Jenner

1749-1823

Killed/inactivated

It was soon discovered that the pathogen needn't be alive to stimulate an immune response. Indeed, provided that it 'resembled' the viable organism a chemically or physically inactivated form of the organism could be used to vaccinate. A vaccine of this type is the inactivated Polio vaccine formulated by Jonas Salk in 1955.



Salk

1914-1995

Live Attenuated

By growing the pathogen outside its host it becomes adapted to these new conditions rendering it less able to infect the original host. This enables the immune system to mount a protective immune response. Maurice Hilleman developed many different vaccines using this approach including the measles, mumps and rubella vaccine (MMR).



Hilleman 1919-

2005

Toxoid

There are several pathogens that depend on a toxin in order to cause disease, e.g. tetanus and diphtheria. The toxin can be inactivated and formulated in a vaccine preparation to stimulate the production of antibodies which serve to effectively 'disarm' the bacterium.

Subunit

A subunit vaccine comprises of a defined antigenic component of a pathogen against which the immune response is stimulated. The subunits can be purified from the original pathogen, but increasingly are made as recombinant proteins. These vaccines have an excellent safety profile but generally are not as immunogenic as attenuated or inactivated vaccines and a need a stronger adjuvant. The recent HPV vaccine is an example of such a vaccine.

Conjugate Vaccines

Many bacteria are protected by an outer polysaccharide coat. Due to their presence on the surface of the bacteria they are attractive targets for the immune system but are usually poorly immunogenic. However, by synthesizing polysaccharides and conjugating them to an immunogenic carrier protein they can act as potent immunogens. Common conjugate vaccines include the HiB, meningitis C and pneumococcal vaccines.

Future

There are several diseases for which there are currently no vaccines, including HIV, malaria and TB. To develop vaccines for these diseases new strategies inducing the cellular and humoral arms of the immune system may need to be employed.

- **DNA Vaccines** – Early gene therapy attempts discovered immune responses directed against injected DNA and its transcripts. DNA vaccines can contain multiple antigens, are cheap and quick to develop.
- **Vectored Vaccines** – Several organisms such as bacteria and viruses can infect cells, they can induce an immune response which is similar to that required to control infection. Vaccine antigens can be vectored into host cells by replication deficient viruses such as Adenovirus and modified Vaccinia Ankara, or bacteria such as Salmonella inducing both B- and T-cell responses.
- **Reverse Vaccinology** – Using modern genome sequencing prospective vaccine candidates can be selected based on predicted immunogenicity