RECENT DEVELOPMENTS IN VACCINES

Development of vaccines along with that of antimicrobials is the major achievement of medical science. Vaccination has eliminated a large part of the infectious diseases that once killed millions of people. A report from the World Health Organization states that today vaccines prevent 2.5 million deaths per year: Every minute five lives are saved by vaccines worldwide. It is not difficult to imagine the impact of vaccination if we just think that in the 20th century smallpox alone killed 300 million people, and that no one dies from it today because the virus has been eradicated thanks to vaccination in 1978. Furthermore, thanks to new technologies, vaccines now have the potential of preventing and treating not only communicable diseases in all ages, but also non-communicable diseases such as cancer and neurodegenerative disorders.

The first typeS of vaccines were based on killed pathogens causative of that particular disease. But because these vaccines could not evoke cellular immunity, the effect was limited in scope and duration. This urged scientists to try live pathogens which were attenuated by chemical treatment or deletion of disease causing genes. These vaccines were very successful and still are but the problems such as reversion and cross reactions were a major issue which made them relatively unsafe and in some cases, led to a significant number of deaths. We now call these two types as traditional vaccines.

The advent of recombinant DNA technology in the late 1970s made it possible to safely transfer the genes of choice into suitable vectors which were either used as vaccines by themselves, or secreted desired proteins which were used as vaccines. Hepatitis B vaccine is prime example of this type of vaccines. Another revolutionary technology was the conjugation of bacterial capsular polysaccharides to carrier proteins to make polysaccharide antigens T-cell dependent and therefore immunogenic, especially in infants. This technology has already allowed the development of vaccines against Haemophilus influenza type B, meningococcus, and pneumococcus. Additional candidates, such as vaccines against group B Streptococcus (GBS) and typhoid fever, are in a late stage of development.

More recently, vaccines based on what is called "reverse vaccinology" have emerged. It is especially useful for those microorganisms which are difficult to grow. In this technique, the entire genomic sequence of pathogens is searched and genes of interest are selected. These genes are excised and used to prepare proteins to be used as vaccines. Reverse vaccinology technology has already allowed the development of vaccine against meningococcus B and advanced preclinical and clinical vaccine studies against several bacteria, including those resistant to antibiotics such as Staphylococcus aureus and E. coli are underway.

The next technology that is likely to profoundly change the way we make vaccines against viral infections is structural vaccinology. Information derived from the 3D structure of viral envelope proteins has been used to design antigens with improved immunogenicity and protection. An extraordinary example of this technology has been the ability to lock the F protein of RSV in the prefusion conformation leading to the development of a vaccine that was badly needed but was not available. Structure-based antigen design recently also hit another milestone, where, for the first time, a peptide epitope from RSV has been shown to induce functional neutralizing antibodies in nonhuman primates, provided that it is inserted into a scaffold that keeps the peptide in a conformation that is thermally stable and recognized with picomolar affinity by antibodies to the native protein.

Another exciting field is synthetic biology that has emerged as a new and potent way to make vaccines. Gene synthesis in the laboratory with less than 1 error in 10,000 bases has been recently used to make a vaccine seed for a potentially pandemic influenza virus in a matter of a few days instead of the typical 2–3 months needed with conventional technologies. The same approach was used to make a completely synthetic RNA vaccine able to induce protective antibody titers in preclinical models in less than 40 days after the discovery of the pandemic H7N9 virus.

It is worth mentioning that not all new and exciting technologies were successful. For instance, some initially promising technologies, such as vaccines based on antiidiotype antibodies, synthetic B- and T-cell epitopes, and DNA vaccines did not lead to vaccine licensure.

Among vaccines against non-communicable diseases, the most significant are those used against cancer. Today we know of two types of cancer. There are those induced by chronic infections, such as those of the stomach, caused by Helicobacter pylori; the liver, caused by human hepatitis B (HBV) and C (HCV) viruses; and the cervix, caused by human papillomavirus (HPV), as well as Burkitt lymphoma and nasopharyngeal caricinoma, caused by the Epstein–Barr virus. These can be eliminated just with vaccination against the infectious agent. HBV and HPV vaccines are already in use and are already preventing cancer. For cancers that are not associated with infectious agents—such as prostate, breast, colon, etc.—experiments in animal models suggest that early vaccination with properly delivered and adjuvanted self-antigens may induce immune responses able to kill the tumorigenic cells before they grow into large tumors. It is therefore possible to think that in the near future we may vaccinate people when they are in their 50s with vaccines that may delay several cancers for 10 to 20 years or even forever. Cancer therapy can also be improved by vaccination. A therapeutic vaccine against prostate cancer has already been licensed.

Finally, a new platform that is going to help all vaccines is the development of novel adjuvants. After a century when the only adjuvants licensed for human use were hydroxide and phosphate salts of aluminium (alum), the licensure of the new adjuvant MF59 has led to the improved effectiveness of seasonal influenza vaccines in the elderly and the creation of vaccines against pandemic influenza strains such as H5N1 or H7N9, that without adjuvants, are not effective. The potential of developing novel adjuvants has increased exponentially with the discovery of innate immune receptors such as Toll-like receptors (TLRs) and nucleotide-binding oligomerization domain-like receptors (NLR).

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