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Sommario/riassunto	Since variolation, conventional approaches to vaccine development are based on live-attenuated, inactivated or purified pathogen-derived components. However, effective vaccines against global health threats such as HIV, parasite infections and tumors are difficult to achieve. On the other hand, synthetic vaccines based on immunogenic epitopes offer advantages over traditional vaccines since they are chemically defined antigens free from deleterious effects. Additionally, in contrast to live-attenuated vaccines, they do not revert to virulence in immunocompromised subjects, and different from genetic vaccines, they do not involve ethical questions. Traditional vaccines contain PAMPs and induce strong immune responses, while recombinant vaccines are less potent. In spite of the immunogenic weakness previously attributed to epitope-based vaccines a synthetic vaccine containing a 17 amino acid-epitope of the Pseudomonas aeruginosa Type IV pilus exceeded the protective potential of its cognate protein composed of 115 amino acids. Therefore, the efficacy yield of a synthetic vaccine can be potentiated by using the proper combination of target epitopes. Recent advances in adjuvant development,

immunogen platforms for DNA vaccines and viral vectors also contributed to optimize immunogenicity. Another constraint to the use of epitope vaccines was their restriction to some MHC or HLA phenotypes. However, epitopes containing 20 or less amino acids of Plasmodium falciparum and Leishmania donovani bind to multiple HLA-DR and MHC receptors. Thus synthetic epitope vaccines may better meet the requirements of the regulatory agencies since they have lower costs and are easier to produce. The classical experimental approach for the development of an epitope-based vaccine involves the use of recombinant domains or overlapping 15-mer peptides spanning the full length of the target antigen, and the analysis of the induced antibody and/or T cell immune responses in vitro or in vivo. On the other hand, in silico tools can select peptides that are more likely to contain epitopes, reducing the number of sequence candidates. T cell epitope prediction dates back to 1980s, when the first algorithm was developed based on the identification of amphipathic helical regions on protein antigens. Since then, new methods based on MHC peptide-binding motifs or MHC-binding properties have been developed. The recent reverse vaccinology concept uses high-throughput genome sequencing and bioinformatics tools to identify potential targets of immune responses. The feasibility of this approach was shown for the first time in the design of a vaccine against Neisseria meningitides that is now in phase III clinical trials. In addition, different computational tools allow the determination of crucial gene(s) through comparative analyses between different pathogenic strains Alternatively, carbohydrates have been considered as key targets in developing safe and effective vaccines to combat cancer, bacterial and viral infections. Tumor associated carbohydrate antigens can be coupled covalently to protein carriers to target MHC receptors and improve immunogenicity and have reached already pre-clinical and clinical studies. In light of the recent availability of genomic tools, we believe that in the near future an increasing number of vaccine candidates, composed of defined epitopes, will be available for synthetic vaccines showing improved protection.