Conclusions

Description

Semi-synthetic approaches

In this section, a panel of strategies to overcome the problems associated to the semisynthetic protein-carrier approach has been presented. Still today, the lack of a fine TACA-protein conjugation control and the problems associated to the characterization of the resulting vaccine construct, together with other difficulties related to the inherent immunogenicity of protein carrier themselves penalize important aspects of protein-conjugated vaccines. Uniformity in terms of TACA display should be reachable and properly detectable since a reproducible and well characterizable vaccine construct impacts its effectiveness.

Highly immunogenic protein carriers can be replaced with different carriers (e.g. VLPs, GNPs, ZPSs), capable to give rise to T-cell dependent immune reactions and generate specific anti-hapten IgG antibodies with reduced toxicity and epitope suppression phenomena. A more tailored approach would allow for a better design of TACA-based anticancer vaccines by addressing both molecular and immunological aspects. For example, by introducing a multivalent TACA display, the enhancement of BCR clustering should translate in improved antigen uptake and processing. Also, the carrier, which has both the role of CD4+ epitope source and scaffold for the TACA’s display, can be reduced to its essential parts to provide a suitable and well-defined tool.

Fully-synthetic approaches

The fully-synthetic approach demonstrated that chemically defined vaccine constructs containing precise oligopeptide TH epitopes, chemically associated with TACAs as B-cell epitopes, could efficiently give rise to high titers of TACA-specific IgG antibodies, with similar efficacy than semi-synthetic vaccines.
In several studies, the produced antibodies demonstrated to be reactive towards human tumor cell lines, and the promising results reported in this section have inspired several other research groups to explore new possibilities in terms of multicomponent vaccine design.

The reliability of solid phase (glyco)peptide syntheses and the advances in the field of chemoselective ligations provided a panel of options for the assembly of different sub-units, facilitating the introduction of convenient antigenic elements ; such as the human universal PADRE epitope, reported to generate carrier-specific antibody response in less lower extent compared to a protein carrier.

The chemical design also allowed the replacement of natural TACA structures with analogs or mimics, able to generate IgG antibodies reactive with native TACAs.
The use of a non-immunogenic scaffold, which supports the versatile introduction of several elements in a convergent manner, represents a useful tool for optimizing the vaccine design in terms of sub-unit composition and multivalency. Examples of multivalent B-cell epitope display have also been reached through dendrimer-like scaffolds, liposome formulations, and self-assembling structures.