Supramolecular Design of Synthetic Vaccines and Injectable Biomaterials.

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Peptide secondary structures can be harnessed to design monomers capable of self-assembling into supramolecular polymers in aqueous media.[1,2] Decorating the surface with immunogenic molecular patterns results in pathogen-mimicking entities and potential vaccine candidates.[3] In the context of antitumor vaccines, the challenge is to overcome self-tolerance mechanisms to enforce an immune response against endogenous, tumor-associated glycopeptide motifs.[4] To this end, a co-stimulation of B cells with Th cells is mandatory, which we aim to achieve using a co-presentation of different epitopes and immunostimulating agents at the surface of multicomponent supramolecular polymers (**Fig.1**). Mucin 1 (MUC1) is well-known for undergoing alterations in O-glycosylation during tumorigenesis,[5] and is thus an excellent tumor-associated target structure for immunotherapy. In this contribution I focus on the use a fully synthetic glycopeptide from the MUC1 tandem repeat sequence. As T cell epitope we chose a small fragment from highly immunogenic tetanus toxin (p30). Additionally, an imidazoquinoline as potent TLR7/8 agonist,[6] was synthesized. These epitopes were conjugated to supramolecular monomers and mixed in aqueous solution to yield a polymeric vaccine formulation. High antibody titers of the IgG type were observed in C57BL/6 mice and FACS analysis confirmed the high binding affinity of the antibodies to T47D tumor cells. These results support the potential of this modular supramolecular platform approach for the development of glycoconjugate vaccines.

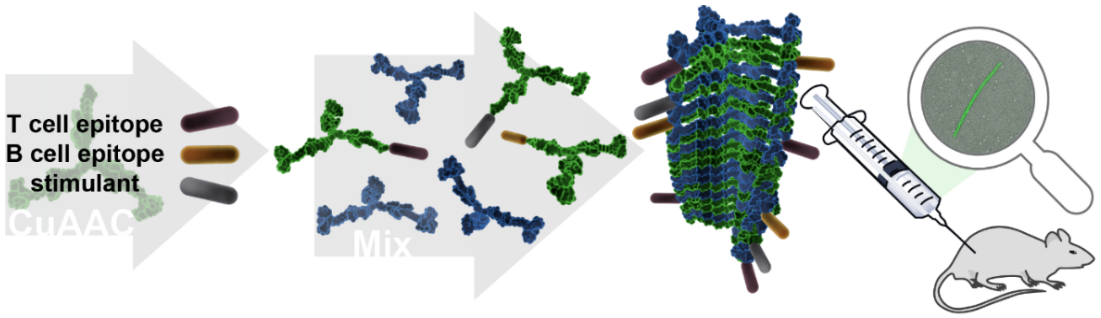

Figure 1. Schematic representation for the design of modular and multicomponent supramolecular vaccines.

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Pol Besenius was born and raised in Luxemburg, and studied Chemistry in Vienna and Glasgow. He received his PhD from the University of Strathclyde in Glasgow (2008) and undertook postdoctoral studies at the Eindhoven University of Technology, as Marie-Curie Fellow (2008-2011). He started his independent research group at the Organic Chemistry Institute at the University of Münster supported by a Liebig Fellowship in 2011, and moved to the Johannes-Gutenberg University of Mainz in 2015 to take up a W2-Professorship of Macromolecular Chemistry. In 2018 he was awarded an ERC Consolidator Grant, a visiting Faculty Program Fellowship at the Weizmann Institute of Science in 2020, and the Forcheur Jean-Marie Lehn Prize in 2022. Since 2018 he acts as Associate Editor for the newly launched Thieme journal 'Organic Materials'. In 2022 he was promoted to W3-Professor of Macromolecular Chemistry at the Department of Chemistry, Johannes-Gutenberg University of Mainz.