The Use of Artificial Glycopeptides for Cancer Vaccines and Diagnostic Tools

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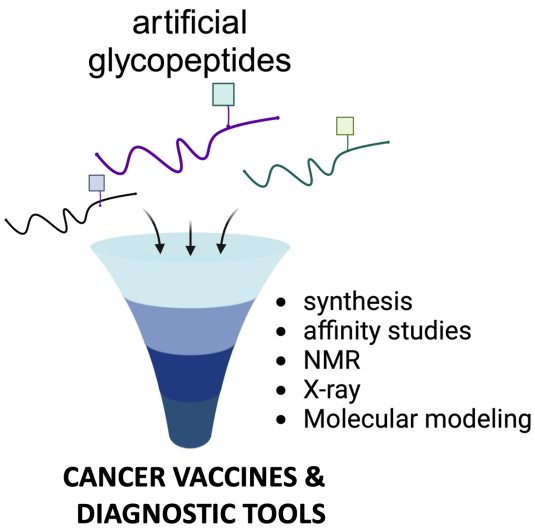
The glycoprotein mucin-1 (MUC1) is located on the surface of epithelial cells. In healthy tissue, MUC1 displays complex oligosaccharides characterized by branched and extended chains of glycans. In contrast, in cancer cells, glycosylated MUC1 residues exhibit altered *O*-glycan profiles where only simple or truncated glycan structures such as GalNAc (*N*-acetylgalactosamine) are attached to the MUC1 peptide scaffold. This change in glycosylation profile exposes different antigens of MUC1 that are otherwise hidden, such as the peptide sequence APDTRP or tumor-associated carbohydrate antigens, including the Tn antigens (α-*O*-GalNAc-S/T). Studies have shown that cancer patients can develop anti-MUC1 antibodies in the early stages of the disease, likely in response to these abnormal glycosylation patterns. Therefore, MUC1 is a promising target for cancer vaccine development and cancer diagnosis. [1,2]



Based on this premise, we have synthesized artificial MUC1 glycopeptides containing unnatural amino acids or modified carbohydrates. Our approach involves structure-based design to optimize the immunogenicity and stability of the glycopeptides using techniques such as NMR (nuclear magnetic resonance), molecular dynamics simulations and X-ray crystallography. These modified glycopeptides are then conjugated to gold nanoparticles or carrier proteins and serve either as cancer vaccines that elicit a robust immune response in mice or as diagnostic tools. [3,4] This presentation will describe several examples of these applications.

References

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