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ABSTRACT BOOK

INVITED LECTURE

Structure-Based Design of Glycopeptides with Applications in Cancer Therapy and Diagnosis

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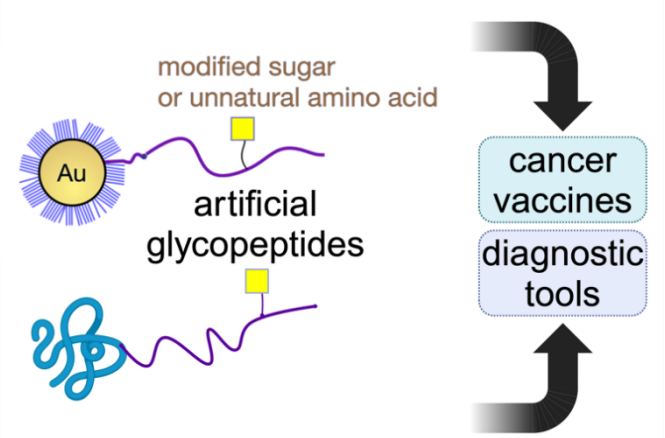
Mucin-1 (MUC1) is a glycoprotein that is highly *O*-glycosylated and expressed on the surface of epithelial cells. In healthy tissue, MUC1 has complex oligosaccharides, but in tumor cells its expression is upregulated, and the protein is decorated with simple and truncated carbohydrates. This altered glycosylation pattern exposes immunogenic peptide fragments and several tumor-associated carbohydrate antigens (TACAs) such as the Tn antigen (alpha-*O*-GalNAc-Ser/Thr), which can elicit a weak immune response.[1] Interestingly, recent studies have shown that early-stage cancer patients have anti-MUC1 antibodies, suggesting that this glycoprotein may be useful for cancer detection.[2] To exploit this potential, we have synthesized artificial MUC1 glycopeptides using a structure-based design, containing unnatural amino acids or modified carbohydrates. Our approach is based on the combination of NMR, molecular dynamics simulations, and X-ray crystallography to fine-tune the antigenicity and stability of the glycopeptides. We then conjugate these glycopeptides with gold nanoparticles or carrier proteins. These conjugates can be used as cancer vaccines that elicit a strong immune response in mice[3] or as diagnostic tools that effectively discriminate between pancreatic cancer patients and healthy volunteers, surpassing the sensitivity and specificity of other clinically used biomarkers.[4]



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