EFFECT OF GLYCOSYLATION ON MUCIN-LIKE PEPTIDES AND IMPLICATIONS FOR MOLECULAR RECOGNITION BY ANTIBODIES

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The mucin 1 (MUC1) is typically overexpressed and aberrantly glycosylated in cancer cells, showing truncated α-*O*-linked saccharides that behave as tumor-associated antigens. Consequently, MUC1 is one of the most promising targets for the development of vaccines to treat cancer (Figure 1).[1] In that respect, it is well known that the glycosylation favors the binding of these molecules to anti-MUC1 antibodies, which may explain why those vaccines based on unglycosylated MUC1-derived peptides fail to evoke a strong immune response. Notably, to date, the molecular basis of these observations remains unclear. There are a variety of likely mechanisms by which antigen glycosylation could influence antibody binding. The carbohydrate could be part of the epitope, [2] the carbohydrate could establish concrete,[3] but non-essential contacts with the antibody which alters affinity or the sugar could change the structure of the antigen.[4] Our group has a great experience in the conformational analysis of MUC1-like glycopeptides in both the free-state and in complex with antibodies.[3] The different mechanisms above-proposed will be discussed applying a multidisciplinary approach based on synthesis, NMR experiments, X-ray crystallography, binding studies and molecular dynamics simulations.

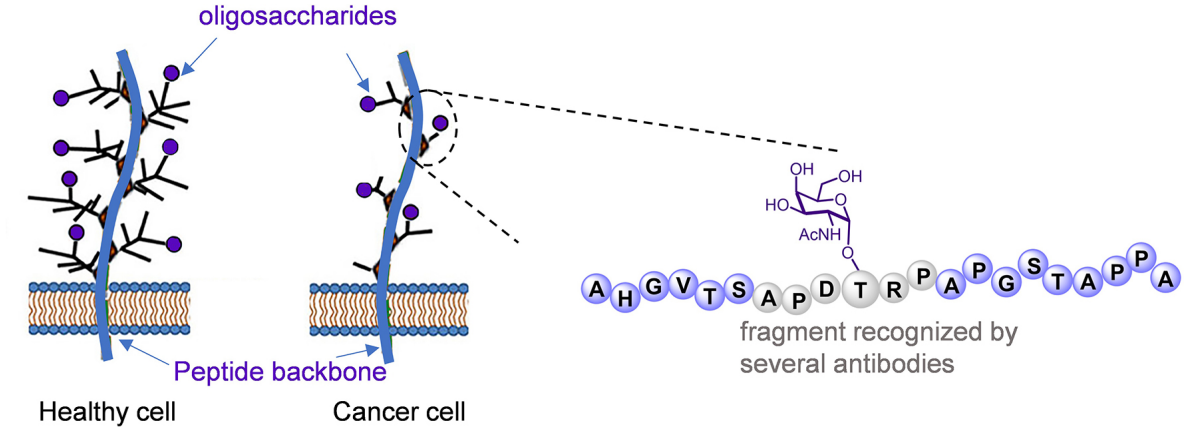

Figure 1. Structure of mucin MUC1 in cancer cells.

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