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ABSTRACTS BOOK

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Structure-based design of new MUC1 derivatives for detection of antibodies in patients with cancer

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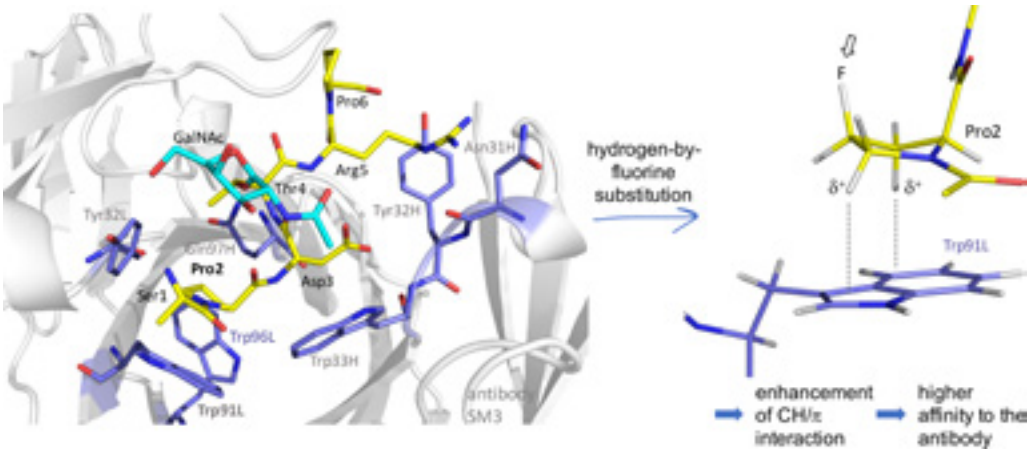
MUC1 is one of the most studied mucins because it is a glycoprotein overexpressed in around 80% of human cancers.[1] Recent studies[2] have demonstrated the presence of anti-MUC1 antibodies in patients who suffer cancer. Therefore, the design of MUC1-based antigens could be used as diagnostic tools for the detection of anti-MUC1 antibodies in human serum.

Within this context, our group has carried out the synthesis of two non-natural MUC1 derivatives featuring fluorinated proline residues.[3] These compounds present a notable enhancement in the binding affinity against two anti-MUC1 antibodies in comparison to the natural antigens and have been successfully used to improve the detection of low concentrations of cancer-associated anti-MUC1 antibodies from serum of patients with prostate cancer. According to X-ray studies and MD simulations, the fluorinated residues stabilize the antigen-antibody complex by enhancing fundamental CH/π interactions (Figure).



Considering the existence of other amino acids in the MUC1 that could be modified to enhance these CH/π interactions, we have synthesized several fluorinated amino acids and incorporated them into the MUC1 sequence to determine their binding affinity against anti-MUC1 antibodies.

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