Rational Design of a Molecularly Imprinted Polymer for Mucin 4 (MUC4) Biomarker

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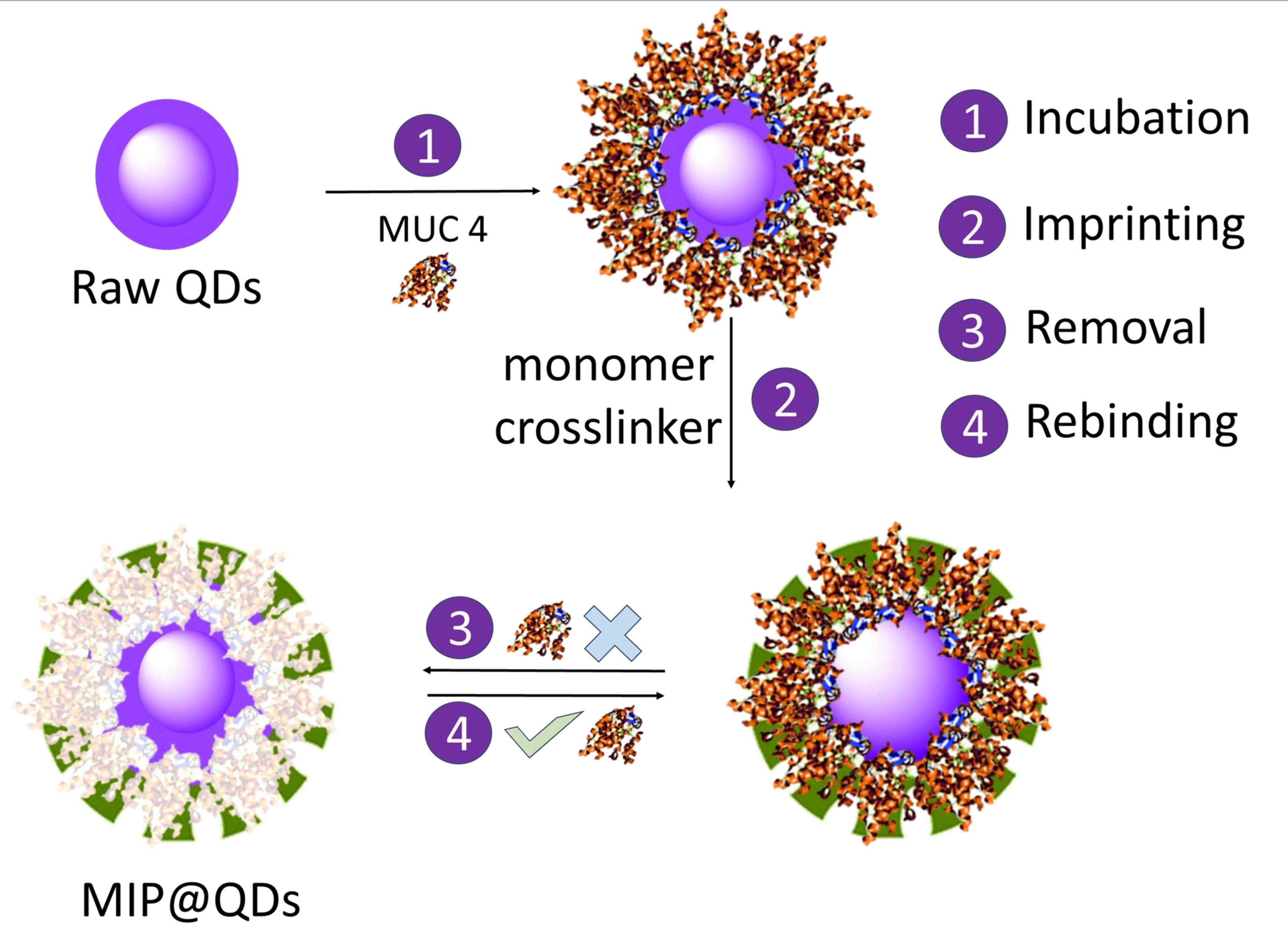
INTRODUCTION

Molecularly imprinted polymers (MIPs) were synthesized around quantum dots (QDs) to detect the protein biomarker MUC4, which is associated with pancreatic cancer(Kaur et al., 2022; Mehrotra et al., 2024). In this approach, MIPs serve as biorecognition elements and are conjugated with cadmium telluride QDs to form the sensing system. The fluorescence of these imprinted polymers is quenched as MUC4 concentrations increase, demonstrating a linear response within the range of 0.12 ng/mL to 16.9 ng/mL in human serum. This range is below the pancreatic cancer diagnostic cut-off values (1.2 to 1.3 ng/mL). The MIPs exhibit good stability and selectivity for MUC4 compared to non-imprinted controls. Additionally, theoretical studies provide valuable insights for the prediction the functional structure of MIPs, enhancing its selectivity for the target, while reducing time and costs associated with laborious benchtop assays, which may provide an effective tool for tailoring MIPs to other biomarkers for clinical diagnosis.

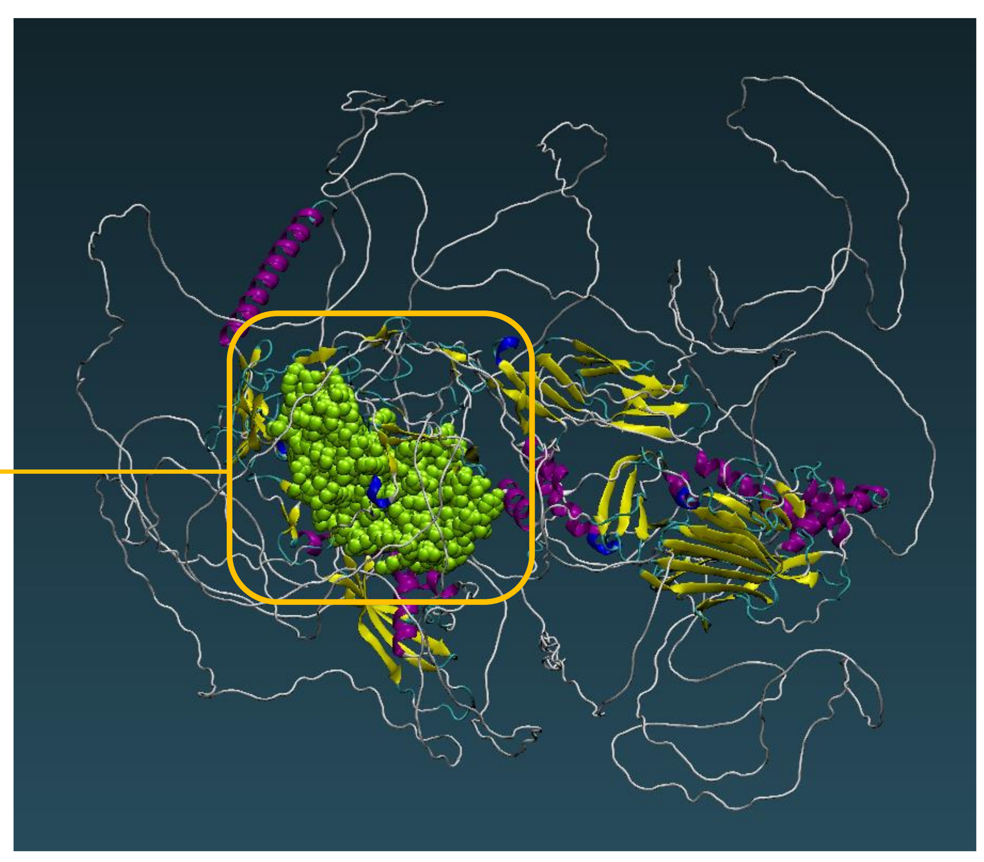
METHODOLOGY



RESULTS

Structure prediction

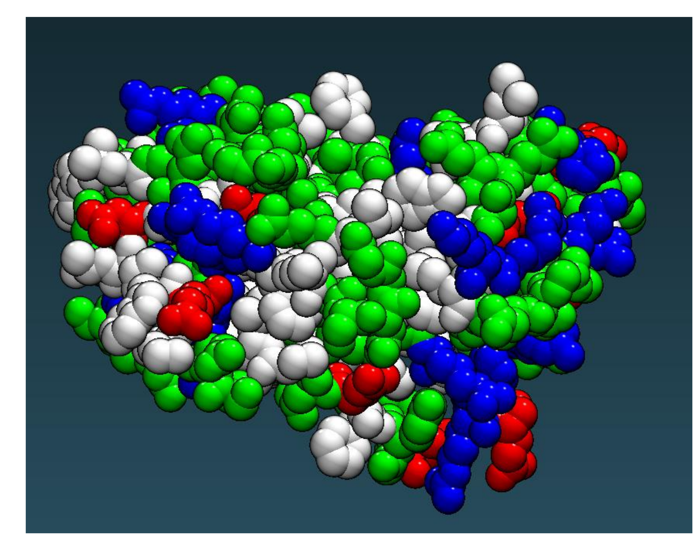
- MUC4 protein structure predicted: **ID AF-Q99102-F1**
- Confidence on the homology model in the tertiary structure : pLDDT > 80
- Sequence Fragment: Pro1154 to Glu1309
- Confidence on the homology model of the fragment: pLDDT > 90

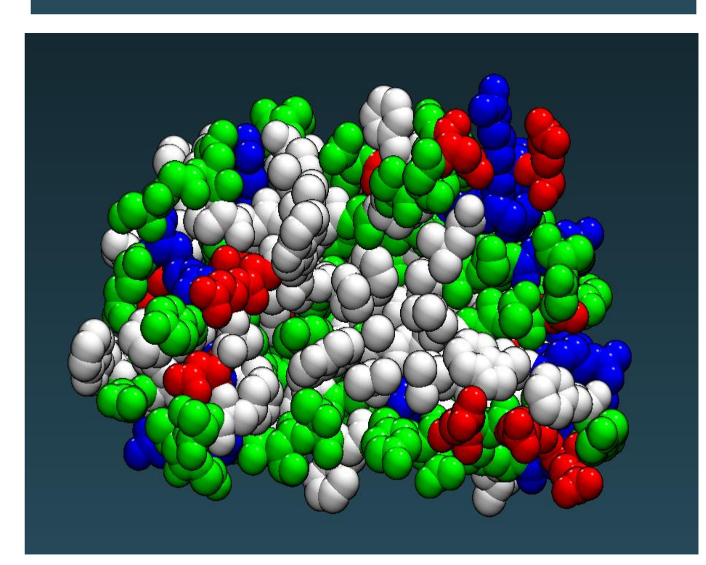


https://www.deepmind.com/open-source/alphafold-protein-structure-database

Protein Surface analysis

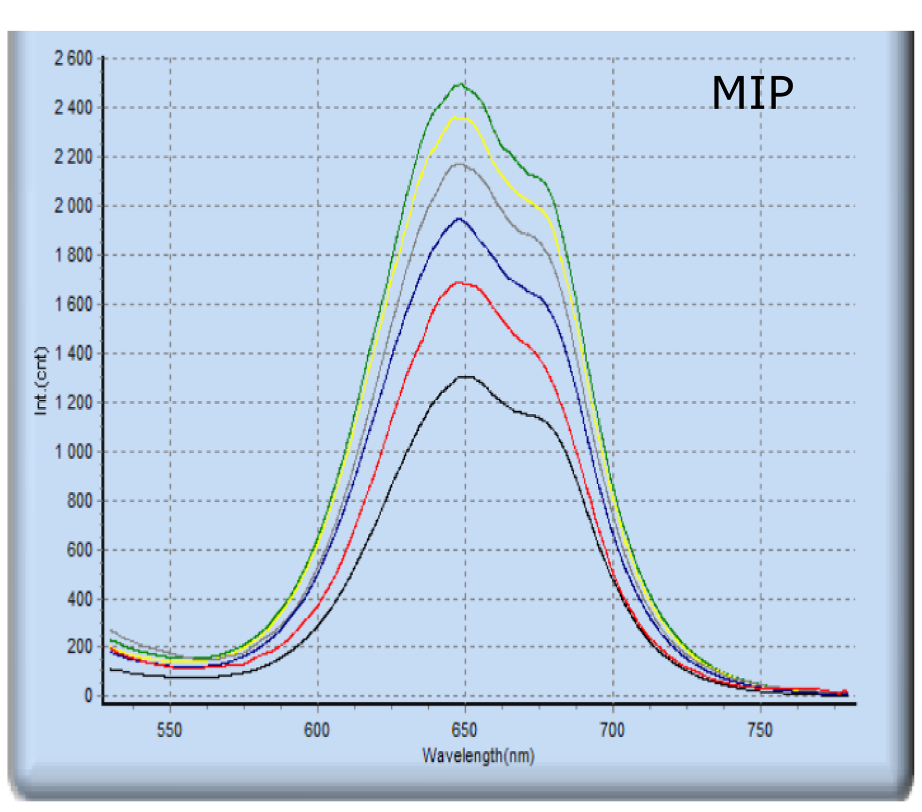
Confidence on the homology model of the fragment: pLDDT > 90
Total surface area = 9359.3A²
Positively charged residues =**13** (LYS, ARG)
Area exposed to the solvent: 1070 A²
Negatively charged residues =**14** (GLU, ASP)
Area exposed to the solvent: 1027 A²

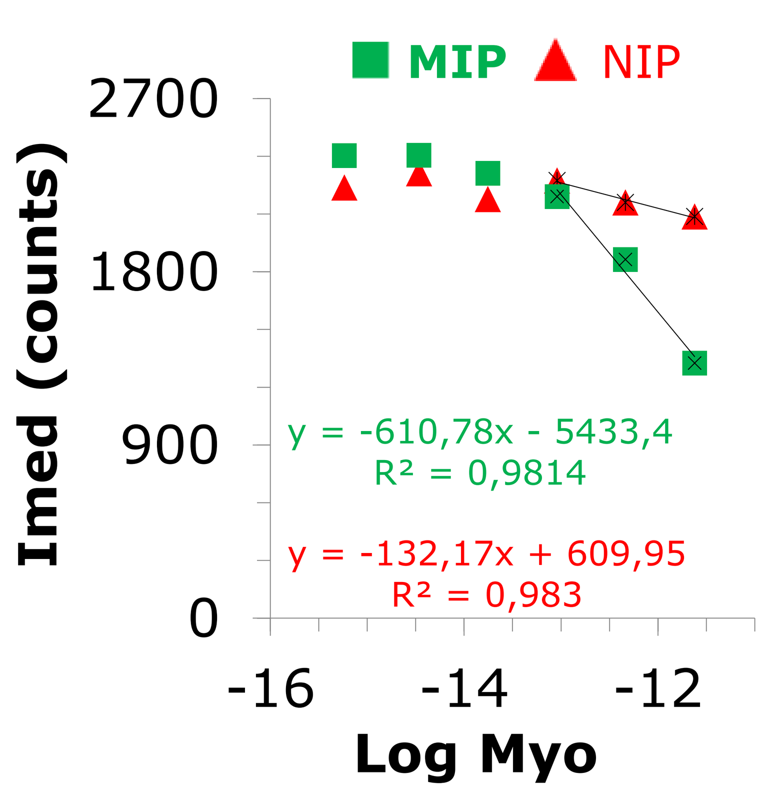




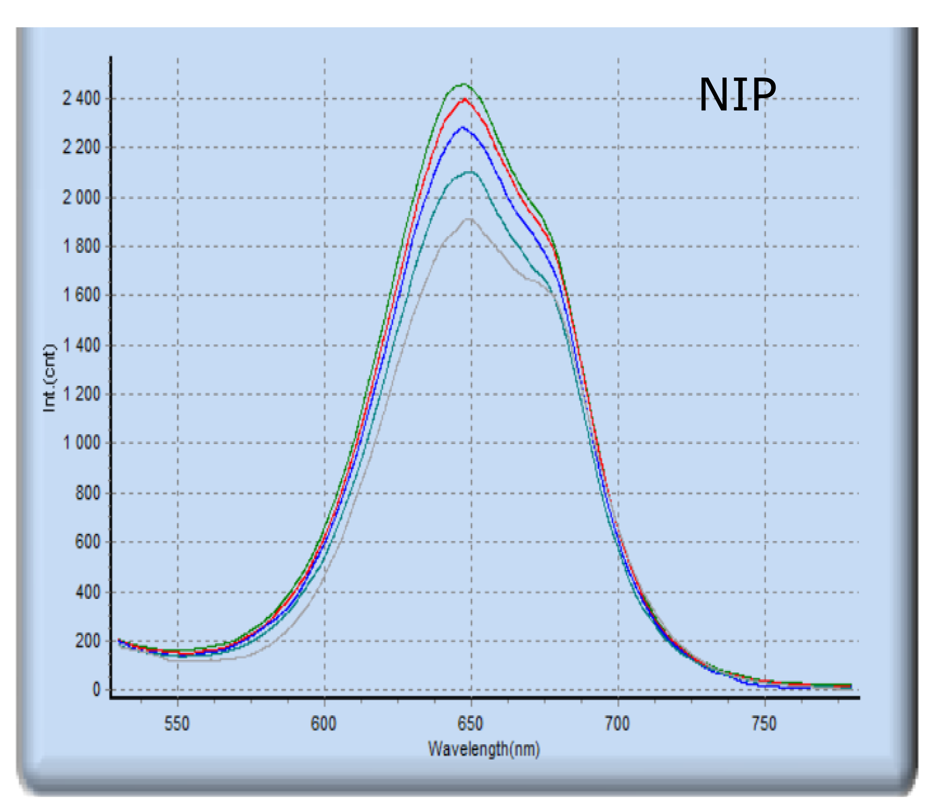
- Positively charged residues (Arg, Lys)
- Negatively charged residues (Asp, Glu)
- Polar residues (Tyr, Asn, Gln)
- Hydrophobic residues

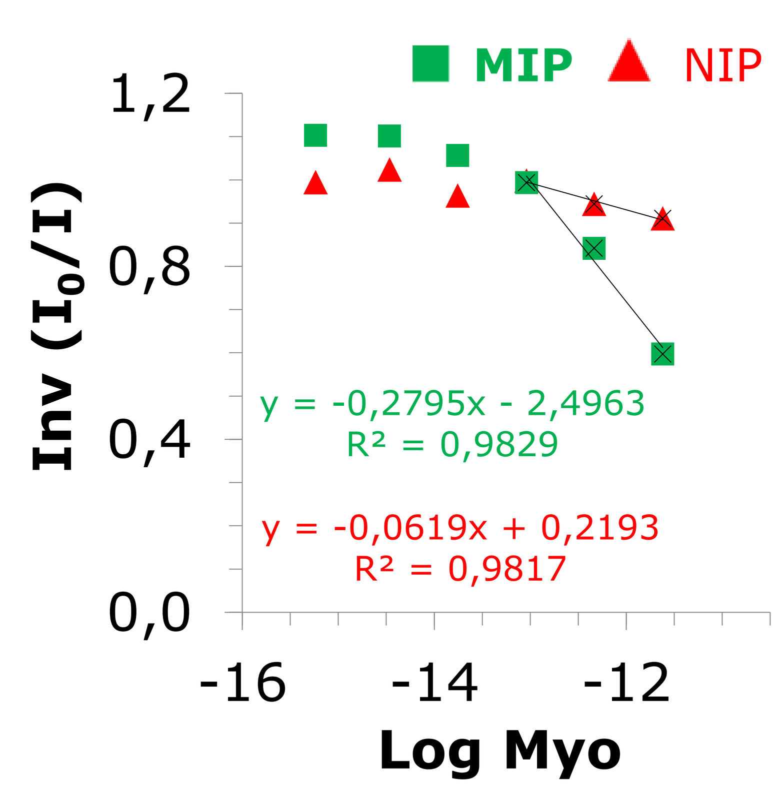
MIP calibrations





NIP calibrations





CONCLUSIONS

Rational design studies help reduce the time and costs associated with the assembly of MIPs. They can predict the optimal imprinting conditions for MIP assembly, enhancing selectivity by choosing the best affinity monomers and crosslinkers for MUC4. Experimental data showed that MIPs respond linearity to the MUC4 biomarker in human serum, below the cutoff range for clinical diagnosis, evidencing the applicability of MIPs to other biomarkers.

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