Targeting SARS-COV-2 Receptor Binding Domain with Stapled Peptides: An *In-Silico* Study

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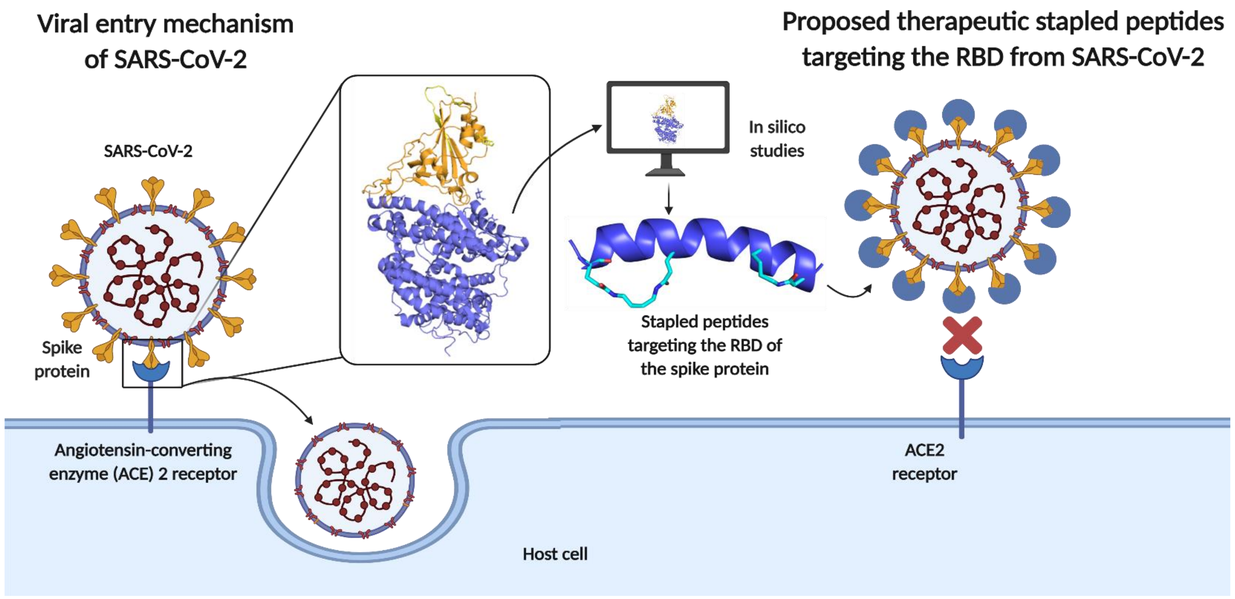
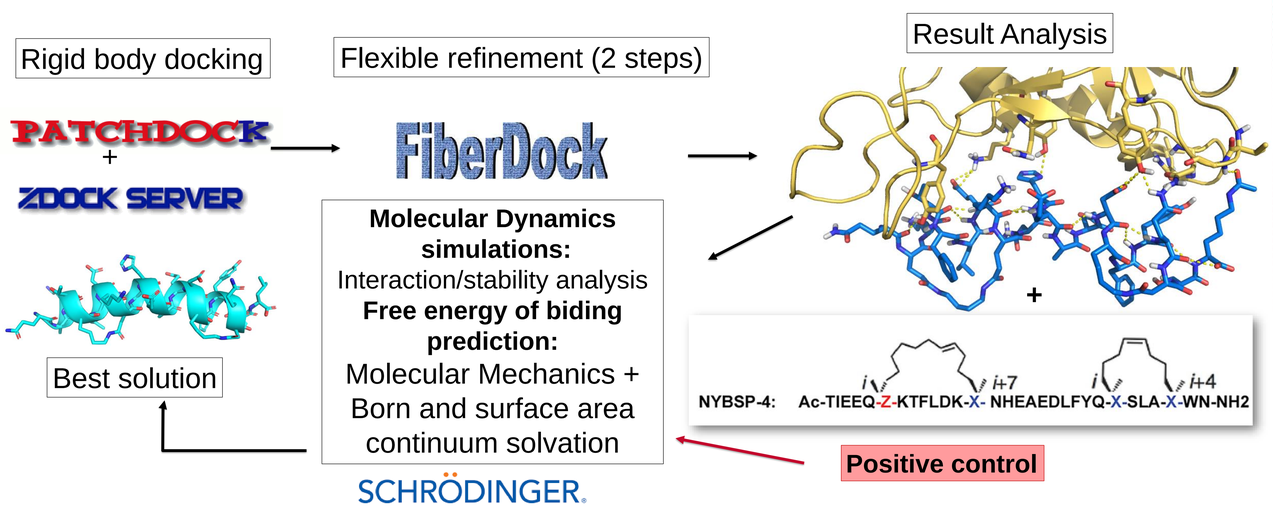
INTRODUCTION / AIMS



SARS-COV-2 enters cells by the interaction of the Receptor Binding Domain (RBD) with the human Angiotensin-Converting Enzyme 2 receptor (hACE2)[1]. In this study, we employed a rational structure-based design and diverse computational techniques aiming to propose 22-mer stapled peptides inhibitors using the structure of the hACE2 α1 helix as template.

METHODS



RESULTS

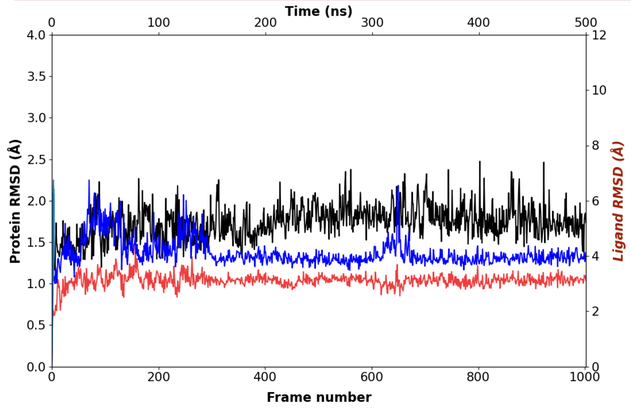


Figure 1. RMSD fluctuations showing a stable profile for Modification 15 (Mod15).

Table 1. Predicted free energies of binding of Mod15 and NYBSP-4 (positive control).

Peptide	ΔGBind
Mod15	-77.67 Kcal/Mol
NYBSP-4	-86.02 Kcal/Mol

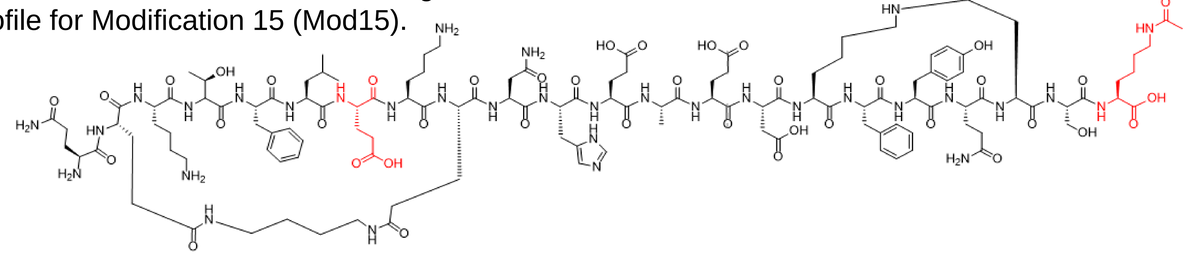


Figure 2. Modification 15 (2D-structure), best predicted stapled peptide inhibitor.

CONCLUSION

Using docking techniques and a refinement protocol we selected the most promising binders to further analysis using MD simulation and MM-GBSA free energy of binding prediction. According to our study we identified modification 15 as our best candidate. We predict this peptide can bind to SARS-COV-2-RBD with similar potency to the control NYBSP-4 (experimentally proven SARS-COV-2-RBD 35-mer peptide binder) showing the advantages of being a smaller peptide.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1 - Wang, C.; Horby, P. W.; Hayden, F. G.; Gao, G. F. *The Lancet* **2020,** *395* (10223), 470-473.

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