SPECIAL INTEREST GROUP
DRUG-DESIGN

IN SILICO ANALYSIS OF THE STRUCTURE AND BINDING SITE FEATURES OF THE 3CL PROTEASE FROM SARS-COV-2: PARAMETERIZATION FOR VIRTUAL SCREENING PROTOCOLS

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Introduction

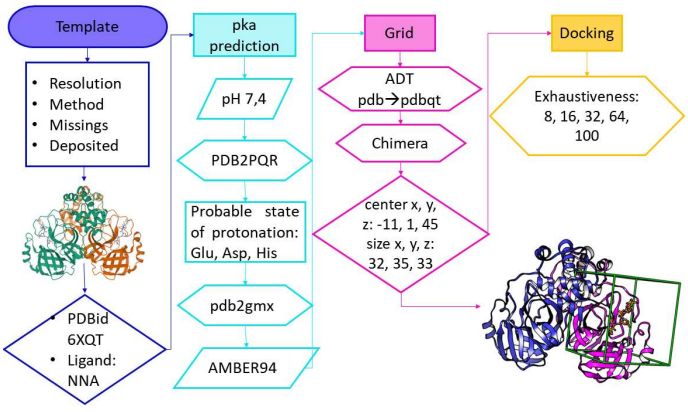
The new SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2) emerged at the end of 2019 as a global emergency. Due to its high rate of transmission and the absence of specific treatment or vaccine, around 1 million people over the world have died, according to World Health Organization until October 2020. Nowadays, thousands of people still get infected every day and many of them do not survive due to the complications of the disease associated with the acute respiratory syndrome. Thus, once the pharmacological therapy has shown to be deficient because of its non-specificity, this work intends to conduct an *in silico* research for possible drugs and bioactive substances, including those belonging to Brazilian biodiversity, that can act as inhibitors of the main viral protease (3CL^{pro}) for the treatment of COVID-19.

Objective

This project aims to prepare and parameterize the 3CL^{pro} protein from Sars-CoV-2 for future virtual screening methodology.

Materials and Methods

The workflow below represents the methodology used to develop this work.



Results and Discussion

The best mode of the redocking result (Table 1) promoted interactions with both the catalytic dyad residues, His41 and Cys145 (Figures 1 and 3).

Table 1: Best mode, docking energy value, RMSD value and exhaustiveness of the redocking of the 3CL^{pro} protease (PDBid: 6XQT).

Mode	Affinity for best distance mode (kcal/mol)	RMSD (Root Mean Square deviation)	Exhaustiveness
1	-10,4	0,97 Å	8

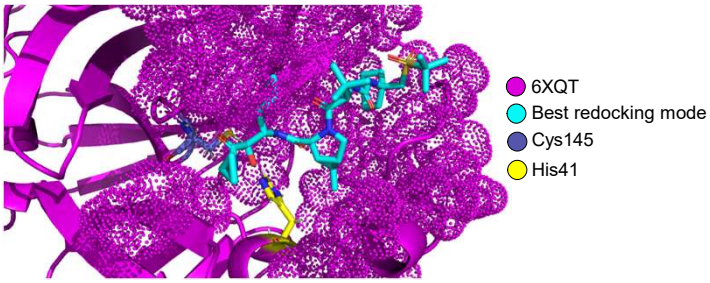


Figure 1: Dock image showing the interaction between the His41 and Cys145 residues of the 3CL^{pro} receptor protein (PDBid 6XQT) with the NNA ligand resulting from the redocking step. In mesh are the residues 5 Å of the ligand.

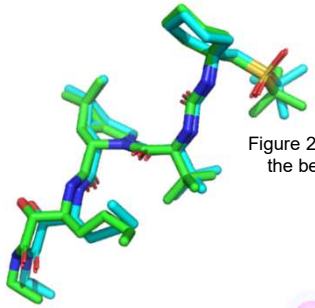


Figure 2: Overlapping of the NNA ligand and the best mode resulting from redocking.

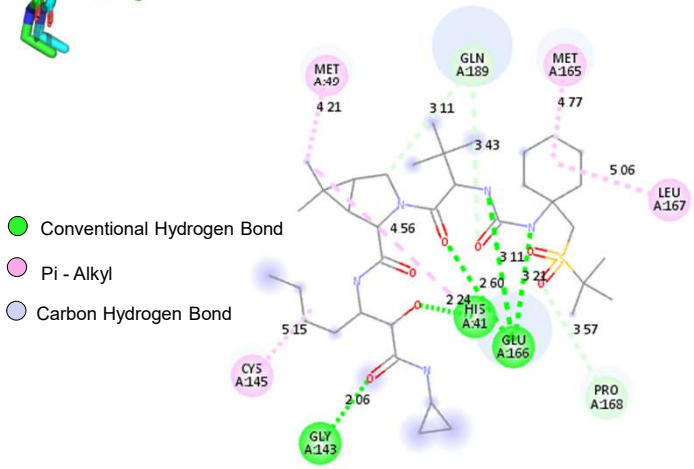


Figure 3: Interaction map of 3CL^{pro} protein residues (PDBid: 6XQT) with the NNA ligand.

Conclusion and Perspectives

It was possible to assess through the performed methodology the parameters for the next stage of virtual screening, whose results are under analysis.

Keywords

SARS-CoV-2; 3CL^{pro}; drugs.

References

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