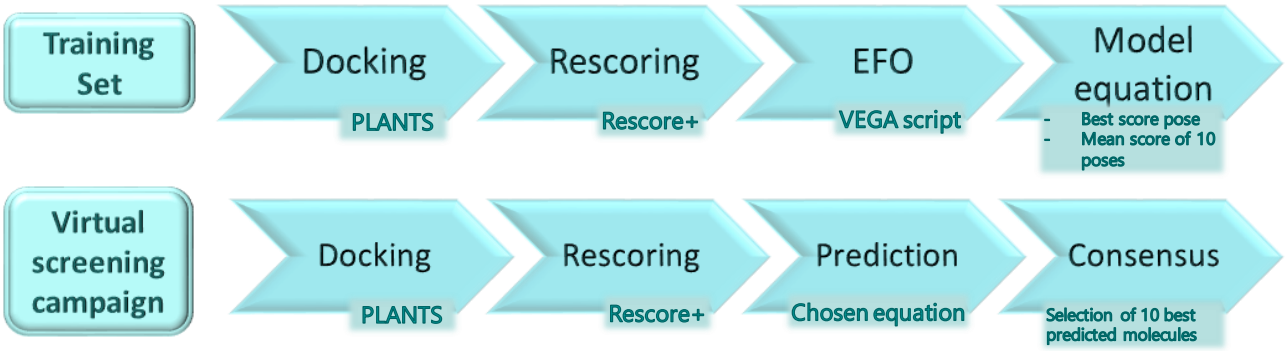
In silico prediction of NSP13 inhibition and virtual screening campaign

Team members:

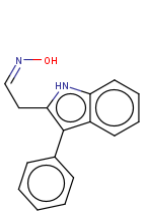
- Asma Alimolaei
- Elnaz Vojoudi Yazdi
- Fateme Sarhandi
- Riham Ibrahim
- Sara Shirvani
- Trishang Udhwani
- Zeinab Salehian

Workflow:



Results:

The first 10 molecules are listed below: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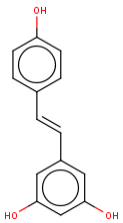
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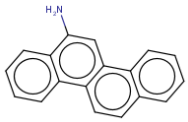
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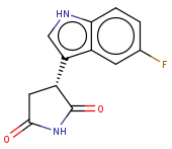
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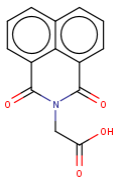
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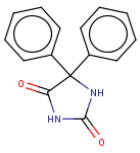
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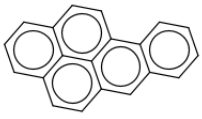
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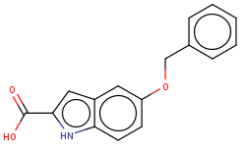
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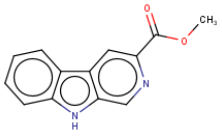
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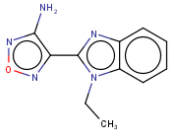
EOS102462

Methods

1. The protein structure (PDB ID 5RM2) was prepared for the following molecular docking studies.
2. The training set was collected including 1% of active molecules (experimental inhibitors of NSP13) and 99% of inactive molecules (decoys from ZINC database). In order to reduce the bias as much as possible, the ZINC database was filtered by considering the physico-chemical properties of the active molecules.
3. The training set was docked into the two binding pockets of NSP13 considering a neighborhood of the co-crystallised ligands.
4. Four predictive models were generated through EFO calculation and the chosen equation was used to predict the activity of OpenScreen dataset (which was properly cleaned and standardised).

Results

The four Enrichment Factors resulted in 50% and 60%, so the models can be considered robust.

The selected equations were used to discriminate which molecules are predicted as active and which molecules are predicted as inactive among OpenScreen dataset. A consensus study was done in order to cross-check the four predictions and to find the best overall results.

In the following diagram, there is the summary of the selection made: