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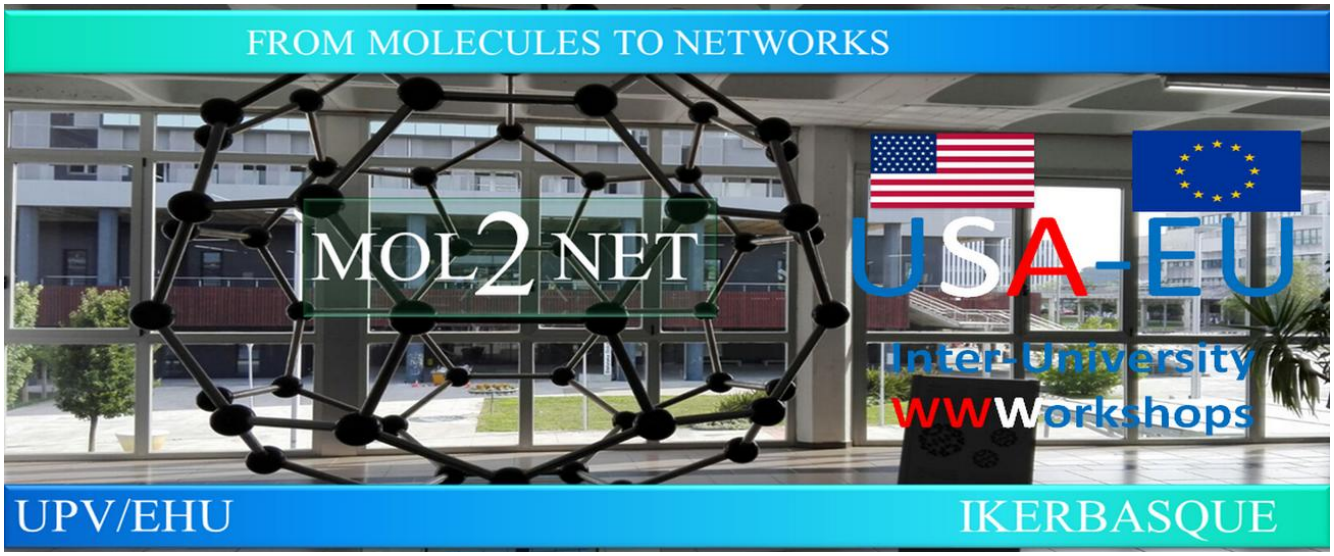

QSARINS Based Computational Identification of SARS-CoV-2 Main Protease Inhibitors

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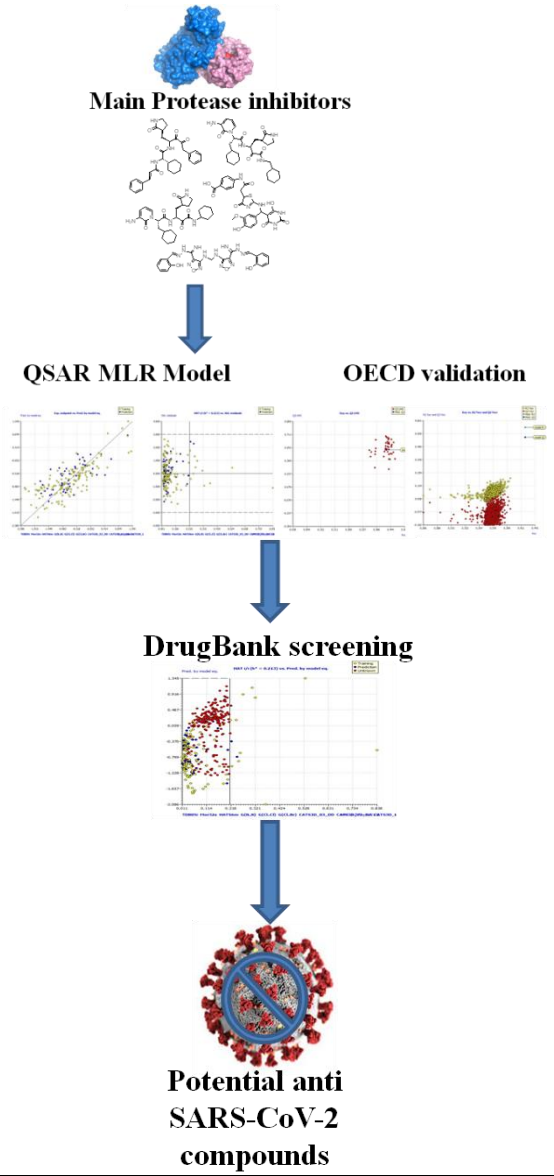
Graphical Abstract



Abstract.

The novel coronavirus SARS-CoV-2 responsible for COVID-19, for which there is no vaccine or any known effective treatment created a sense of urgency for novel drug discovery approaches. One of the most important COVID-19 protein targets is the 3C-like (main) protease for which the crystal structure is known. In this study, we used QSAR methodology to identify compounds with potential inhibition activity for 3C-like protease. First we collect a dataset of 204 compounds, with experimental report of inhibition against SARS-CoV main protease, to develop a predictive model, using Multiple Linear Regression and a Genetic Algorithm for the selection of variables, implemented in the QSARINS software. The model was assessed and validated using the OECDs principles. The best model showed good value for the determination coefficient (R^2=0.61), and others parameters were appropriate for fitting (s=0.47 and $RMSE_{tr}$=0.45). The validation results confirmed that the model has good robustness (Q^2_{LOO}=0.53) and stability (R^2–Q^2_{LOO}=0.08) with low correlation between the descriptors (K_{XX}=0.41), an excellent predictive power (R^2_{ext}=0.54) and was product of a non-random correlation (R^2_{Yscr}=0.06). This model is employed for the virtual screening of the Drug Bank database and several compounds, which belong to the applicability domain of the models, were identified as potential 3C-like protease inhibitors and proposed to further experiments to corroborate the predicted activity.

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