
# XXVI National Meeting in Medicinal Chemistry

## XII Young Medicinal Chemists' Symposium

# ABSTRACT BOOK

# TOWARD ENRICHED *VHTS* FOR CDK2 INHIBITORS: MOLECULAR DYNAMICS, PHARMACOPHORE MODELLING, AND DOCKING

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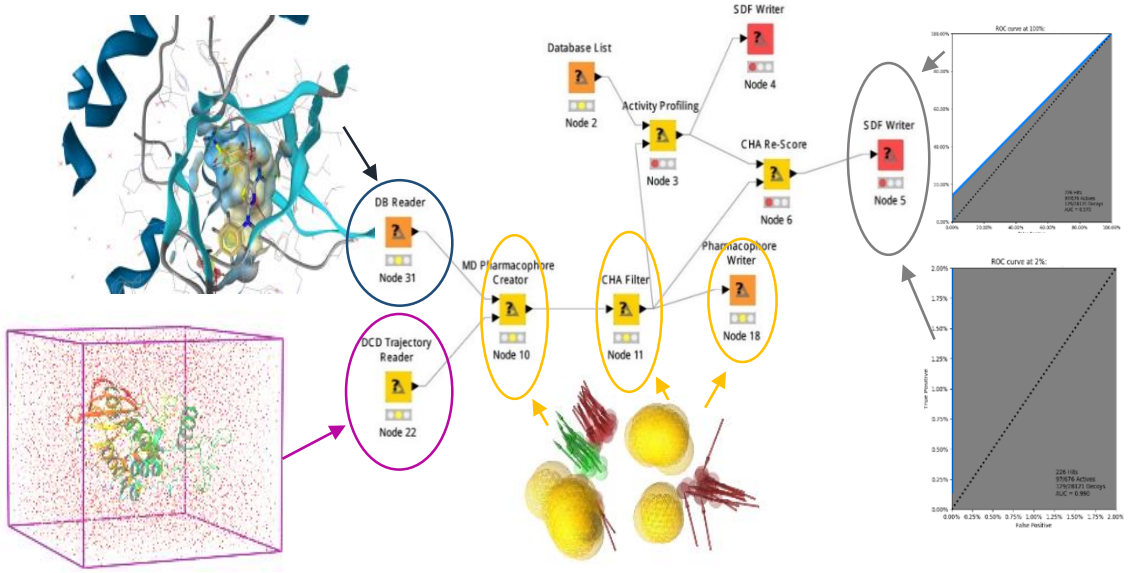
Cyclin-Dependent Kinases-2 (CDK2) are members of the serine/threonine protein kinases family. They play an important role in the regulation events of the eukaryotic cell division cycle, especially during the G1 to S phase transition. Experimental evidence indicates that excessive expression of CDK2s should cause abnormal cell cycle regulation. Therefore, since a long time, CDK2s have been considered potential therapeutic targets for cancer therapy. In this work, we collected one-hundred and forty-nine complexes of inhibitors bound in the CDK2-ATP pocket submitting to short MD simulations (10ns) and free energy calculation by means of MM-GBSA. The calculate ΔG values have been compared with experimental data ($K_i$, $K_d$, and $IC_{50}$). Information collected on short MD simulations of protein-ligand complexes has been used to perform molecular modeling approaches that incorporates flexibility into structure-based pharmacophore modeling (Common Hits Approach, CHA,[1] and Molecular dYnamics SHAred PharmacophorE, MYSHAPE[2] approach) and constraints docking, to enrich the hits list of virtual screening. Short simulations proved to be exhaustive to examine the crucial ligand-protein interactions within the complexes.




## References

1. Wieder, M.; Garon, A.; Perricone, U.; Boresch, S.; Seidel, T.; Almerico, A.M.; Langer T., "Common Hits Approach: Combining Pharmacophore Modeling and Molecular Dynamics Simulations", *J. Chem. Inf. Model.* **2017**, *57*, 365-385.
2. Perricone, U.; Wieder, M.; Seidel, T.; Langer T.; Padova, A.; Almerico, A.M.; Tutone, M., "A Molecular Dynamics-Shared Pharmacophore Approach to Boost Early-Enrichment Virtual Screening: A Case Study on Peroxisome Proliferator-Activated Receptor α", *ChemMedChem* **2017**, *12*, 1399-1407.