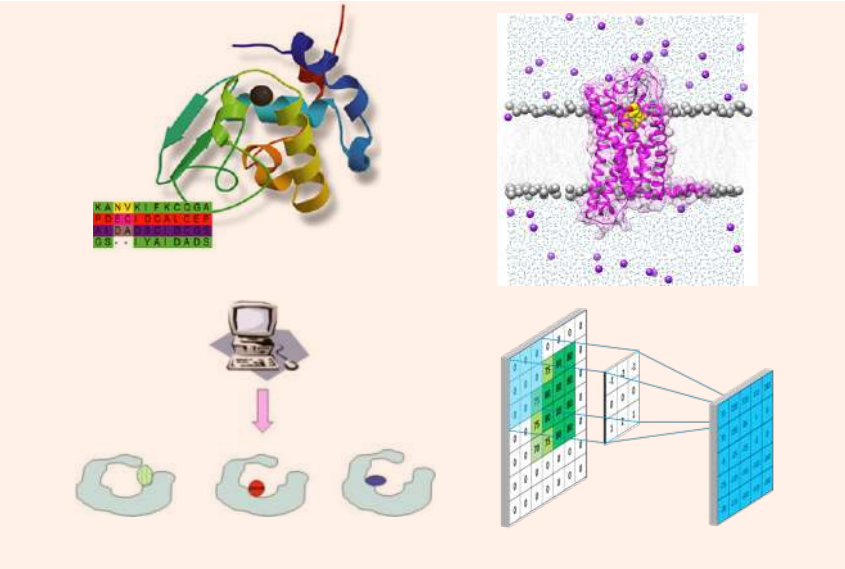
Computational Modeling of Protein-Ligand Interactions



Hao FAN

https://web.bii.a-star.edu.sg/~fanh

https://www.a-star.edu.sg/bii/research/bsmd/sldd

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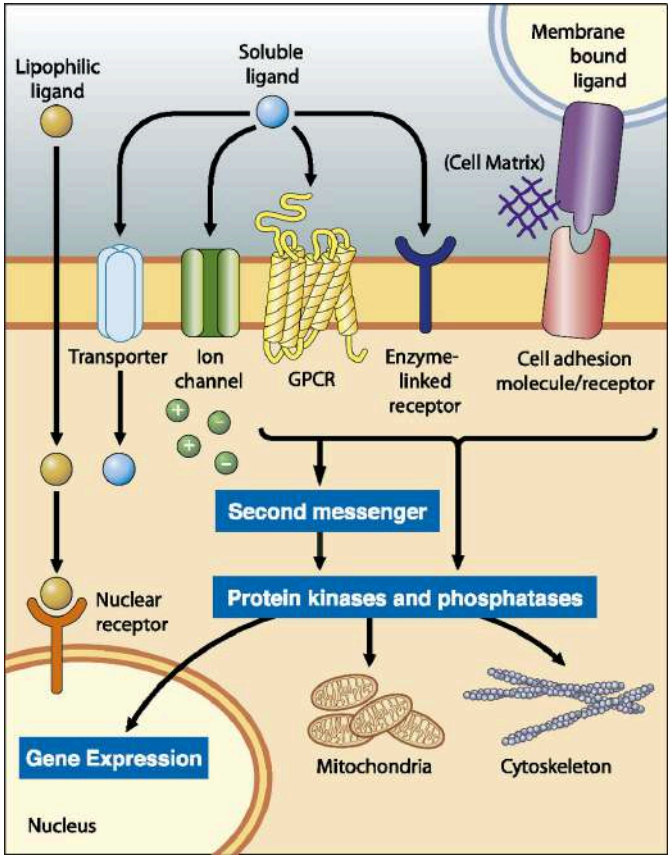
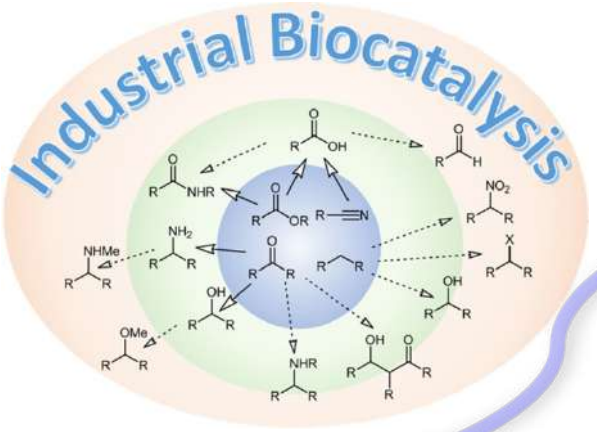
Mechanism – Engineering – Discovery – Safety

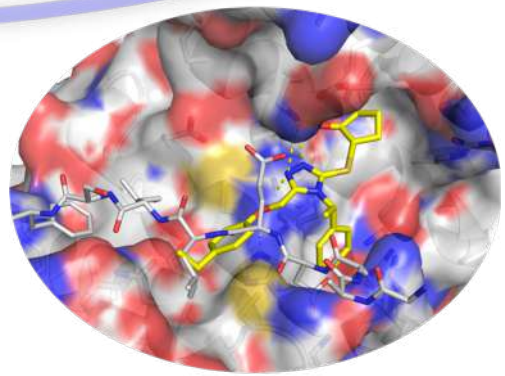


Structure & Function Mechanism

Enzyme Engineering

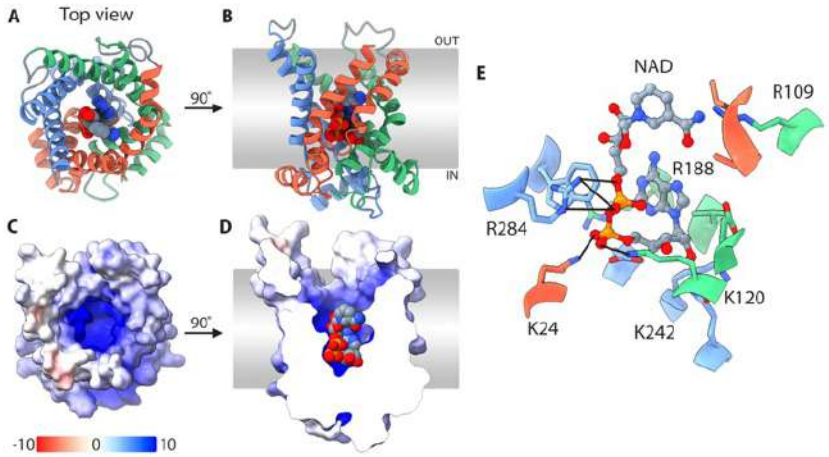


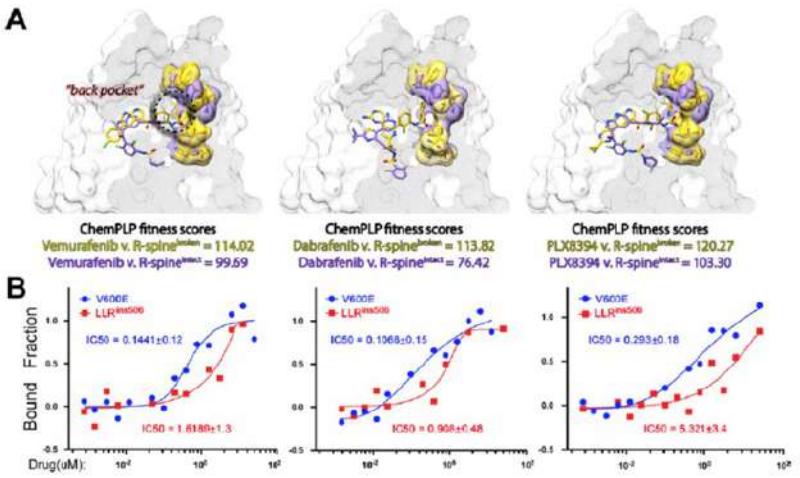
Chemical Safety

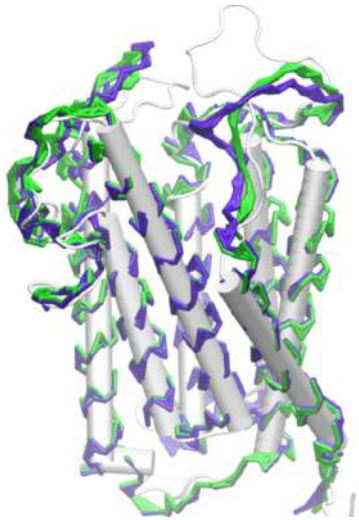


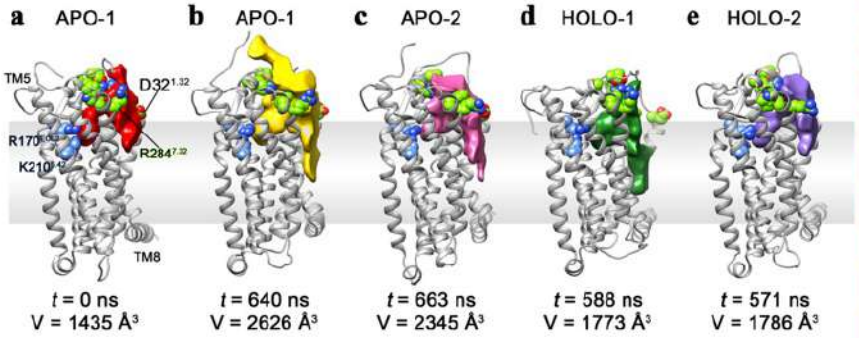
Ligand Discovery

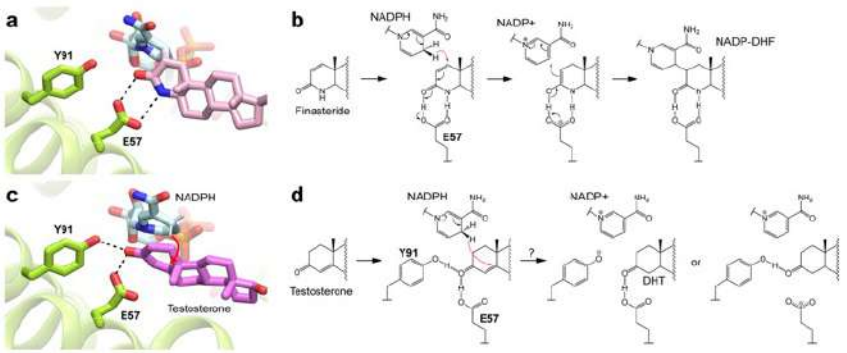
Structure & Function Mechanism (Pittsburg, Tsinghua, DUKENUS)



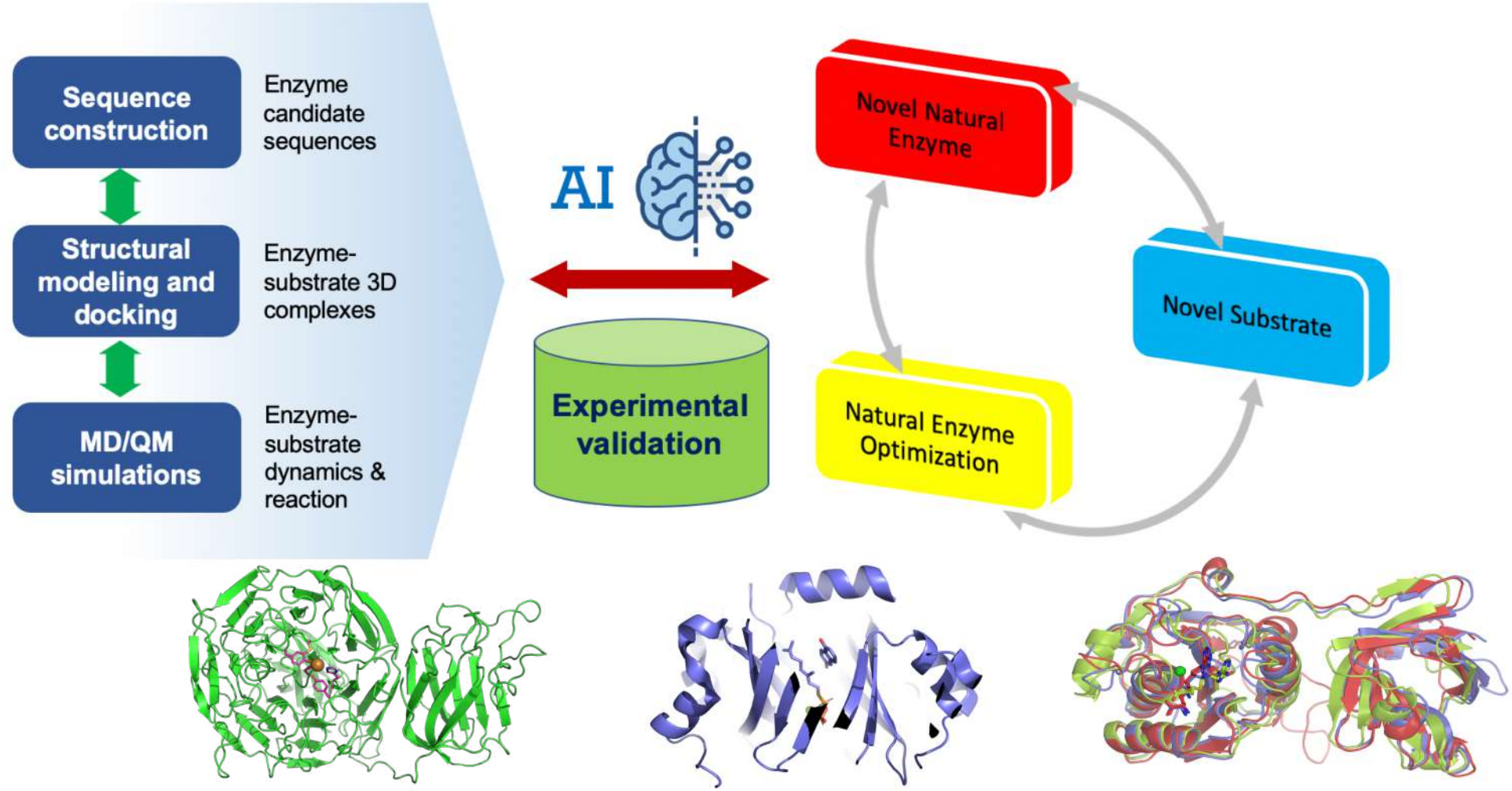




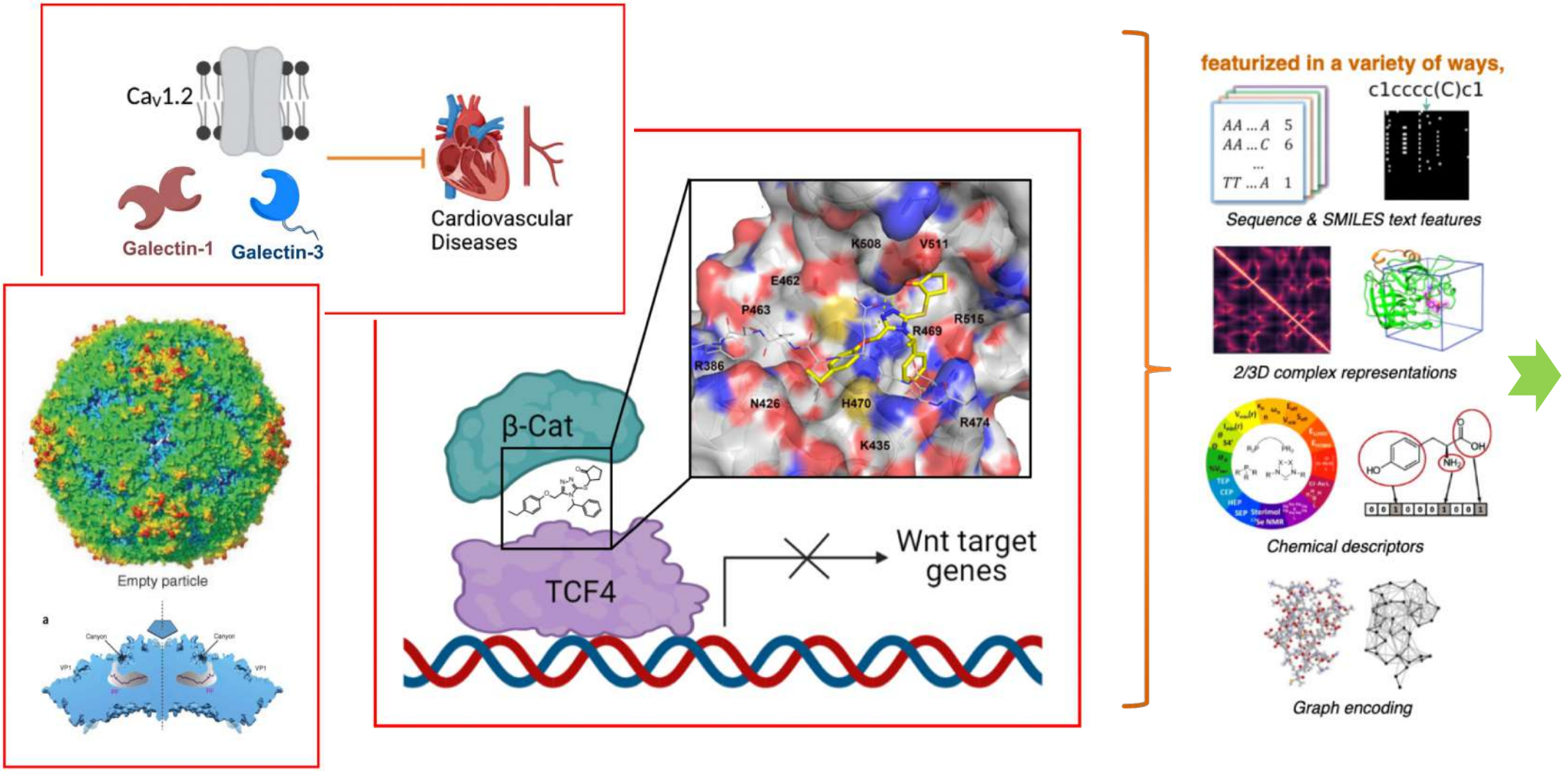




Enzyme Engineering (NUS, BII, ISCE2, SIFBI)

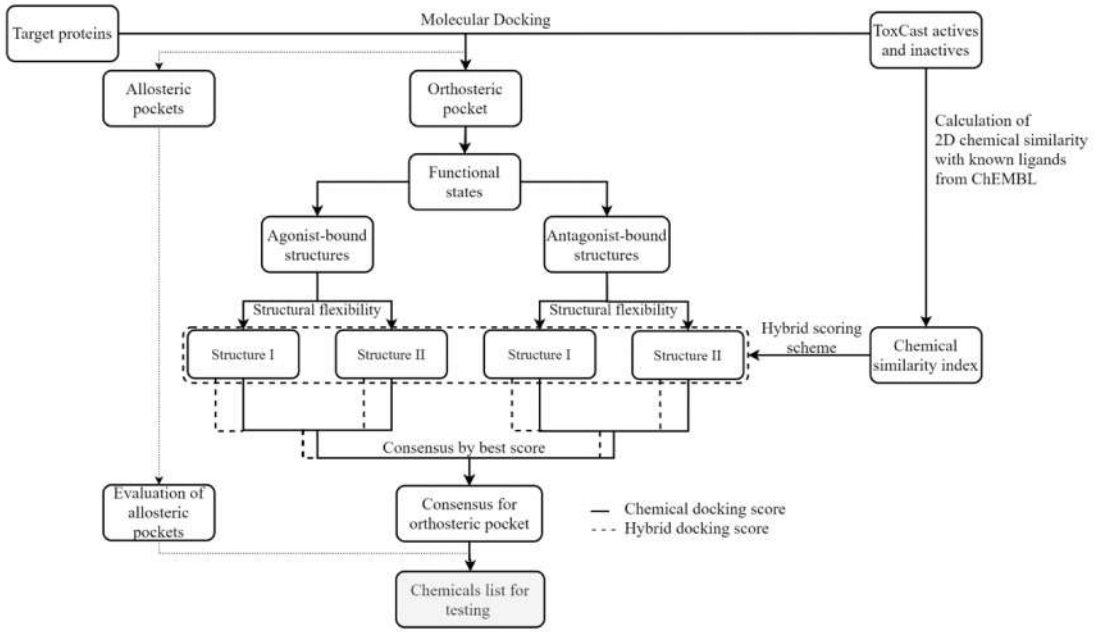


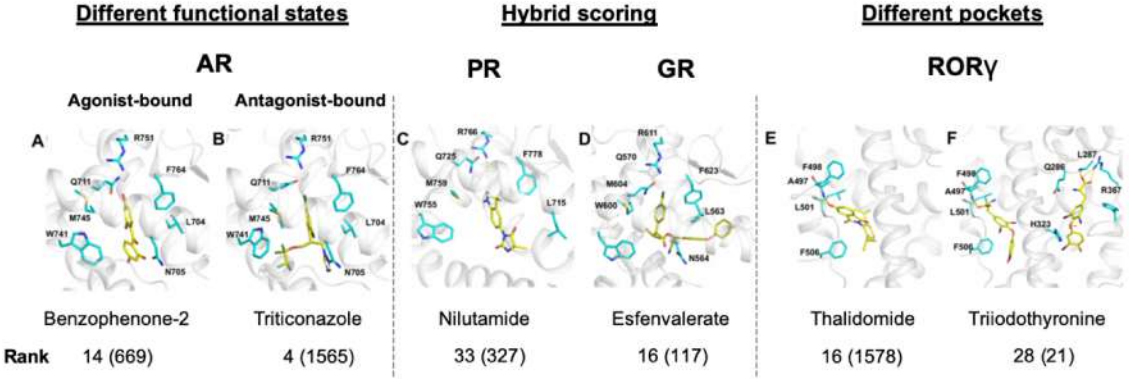
Ligand Discovery (GIS, NCCS, NUS, BII)

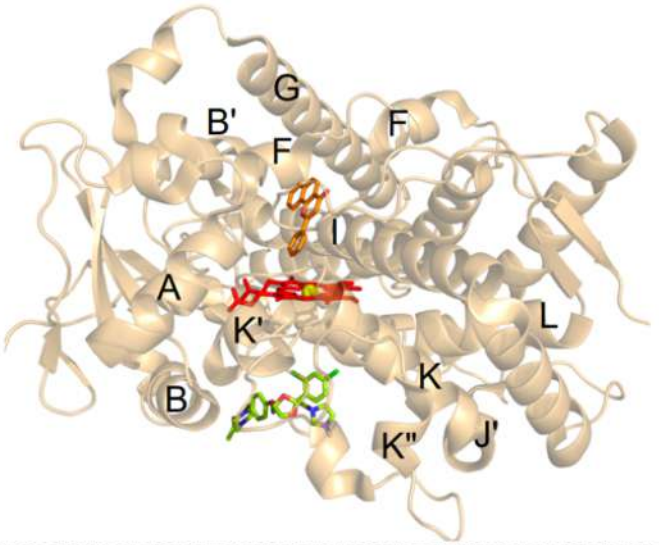


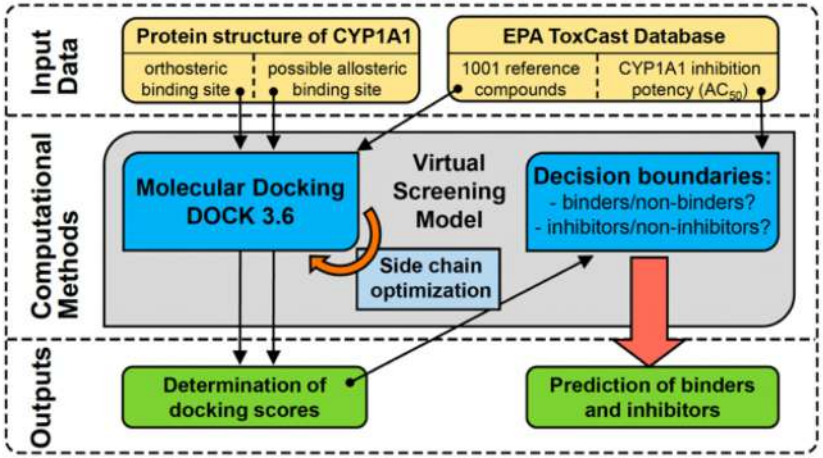
Chemical Safety

(IMCB, BII, NUS, DSO)









Publications and Inventions

➢ Structure & Function Mechanism (Krishna, Shreyas, Ravi)

1) Hepatic mitochondrial NAD+ transporter SLC25A47 activates AMPKα mediating lipid metabolism and tumorigenesis. **Hepatology**. 2023
2) The stability of R-spine defines RAF inhibitor resistance: A comprehensive analysis of oncogenic BRAF mutants with in-frame insertion of αC-β4 loop. **Science Advances**. 2021
3) Molecular basis for lipid recognition by the prostaglandin D2 receptor CRTH2. **PNAS**. 2021
4) Structure of human steroid 5α-reductase 2 with the anti-androgen drug finasteride. **Nature Communications.** 2020
5) Structure of formylpeptide receptor 2-Gi complex reveals insights into ligand recognition and signaling. **Nature Communications**. 2020

➢ Enzyme Engineering (Yossa, Shreyas, Ravi)

1) Lim et al. Structure-guided engineering of prenyltransferase NphB for high-yield and regioselective cannabinoid production. **ACS Catalysis**. 2022
2) https://chemrxiv.org/engage/chemrxiv/article-details/63ec488ffcfb27a31fccf1e4
3) **Patent** No. 10202260537Q. Title: “A computational-experimental workflow to increase enzyme evolution speed”.

➢ Ligand Discovery (Chaitanya, Weina, Lina)

1) **Inventory disclosure** SHIP Ref No TEC-20-85. Title: “The discovery of a BRAF-specific allosteric inhibitor, T009 for treating cancers that have developed resistance to RAF inhibitors”.
2) Low et al. Molecular docking-aided identification of small molecule inhibitors targeting β-catenin-TCF4 interaction. **iScience**. 2021
3) **Patent** No. PCT/SG2020/050512. Title: “Heterocyclic Compounds as Modulators of Beta-Catenin/Tcf4 Interaction”.
4) **Patent** No. SP106288SG. Title: ”Galectin-based peptide cocktail therapy for hypertension and heart failure”.
5) In-Silico Identified New Natural Sortase A Inhibitors Disrupt S. aureus Biofilm Formation. **Int. J. Mol. Sci**. 2020

➢ Chemical Safety (Ravi, Wan, Chaitanya, Julian)

1) Direct and Sequential Bioactivation of Pemigatinib to Reactive Iminium Ion Intermediates Culminates in Mechanism-Based Inactivation of Cytochrome P450 3A. **Drug Metab Dispos**. 2022
2) Differential Reversible and Irreversible Interactions between Benzbromarone and Human Cytochrome P450s 3A4 and 3A5. **Mol Pharmacol**. 2021
3) Structure-based virtual screening of CYP1A1 inhibitors: towards rapid tier-one assessment of potential developmental toxicants. **Arch. Toxicol**. 2021
4) Mechanism-based Inactivation of Cytochrome P450 3A4 by Benzbromarone. **Mol Pharmacol**. 2021
5) Virtual screening of potentially endocrine-disrupting chemicals against nuclear receptors and its application to identify PPARg-bound fatty acids. **Arch. Toxicol**. 2020

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