🔬 **Predicting Competitive Inhibition Outcomes in an Evolving Enzyme**

In our study, **"A Thermodynamic Cycle to Predict the Competitive Inhibition Outcomes of an Evolving Enzyme,"** we developed a framework linking competitive inhibition to alchemical free energy perturbation (FEP) calculations, focusing on *Escherichia coli* dihydrofolate reductase (DHFR) and its inhibition by trimethoprim (TMP).

🔬 **Key Tools & Theories Used:**

- **Alchemical Free Energy Perturbation (FEP) Calculations:** We employed FEP to estimate free energy differences associated with wild-type and mutant DHFR forms, enabling precise predictions of binding affinities and inhibition constants.
- **Thermodynamic Cycles:** By constructing thermodynamic cycles, we linked experimentally measured binding constants (K_i and K_m) to the free energy differences from FEP calculations, providing a comprehensive understanding of TMP resistance.

Our findings emphasize the role of **local conformational dynamics in competitive inhibition** and demonstrate how combining thermodynamic cycles with FEP calculations can predict inhibition outcomes in evolving enzymes.

📎 Read more: DOI Link

#EnzymeInhibition #ThermodynamicCycles #FreeEnergyPerturbation #ComputationalBiology #DrugResistance #Biochemistry #Research