



# Can evolution solve TrmD inhibition problem?

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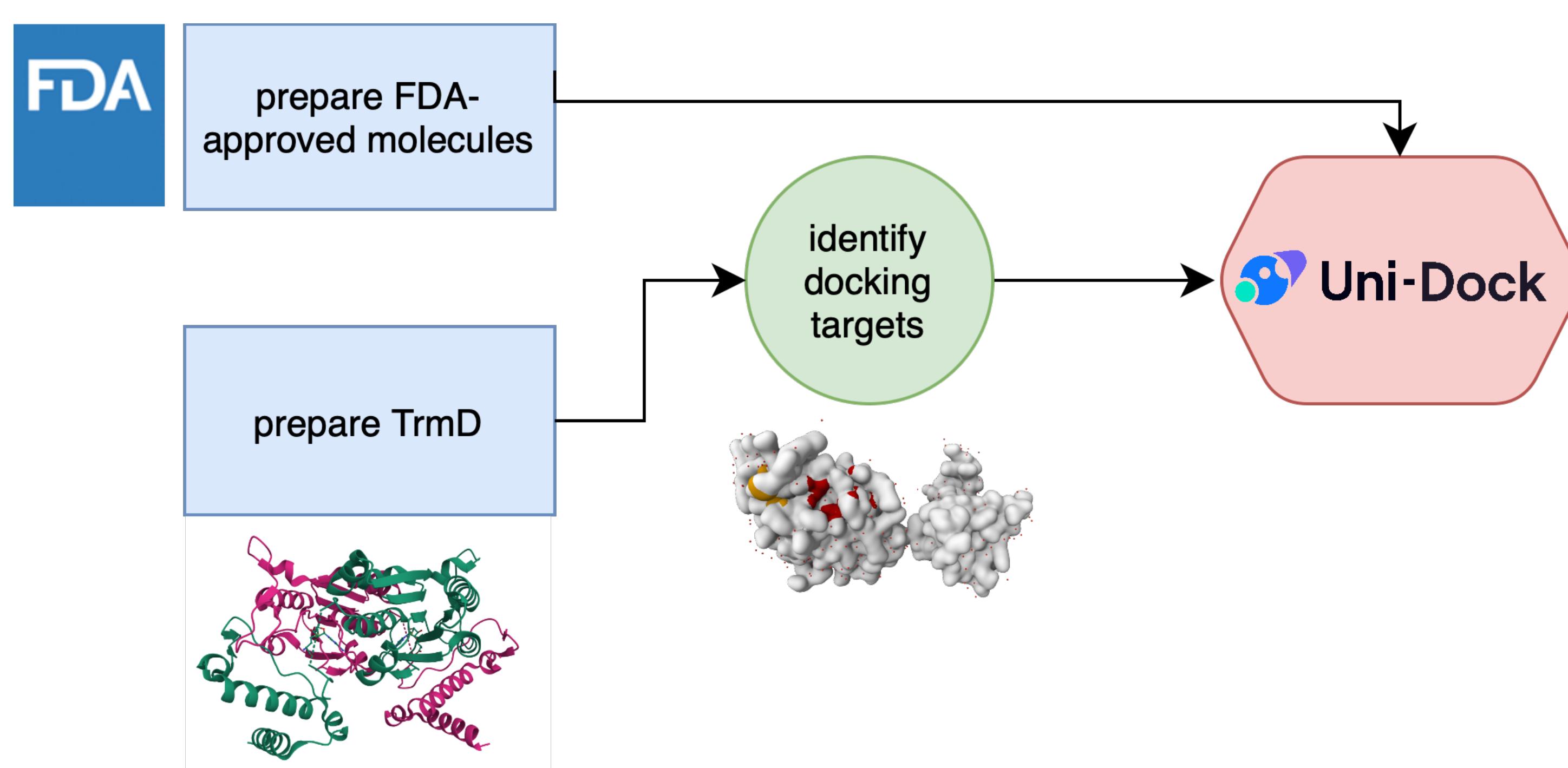
## INTRODUCTION

TrmD is a bacterial tRNA methyltransferase structurally distinct from its human counterpart, making it an attractive antibiotic target. This project utilizes structural bioinformatics, docking simulations, and virtual screening to identify potential TrmD inhibitors. We have developed computational pipeline that includes pocket analysis, docking with FDA-approved molecules, and modeling using genetic algorithm. And this is us:



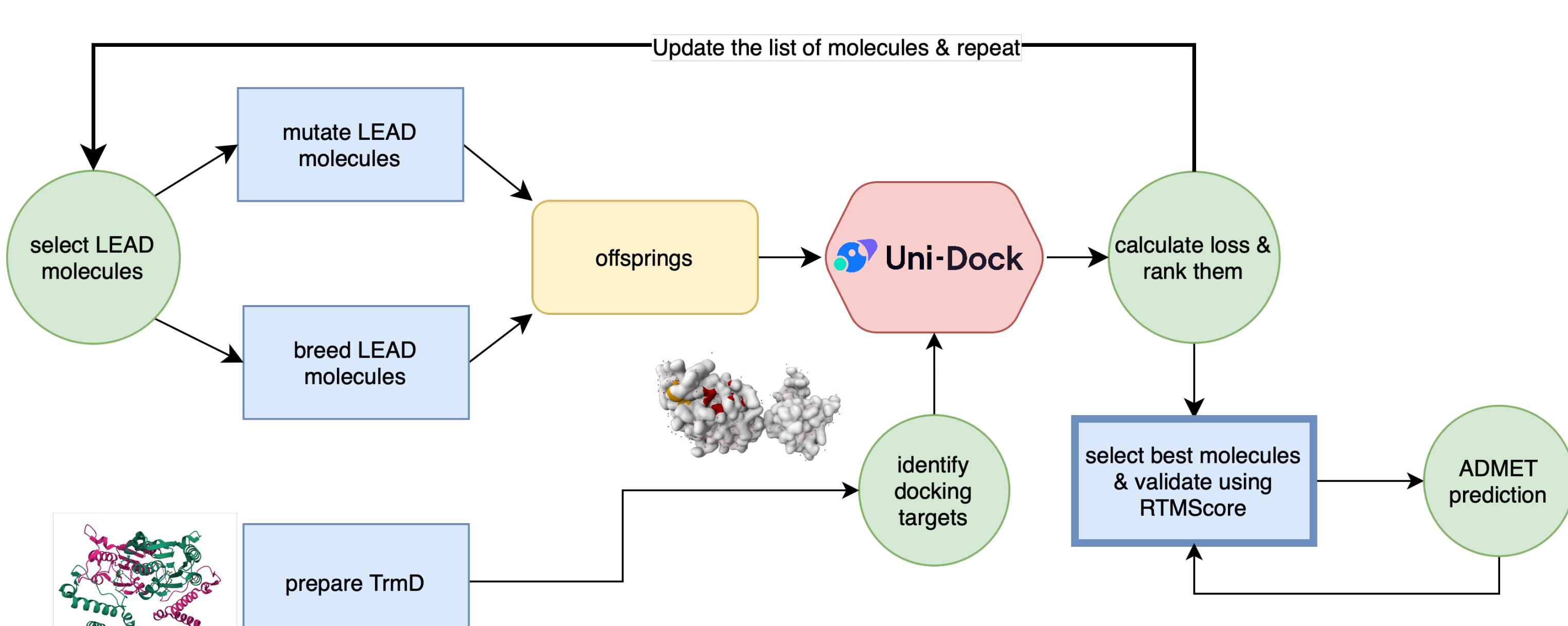
## METHODS & WORKFLOW

### (a) FDA approved molecules docking → benchmarking



The diagram represents a docking workflow where **FDA-approved molecules** are sanitized, ensuring chemical validity, protonated with 3D hydrogen coordinates, and assigned Gasteiger charges for proper charge distribution. The TrmD protein is prepared by removing water molecules (HOH residues) to avoid docking interference and adding hydrogen atoms for correct protonation. **Three docking sites** (AdoMet, tRNA and dimerization spot) are identified, and **UniDock** is used to perform docking.

### (b) EvoFLOPA



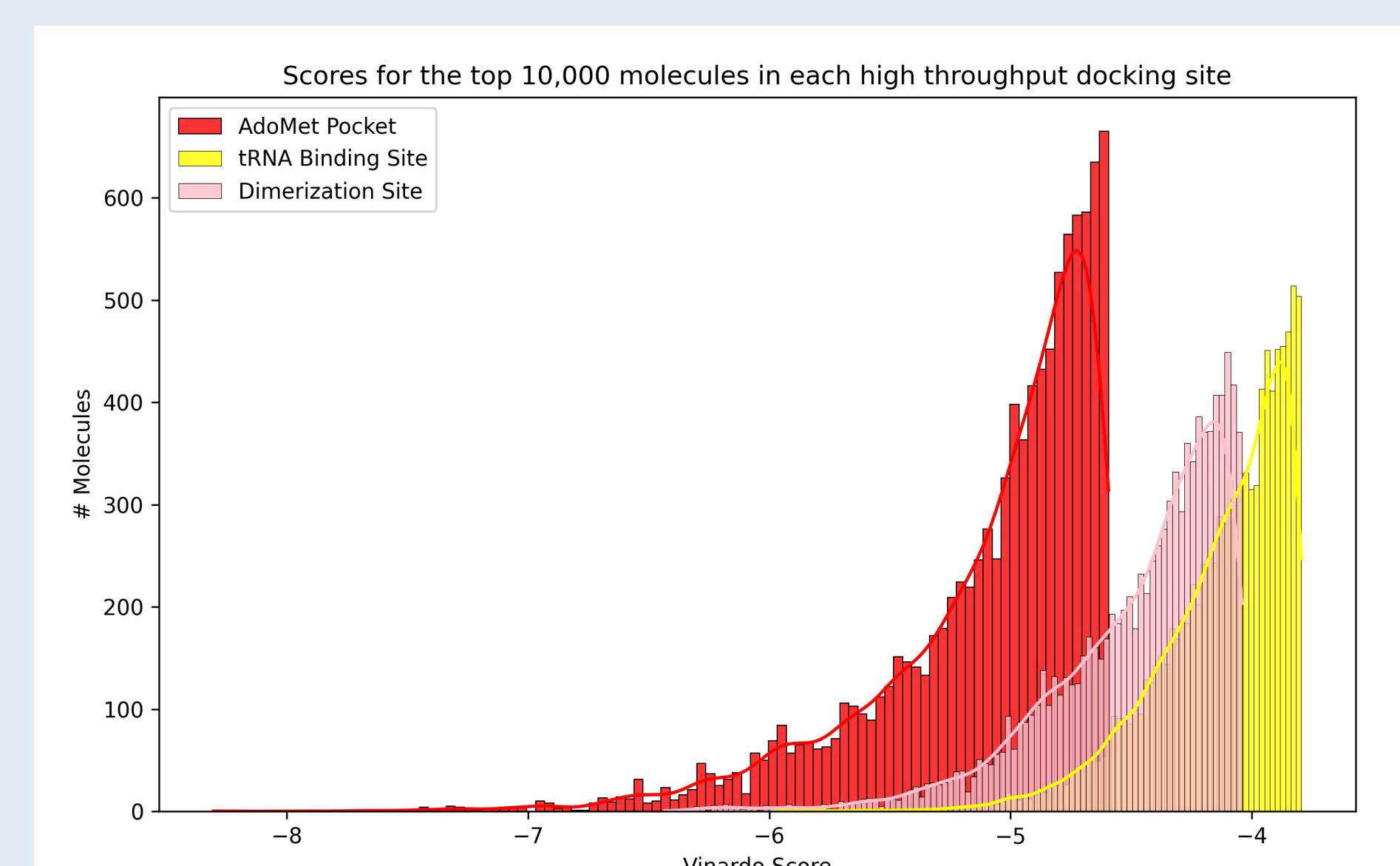
**EvoFLOPA** selects top molecules, mutates them with a modified STONED algorithm, docks them (UniDock), and ranks them by a weighted loss of docking scores, synthetic accessibility, and drug-likeness. The best hits are validated with RTMScore and iterated to optimize binding and drug properties.

### RTMScore

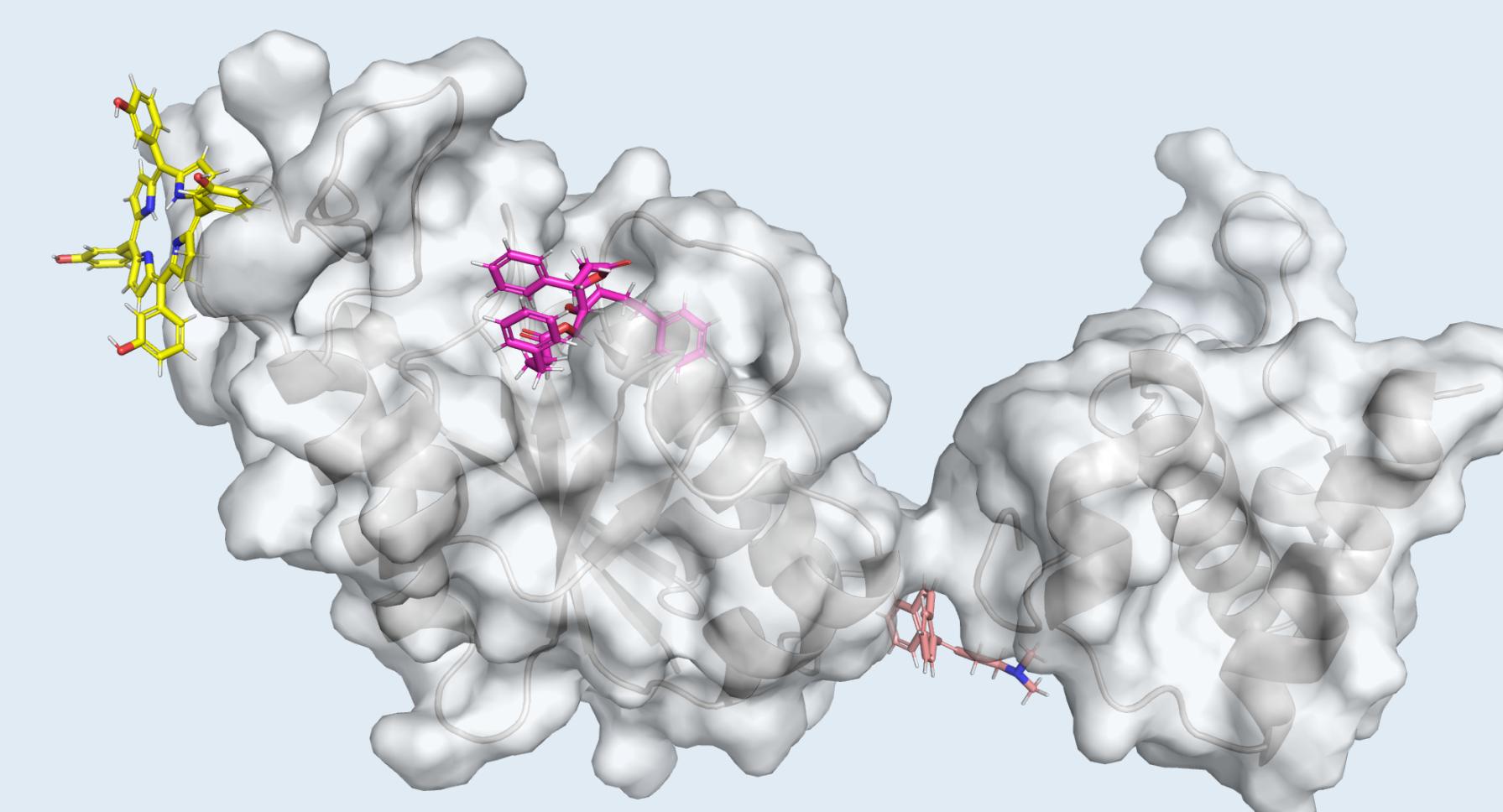
RTMScore is a **deep learning** scoring function for rescoring and verifying binding poses. Unlike Vina's empirical approach, RTMScore learns from experimental protein-ligand complexes. For **AdoMet** the score is **27,65**.

## RESULTS

### (a) Results of FDA-approved approach

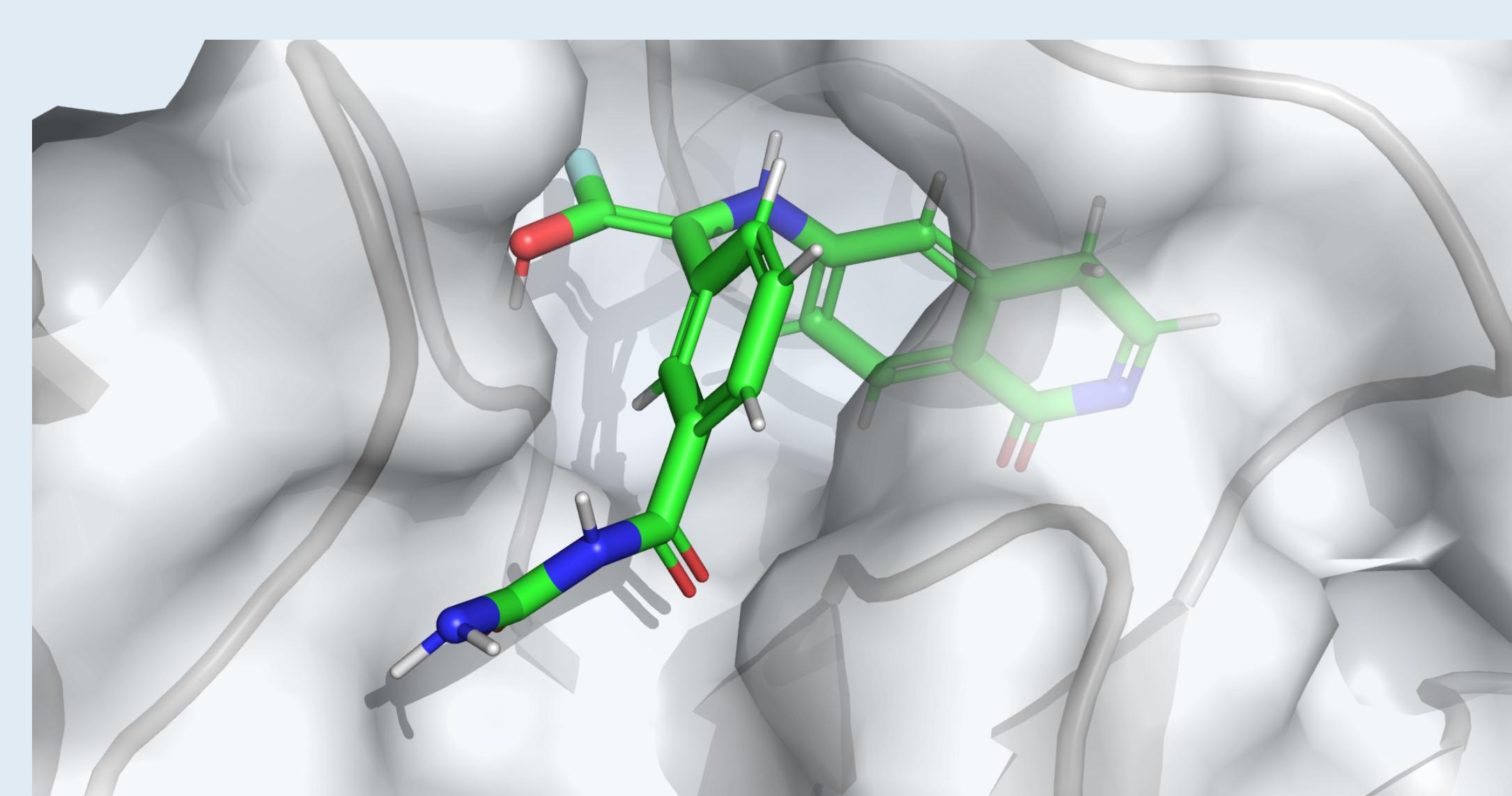


This histogram shows docking-score distributions for three TrmD binding sites. More negative scores indicate stronger predicted binding affinity.

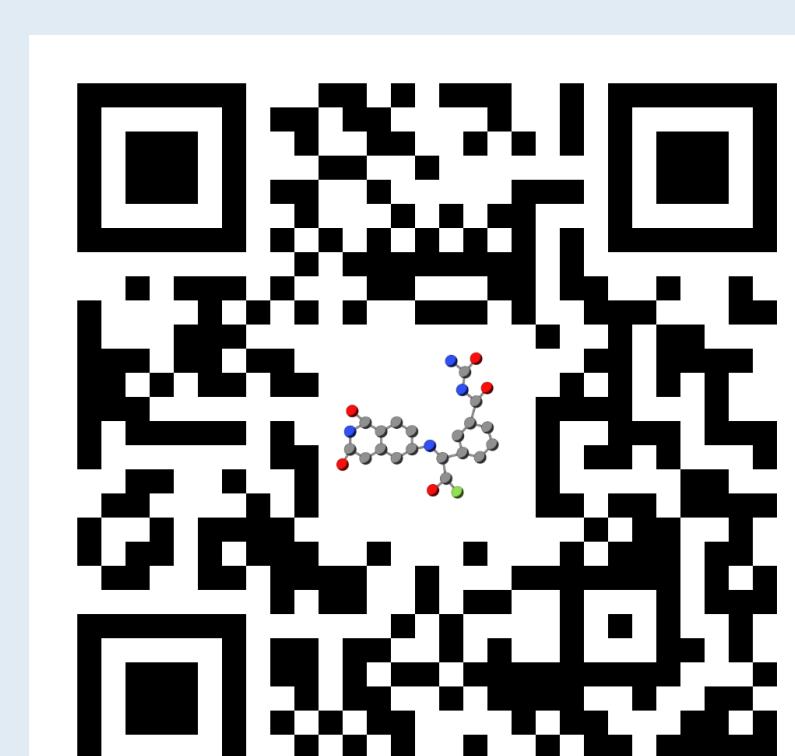


The image shows the **best docking results** bound to the three identified sites of the TrmD protein.

### (b) Results of EvoFLOPA



**YF compound**  
Score: -12,72 kcal/mol  
RTMScore: 42,767  
SA: 3,05  
QED: 0,603



[View our molecules here!](#)

## CONCLUSION

The EvoFLOPA has shown that evolution algorithms can be utilized for improving the binding affinity of lead molecules and in our case has been able to achieve **better results** than classical database virtual screening approaches. While using this method, EvoFLOPA has successfully identified novel TrmD protein inhibitors with high affinity and good synthetic accessibility.

