

**Electronic Supplementary Information**

**Yb(OTf)<sub>3</sub> mediated MCR: a new and regioselective approach  
towards polysubstituted pyrroles of pharmacological interest**

G. Rajeshwar Reddy,<sup>a,b</sup> T. Ram Reddy,<sup>a</sup> Suju C. Joseph,<sup>a</sup> K. Sateesh Reddy,<sup>a</sup> Chandana Lakshmi  
T. Meda,<sup>c</sup> Ajit Kandale,<sup>c</sup> D. Rambabu,<sup>c</sup> G. Rama Krishna,<sup>d</sup> C. Malla Reddy,<sup>d</sup> Kishore V.L.Parsa,<sup>c</sup>  
K. Shiva Kumar,<sup>c</sup> and Manojit Pal<sup>\*,c</sup>

*<sup>a</sup>Custom Pharmaceutical Services, Dr. Reddy's Laboratories Limited, Bollaram Road Miyapur,  
Hyderabad 500 049, India*

*<sup>b</sup>Chemistry Division, Institute of Science and Technology, JNT University, Kukatpally,  
Hyderabad 500072, Andhra Pradesh, India*

*<sup>c</sup>Institute of Life Sciences, University of Hyderabad Campus, Gachibowli, Hyderabad, 500046,  
India.*

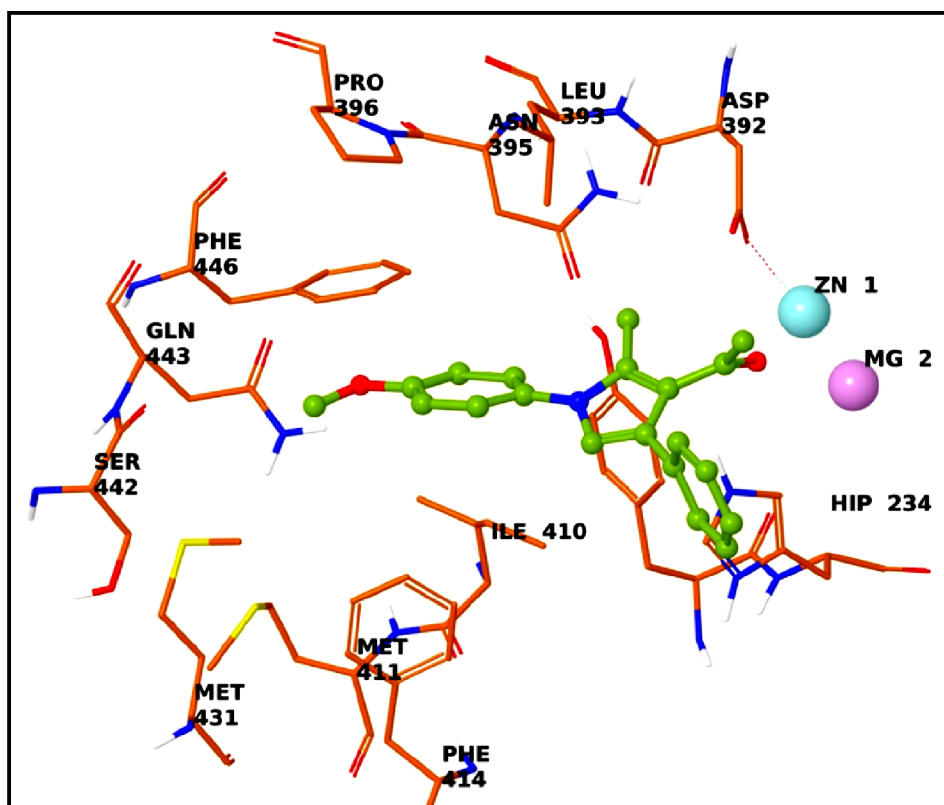
*<sup>d</sup>Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata,  
West Bengal, 741252, India.*

*E-mail: manojitpal@rediffmail.com*

**Docking study**

**Method:** We docked all the molecules by using Schrödinger 2011 software. The results are compared with the cocrystal ligand and *In vitro* activity. The PDB ID 3O0J was used for the docking study. The protein was prepared by giving preliminary treatment like adding hydrogen, adding missing residues, refining the loop with prime and finally minimized by using OPLS 2005 force field. The search grid was generated by picking the cocrystal ligand upto 20 Å search area. The hydroxyl groups of search area were allowed to move.

All the molecules were minimized by using macromodule application. We used 1000 iteration for minimization using OPLS 2005 force field and charges were also added from force field only. The PRCG (Polak-Ribier conjugate gradient) method was used for minimization. All the molecules were docked by using glide XP (extra precision) dock application. We performed flexible docking by allowing sample ring conformations and sample nitrogens to move to possible extent in docking. 10 poses were generated for each ligand. The docking results are documented and analyzed.



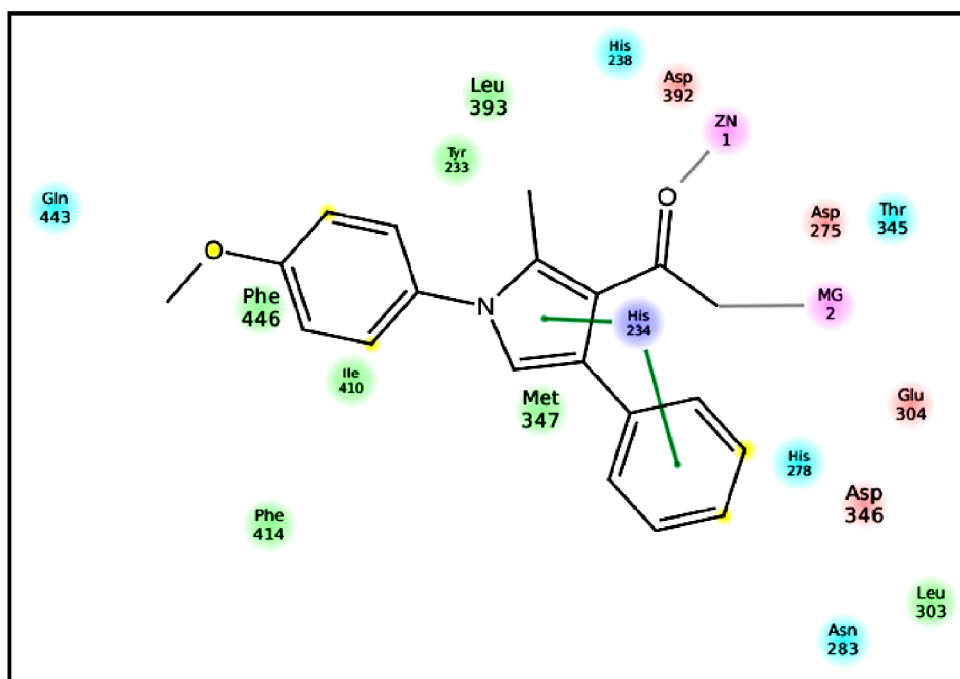
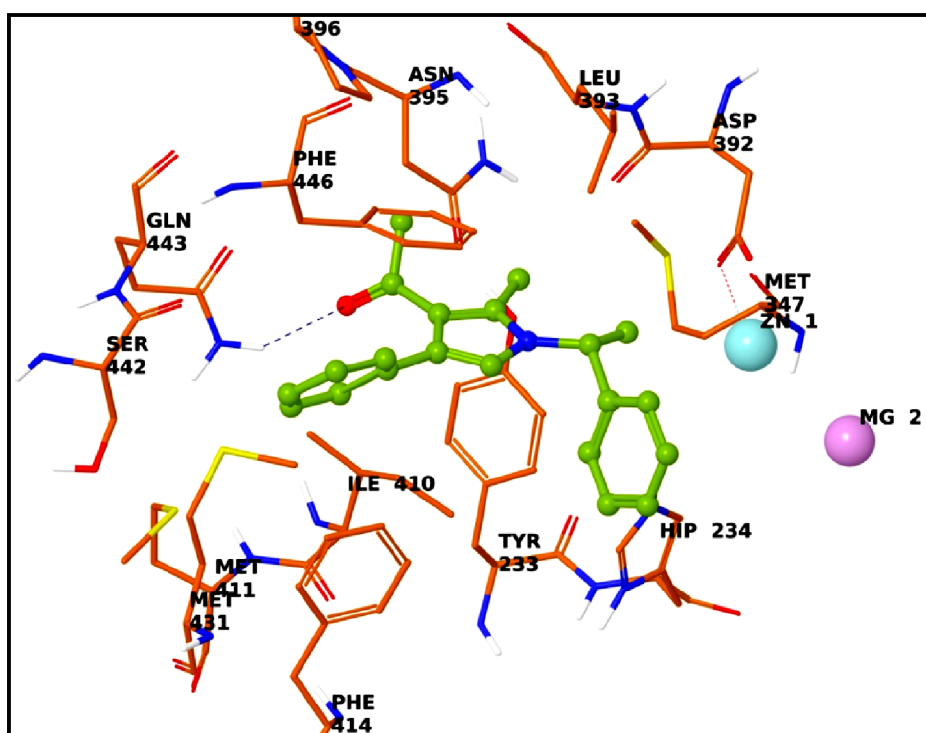
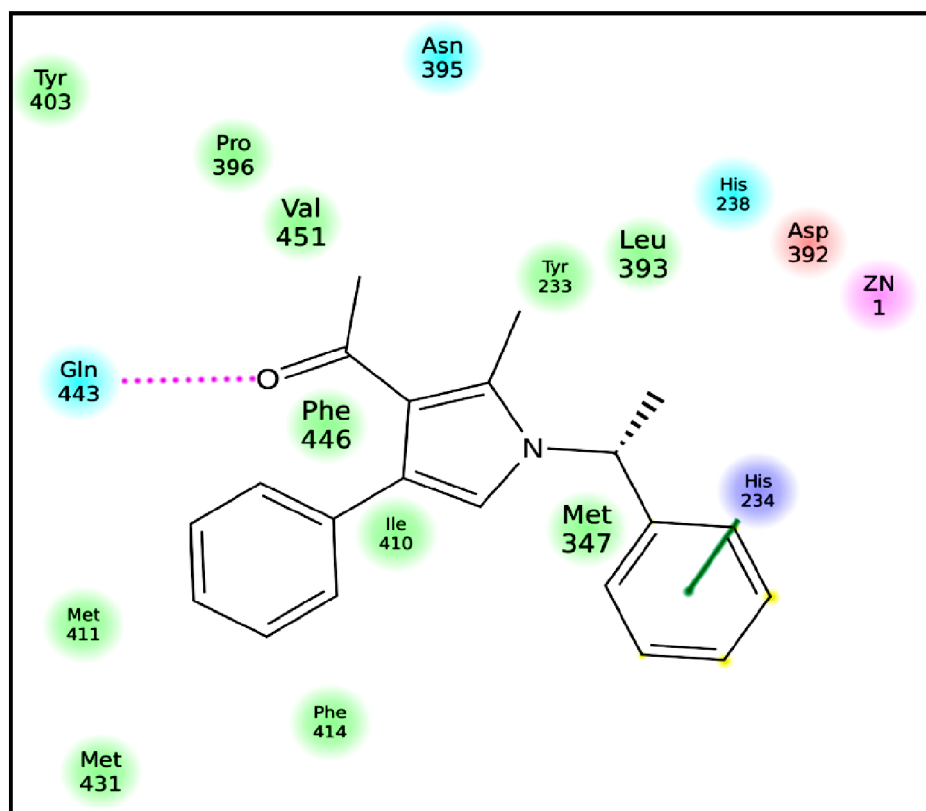


Fig. 5. Docking of 4g at the active site of PDE4B.





**Fig. 6.** Docking of **4n** at the active site of PDE4B.

The docking studies were carried out using the compounds **4g** and **4n**. The Glide scores obtained after docking of compounds **4g** and **4n** with PDE4B protein are summarized in the following Table. The data shown in the Table clearly suggests that these molecules interact well with the PDE4B protein.

**Table:** Glide scores and other parameters of compounds after docking with PDE4B

| Compound  | Glide score<br>(Kcal/mol) | E-1 <sup>a</sup><br>(Kcal/mol) | E-2 <sup>b</sup><br>(Kcal/mol) | E-3 <sup>c</sup><br>(Kcal/mol) |
|-----------|---------------------------|--------------------------------|--------------------------------|--------------------------------|
| <b>4g</b> | -5.26                     | -3.65                          | 0                              | -2.19                          |
| <b>4n</b> | -7.04                     | -4.76                          | -0.62                          | -0.09                          |

<sup>a</sup>E-1 = Chemscore lipophilic term and fraction of total van der Waals energy.

<sup>b</sup>E-2 = Hydrophobic reward.

<sup>o</sup>E-3 = Electrostatic reward.