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SUPPLEMENTAL DATA

Virtual screening of marine coumarins and xanthenes identifies novel acid-suppressive leads targeting histamine H_2 receptor and gastric proton pump

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Full article is available at the following link: Virtual screening of marine coumarins and xanthenes identifies novel acid-suppressive leads targeting histamine H_2 receptor and gastric proton pump

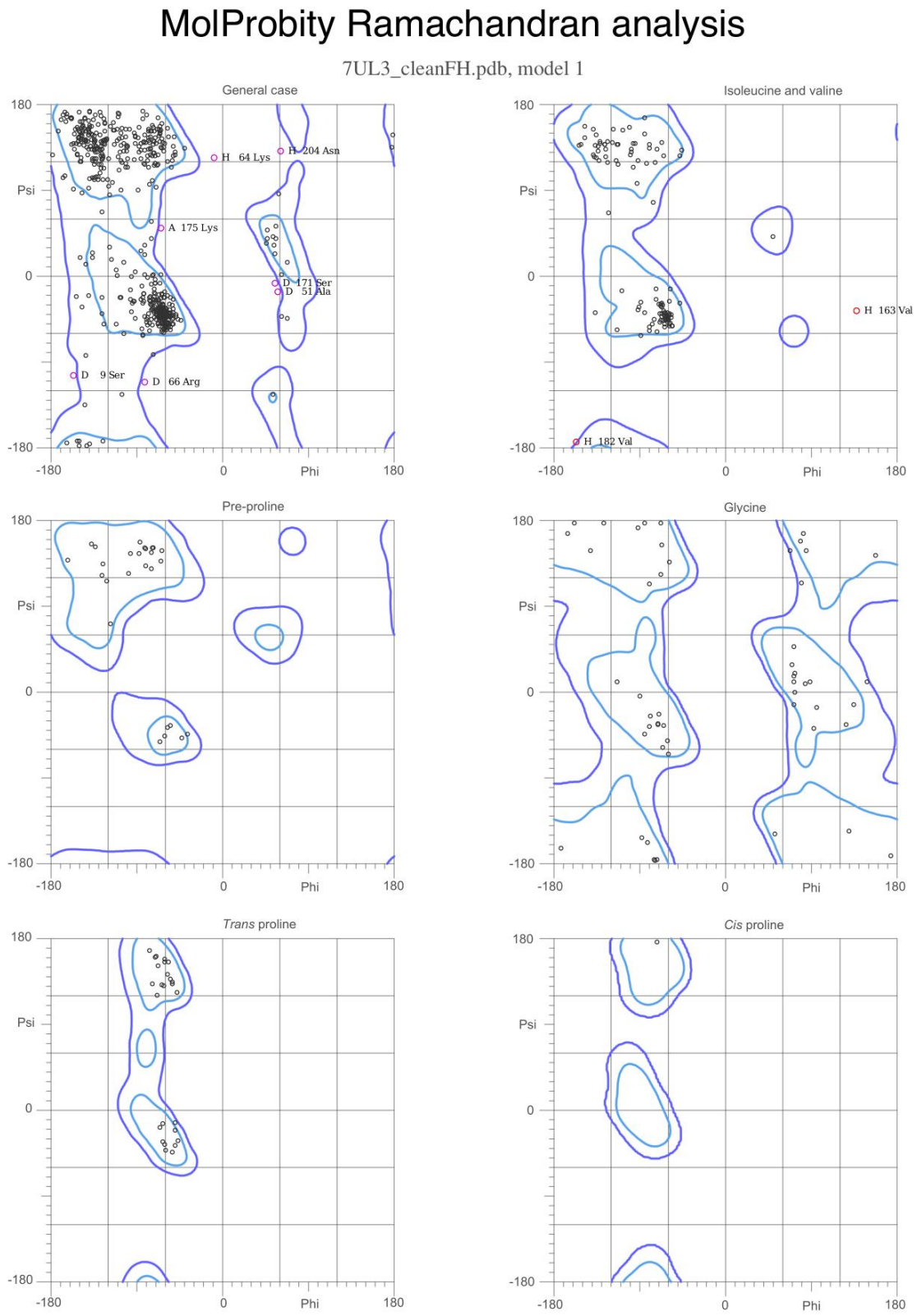

Figure S1. MolProbity Ramachandran validation of the prepared histamine H_2 receptor model used for docking (PDB ID: 7UL3). Backbone dihedral angle distribution (Phi and Psi) was evaluated using high-accuracy Ramachandran criteria

as implemented in MolProbity (Lovell et al., 2003). The refined receptor model shows 92.9% (705/759) residues in favored regions and 98.8% (750/759) in allowed regions. Nine residues are classified as outliers (Phi, Psi): A175 Lys (−66.0, 51.3); H64 Lys (−10.0, 125.9); H163 Val (13.86, −36.9); H182 Val (−157.9, −174.4); H204 Asn (61.4, 132.3); D9 Ser (−157.4, −104.3); D51 Ala (58.9, −16.5); D66 Arg (−82.4, −111.1); D171 Ser (55.2, −7.3). Overall, the stereochemical quality supports the suitability of the prepared receptor structure for subsequent docking analyses. **Abbreviations**: H_2: Histamine H_2; PDB: Protein Data Bank; Ala: Alanine; Arg: Arginine; Asn: Asparagine; Lys: Lysine; Ser: Serine; Val: Valine.

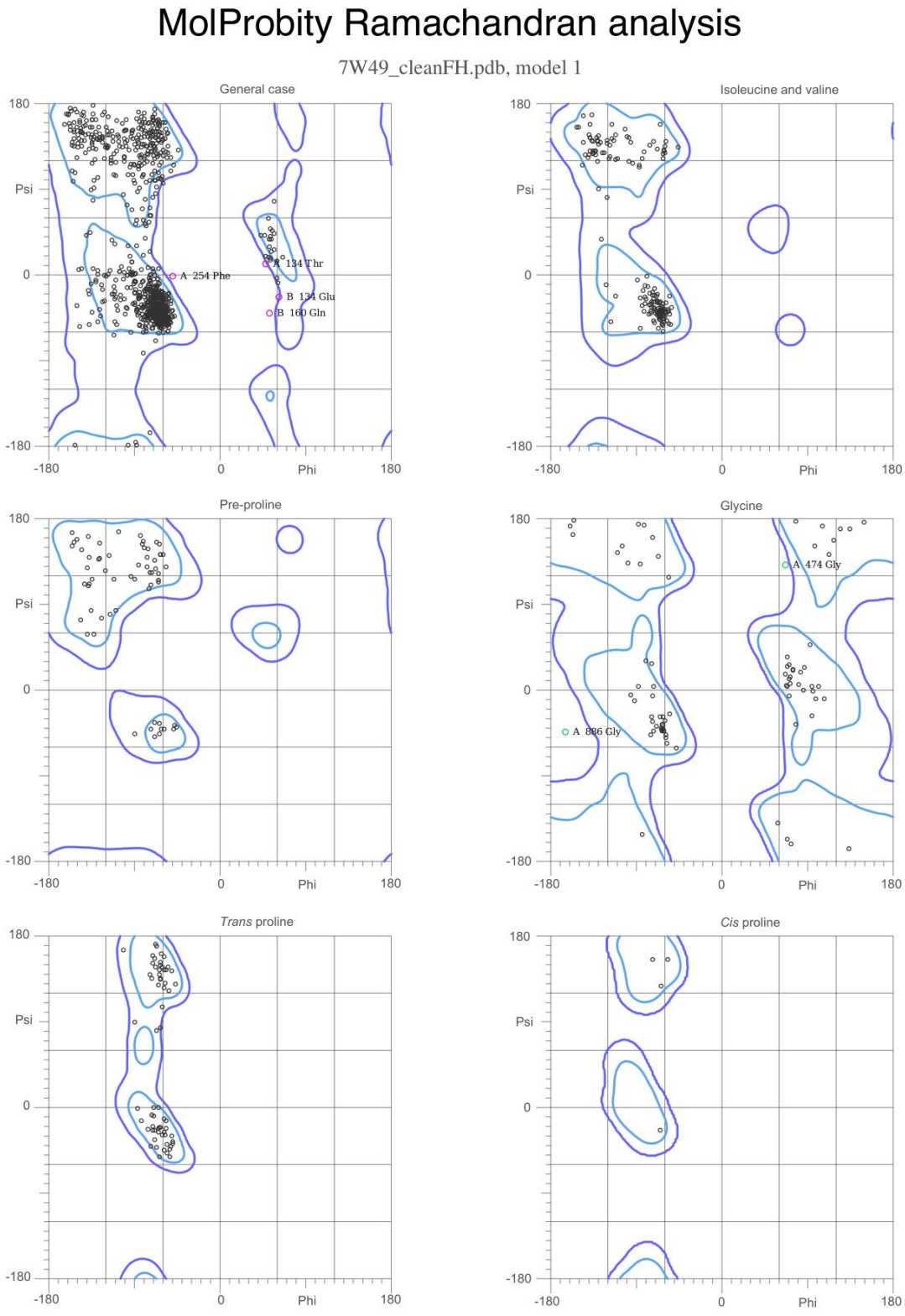

Figure S2. MolProbity Ramachandran validation of the prepared gastric proton pump structure used for docking (PDB ID: 7W49). Backbone dihedral angle distributions (Phi and Psi) were evaluated using the high-accuracy Ramachandran criteria implemented in MolProbity (Lovell et al., 2003) to assess stereochemical

quality after target preparation and refinement. The refined H^+/K^+-ATPase model shows 94.4% (1172/1242) of residues in favored regions and 99.5% (1236/1242) in allowed regions. Six residues are classified as outliers (Phi, Psi), mapped to the corresponding protein chains: A134 Thr (48.9, 12.5); A254 Phe (−50.7, −1.2); A474 Gly (67.3, 132.2); A886 Gly (−165.6, −44.2); B134 Glu (62.5, −23.0); B160 Gln (52.1, −40.1). Overall, these stereochemical statistics support the suitability of the prepared proton pump model for subsequent docking analyses. **Abbreviations**: H^+/K^+-ATPase: Gastric H^+/K^+ adenosine triphosphatase (proton pump); PDB: Protein Data Bank; Thr: Threonine; Phe: Phenylalanine; Gly: Glycine; Glu: Glutamate; Gln: Glutamine.

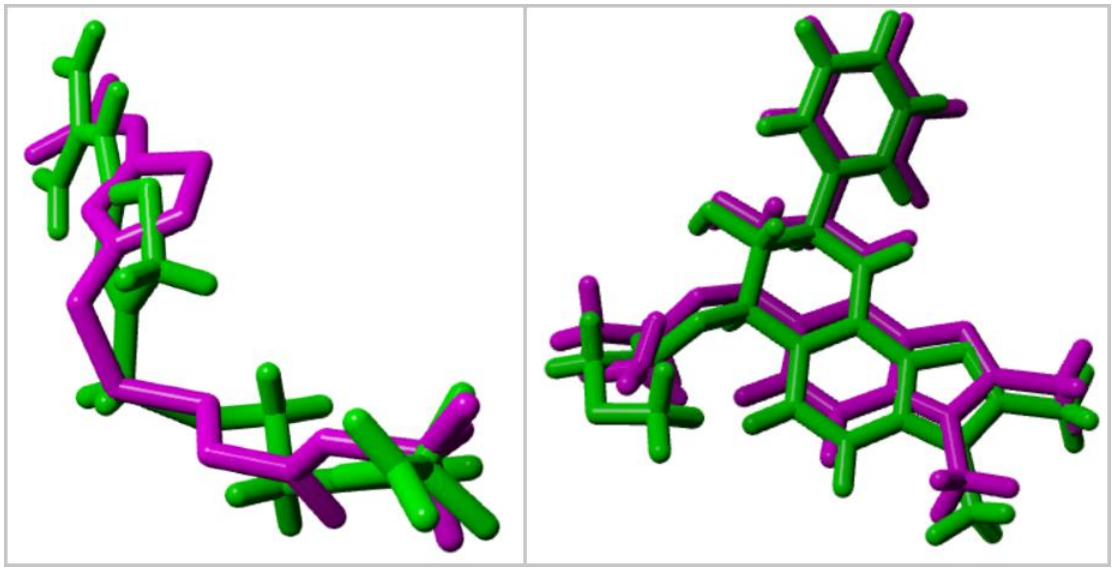

Figure S3. Redocking validation of the docking protocol. Superposition of the co-crystallized ligand poses (green) and the best-ranked redocked poses (magenta) for famotidine in the histamine H_2 receptor (left) and soraprazan in the gastric proton pump (right), demonstrating close agreement between experimental and redocked binding conformations. **Abbreviation**: H_2: Histamine H_2.