Electronic Supplementary Material (ESI) for RSC Advances.

Molecular basis of ligand selectivity for melatonin receptors

Wenqiang Cui[1, 2], Junlin Dong[1, 2], Shiyu Wang[1, 2], Horst Vogel[1], Rongfeng Zou[1 *], Shuguang Yuan[1 *]

1 The Research Center for Computer-aided Drug Discovery, Institute of Biomedicine and Biotechnology, The Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, Shenzhen 518055, China

2 University of Chinese Academy of Sciences, Beijing 100049, China

**Correspondence to:*

Shuguang Yuan

Email: shuguang.yuan@siat.ac.cn

Rongfeng Zou

Email: rf.zou@siat.ac.cn

Figure S1

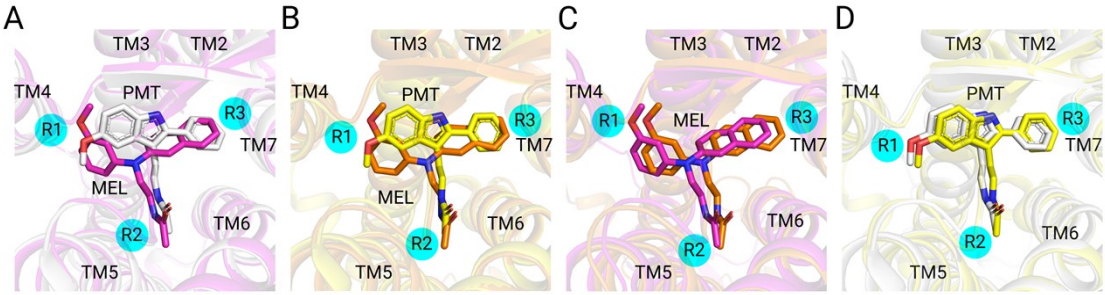

Figure S1. (A) The poses of MEL (magenta) and PMT (gray, PDB Code: 6ME3) in MT1 system. (B) The poses of MEL (orange) and PMT (yellow, PDB Code: 6ME6) in MT2 system. (C) The poses of MEL (magenta) in MT1 system and MEL (orange) in MT2system. (D) The poses of PMT (gray) in MT1 system and PMT (yellow) in MT2 system. Ligands are displayed as sticks model. Proteins are displayed as cartoon model.

Figure S2

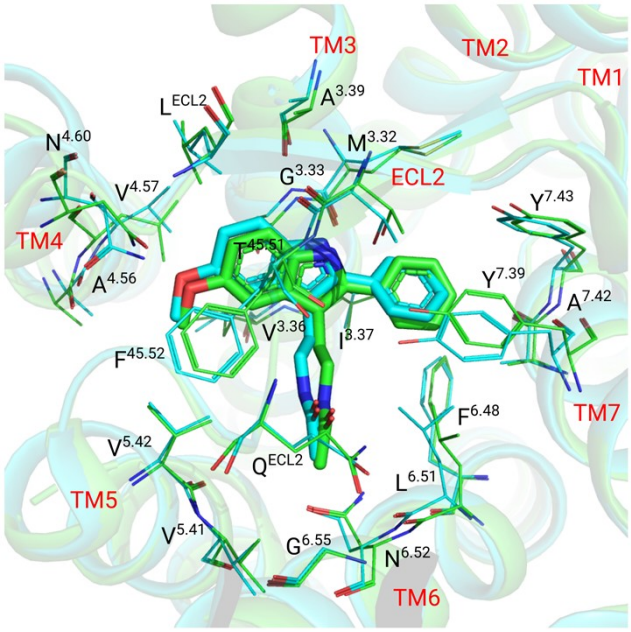

Figure S2. The amino acids within 5 Å of ligand in the inactive MT1 (PDB Code: 6ME3) and MT2 (PDB Code: 6ME6).

Table S1

The parameters used in PLUMED for the systems in the present work

Type	**MT1**	**MT2**
Angle	Atom C13 = 4831; Atom C21 = 4839 Atom 1 = (0, 0, -8); Atom 2 = (5, 5, -8)	Atom C12 = 4755; Atom C20 = 4763 Atom 1 = (0, 0, -8); Atom2 = (5, 5, -8)
TM6	Atoms=3499-3770 Atoms=4320-4522	Atoms=3412-3683 Atoms=4219-4418
TM1	Atoms=45-204 Atoms=4118-4301	Atoms=1-155 Atoms=4027-4197

Sandwich	MEL/Y285$^{7.43}$/L34$^{1.39}$	MEL/Y298$^{7.43}$/L47$^{1.39}$

Movie S1. The conformation of this naphthalene ring in MEL changed: the hydrophobic interaction with Y2857.43 was disrupted because of the fast movement of water molecules during the long-time scaled MD simulations.