Scientific recognition for Dr. Zohreh Fallah

A paper by Dr. Zohreh Fallah with her collaborations entitled “Molecular dynamics-guided discovery of an ago-allosteric modulator for GPR40/FFAR1” has been accepted for publication in the PNAS journal (IF= 9.504). The School of Nano Science congratulates this achievement to Dr. Fallah , and her colleagues.

Description:

The long-chain fatty acid receptor FFAR1/GPR40 binds agonists in both an interhelical site between the extracellular segments of transmembrane helix (TM)-III and TM-IV and a lipid-exposed groove between the intracellular segments of these helices. Molecular dynamics simulations of FFAR1 with agonist removed demonstrated a major rearrangement of the polar and charged anchor point residues for the carboxylic acid moiety of the agonist in the interhelical site, which was associated with closure of a neighboring, solvent-exposed pocket between the extracellular poles of TM-I, TM-II, and TM-VII. A synthetic compound designed to bind in this pocket, and thereby prevent its closure, was identified through structure-based virtual screening and shown to function both as an agonist and as an allosteric modulator of receptor activation. This discovery of an allosteric agonist for a previously unexploited, dynamic pocket in FFAR1 demonstrates both the power of including molecular dynamics in the drug discovery process and that this specific, clinically proven, but difficult, antidiabetes target can be addressed by chemotypes different from existing ligands.

- **Michael Lückmann, Mette Trauelsen, Marie A. Bentsen, Tinne A. D. Nissen, Joao Martins, Zohreh Fallah, Mads M. Nygaard, Elena Papaleo, Kresten Lindorff-Larsen, Thue W. Schwartz, and Thomas M. Frimurer "Molecular dynamics-guided discovery of an ago-allosteric modulator for GPR40/FFAR1", PNAS,**
  https://doi.org/10.1073/pnas.1811066116