Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

Seminar

Drug binding and subtype selectivity in G-protein-coupled receptors

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Acetylcholine, the first neurotransmitter to be identified, exerts many of its physiological actions via activation of the muscarinic acetylcholine receptor (mAChR) family of G-protein-coupled receptors (GPCRs). The development of small molecule ligands that selectively act on one of the five mAChR subtypes (M1–M5) has proven extremely challenging, primarily owing to the high degree of sequence similarity in the transmembrane core of these receptors. Using molecular dynamics simulations, we characterized the pathway by which drugs bind to and dissociate from the M2 and M3 receptors. These simulations suggest a metastable drug-binding site in the extracellular vestibule of both receptors, and also provide a potential rationale for the slower dissociation rates of certain M3 antagonists. Our findings may facilitate the design of improved subtype-selective therapeutics targeting these critical receptors.

Tuesday, Dec 5th 2017

11:30 AM (Tea/Coffee at 11:15 AM)

Auditorium, TIFR-H