**INTRODUCTION**

The 7C subunit of serotonin receptors (5HT) is a member of the G protein-coupled receptor (GPCR) superfamily of seven transmembrane helix proteins. The cascade of events in which a GPCR changes from its inactive (R) to its active state (R*) has not yet been elucidated. The efficacy of agonists, partial agonists, antagonists and inverse agonists in eliciting responses from binding to GPCRs relates to their ability to modify the equilibrium between R and R*, stabilizing one or the other to a different extent. Binding of the endogenous ligand 5HT to its 5HT2C receptor has been known previously to involve residues D3.30 [1], S3.32 [2], and P6.53 [3] (Figure 1a and 2).

The propagation of the ligand-binding signal through the receptor structure involves a "sensor" of its interaction at the binding site. Partial agonists are those that trigger a change in the relative population of R and R* without selectively stabilizing one or the other. In the absence of 5HT, the active conformation is preferred, resulting in the perpendicular orientation of W6.48 with respect to the membrane associated with the inactive form R of the receptor [5]. In the absence of 5HT, the active conformation is preferred, resulting in the perpendicular orientation of W6.48 with respect to the membrane associated with the inactive form R of the receptor [5]. In the presence of 5HT, the conformational changes around W6.48 favor a more parallel orientation with respect to the membrane [6]. The side chain conformations for W6.48 and W6.52 computed from the MD trajectories are shown in graphs 3-6.

**RESULTS**

1. **INACTIVE**

![Graph 1](image1.png)

**ACTIVE**

![Graph 2](image2.png)

**REFERENCES**

[1] Javitch, J.A., J.A. Ballesteros, H. Weinstein, and J. Chen, A cluster of aromatic residues in the sixth membrane-spanning segment of the dopamine D2 receptor is accessible in the binding-site conformation when 5-HT is present, resulting in an orientation of 5HT parallel to the membrane.


