3D-model structure of the D2 dopamine receptor bound to the atypical antipsychotic drug risperidone

Dillon T. Rubalcava, Brittany L. Daniel, and Matt J. DePoalo

This 3D model creates an easy visualization of the D2 dopamine receptor and its interactions after the inverse-agonist Risperidone has bound. Risperidone attaches to the binding pocket of DRD2 and causes a conformational change in a nearby residue known as I184 (located on extracellular loop 2). I184 undergoes a small helical turn to reach across the binding pocket and interact with residues Trp100 (located on extracellular loop 1) and L94. The interactions between these three residues form a hydrophobic patch above the binding pocket of DRD2. This hydrophobic patch then prevents other molecules from binding to the D2 dopamine receptor, enhancing the affinity and efficacy of Risperidone and highlighting the mechanism that leads to its inverse-agonist nature. Due to the implications of dysfunction of the dopaminergic system that are present in diseases such as Schizophrenia and Parkinson's disease, this Risperidone-DRD2 model is important for understanding structural changes that are essential for Risperidone and similar antipsychotic drugs used as treatment. Furthermore, this 3D model provides a visual representation that is frequently difficult to depict, therefore encouraging a greater understanding of this ligand-receptor interaction.