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Effects of Mutagenesis of Highly Conserved Tyrosine Residues on the Function of m1 Muscarinic Receptor

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Muscarinic acetylcholine receptors contain two highly conserved tyrosine residues which are located within or at the extracellular border of the second transmembrane domain. These tyrosine residues are located at positions 82 and 85 of the sequence of the m1 subtype of muscarinic receptors. In this wok, we studied the involvement of these two residues in ligand binding to and agonist-induced activation this receptor subtype. our data suggest an important role for these two tyrosines in these processes, with a more prominent role for the tyrosine residue located at position 82 than that located at position 85. Evidence is also provided that while the aromatic moiety of these tyrosine residues is important for antagonist binding, both this moiety and the tyrosine phenolic hydroxyl group are involved in agonist binding and receptor activation.