Neurophysiology

The Nicotinic Acetylcholine Receptor





Figure 4. Ribbon diagrams of a single subunit (a) viewed parallel with the membrane plane, in orientations such that the central axis of the pentamer (vertical line) is (left) at the back and (right) to the side. The a-helices are in yellow; the bstrands composing the b-sandwich are in blue (inner) and red (outer). Locations of the N and C termini, aTrp149, aV46, the Cys- loop disulphide bridge and the membrane (horizontal bars) are indicated. Part of the M3-M4 loop (connecting MA to M3) is missing.

> Ligand-gated channels in the "cys-loop" superfamily have similar molecular structures:

> > nAChR **GABA**_A 5-HT₃ glycine receptor



Figure 8. Central sections showing the inner surfaces of (a) the extracellular and (b) the intracellular vestibules. Both vestibules are lined by an excess of negatively charged groups, promoting a cation-stabilising electrostatic environment. (a) A view looking towards the alpha-beta subunit-subunit interface; (b) a view looking towards the alpha subunit. Labels identify exposed charged side-chains. The locations of the membrane pore (arrows) and the membrane surfaces (horizontal bars) are indicated. Red, negative charges; blue, positive charges.







Figure 12. Interpretation of the ACh-binding region of the closed channel at the interface between the alpha and gamma subunits, showing the loops B and C (alpha subunit), the adjacent strands, b5 and b6 (gamma subunit) and the attached amino acid side-chains. The slab is of the upper part of the ACh-binding region, viewed from the synaptic cleft. Some key residues implicated in ACh binding are labelled. The C backbone and side-chains are in red (alpha) and blue (gamma). As indicated, a salt-bridge between D152 and R78 may be involved in stabilising the B loop. The experimental densities show weak features associated with the C loop.



Sources:

Unwin, N (2005) Refined Structure of the Nicotinic Acetylcholine Receptor at 4 Å Resolution. J. Mol. Biol. 346: 967-989.

Albuquerque, E.X. et al. (2009) Mammalian Nicotinic Acetylcholine Receptors: From Structure to Function. Physiol. Rev. 89: 73–120. (lower right figure only)

Figure 7. Electrostatic potential surface representations showing entry/exit windows for cations between the MA helices of different subunits on the intracellular side of the membrane. The windows formed between delta and beta, and between gamma and alpha, are on the left and right, respectively. Labels identify exposed charged side-chains. The location of the intracellular membrane surface is indicated (horizontal bars). The sphere in the delta-beta window is the size of a potassium ion (2.7 Å diameter).

