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LGIC

Overview: Ligand-gated ion channels (LGICs) are integral membrane proteins that contain a pore that allows the regulated flow of selected ions across the plasma membrane. The channels are opened, or gated, by the binding of a neurotransmitter that triggers a conformational change that results in the conducting state. LGICs mediate fast synaptic transmission, on a millisecond time scale, in the nervous system and at the somatic neuromuscular junction, but the expression of some LGICs by non-excitable cells is suggestive of additional functions. By convention, the LGICs comprise the excitatory, cation-selective, nicotinic acetylcholine (Millar and Gotti, 2009), 5-HT_3 (Barnes *et al.*, 2009), ionotropic glutamate (Lodge, 2009) and P2X receptors (Jarvis and Khakh, 2009) and the inhibitory, anion-selective, $GABA_A$ (Olsen and Sieghart, 2008) and glycine receptors (Lynch, 2009). The nicotinic acetylcholine, 5-HT_3, $GABA_A$ and glycine receptors (and an additional zinc-activated channel) are pentameric structures and are frequently referred to as the Cys-loop receptors due to the presence of a defining loop of residues formed by a disulphide bond in the extracellular domain of their constituent subunits. However, the prokaryotic ancestors of these receptors contain no such loop, and the term pentameric ligand-gated ion channel (pLGIC) is gaining acceptance in the literature (Hilf and Dutzler, 2009). The ionotropic glutamate and P2X receptors are tetrameric and trimeric structures respectively. Multiple genes encode the subunits of LGICs, and the majority of these receptors are heteromultimers. Such combinational diversity results within each class of LGIC in a wide range of receptors with differing pharmacological and biophysical properties and varying patterns of expression within the nervous system and other tissues. The LGICs thus present attractive targets for new therapeutic agents with improved discrimination between receptor isoforms and a reduced propensity for off-target effects. The development of novel, faster screening techniques for compounds acting on LGIcs (Dunlop *et al.*, 2008) will greatly aid in the development of such agents.

Further Reading

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