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ION CHANNELS

Overview: Ion channels are pore-forming proteins that allow the flow of ions across membranes, either plasma membranes or the membranes of intracellular organelles. Many ion channels (such as most Na, K, Ca and some Cl channels) are gated by voltage, but others (such as certain K and Cl channels, TRP channels, ryanodine receptors and IP_3 receptors) are relatively voltage-insensitive and are gated by second messengers and other intracellular and/or extracellular mediators. As such, there is some blurring of the boundaries between 'ion channels' and 'ligand-gated channels' that are compiled separately in this guide. Many ion channels (e.g. K, Na, Ca, HCN and TRP channels) share several structural similarities. These channels are thought to have evolved from a common ancestor and have been classified together as the 'voltage-gated-like (VGL) ion channel chanome' (see Yu *et al.*, 2005). Other ion channels, however, such as Cl channels, aquaporins and connexins, have completely different structural properties to the VGL channels, having evolved quite separately. Currently, ion channels (including ligand-gated ion channels) represent the second largest target for existing drugs after G protein-coupled receptors (Overington *et al.*, 2006). However, the advent of novel, faster screening techniques for compounds acting on ion channels (Dunlop *et al.*, 2008) suggests that these proteins represent promising targets for the development of additional, novel therapeutic agents in the near future.

Further Reading

Dunlop J, Bowlby M, Peri R, Vasilyev D, Arias R (2008). High-throughput electrophysiology: an emerging paradigm for ion channel screening and physiology. *Nat Rev Drug Discov* **7**: 358–368.

Hille B (2001). *Ion Channels of Excitable Membranes*, 3rd Edition. Sinauer Associates: Sunderland, MA.

Overington JP, Al-Lazikani B, Hopkins AL (2006). How many drug targets are there? *Nat Rev Drug Discov* **5**: 993–996.

Yu FH, Yarov-Yarovoy V, Gutman GA, Catterall WA (2005). Overview of molecular relationships in the voltage-gated ion channel superfamily. *Pharmacol Rev* **57**: 387–295.