MOLECULAR PHYSIOLOGY OF ION CHANNELS

Classes of ion channels can be distinguished on the basis of electrophysiology, pharmacological, and physiological ligands, intracellular messengers, and sequence homology

Electrophysiology:

1. analyzing ionic currents by voltage clamp techniques
2. Characterization of channels accdg to:
    a. Selectivity (most striking difference)
    b. Voltage dependence
    c. Kinetics of gating behavior

Pharmacologic ligands:

Sensitivity to:

1. u-conotoxin
    a. strongly inh. Na in skeletal muscles
    b. little effect Na channels of neurons and cardiac myocytes
2. conotoxin
    a. inhibits voltage gated Ca2+ channels in spinal cord
3. Ziconitide: treatment of neuropathic pain in patients

Physiological ligands

Channels are activated by binding to an agonist

Example: Vertebrate Neuromuscular Junction

1. Presynaptic nerve terminus secretes ACh
2. Ach binds to Ach receptor
3. Ach receptor opens

Intracellular messengers

Physiological regulation by intracellular messengers

Example:

Ca 2+ gated K+

Ca2+ gated Cl-

Intracellular cyclic guanosine monophosphate

Sequence Homoogy

Many channels are formed by a radially symmetric arrangement of subunits or domains around a central pore

Essential function of a channel is to facilitate passive flow of ions across the hydrophobic membrane layer

General characteristics of Pores:

Aqueous pores

Location: center of an oligomeric rossetter like arrangement of homologous subunits int the plane of a membrane

Characteristic: weaves thru the membrane several times

Two special kinds of pores:

1. Gramicidin
    a. Forms a unique helix dimer
    b. Spans the membrane
    c. Hollow cylindrical region inside the helix is the channel pore
2. Porin
    a. Found in gram negative bacteria and outer membranes of the mitochondria
    b. Forms a large pore
    c. Surrounding the large pore are: