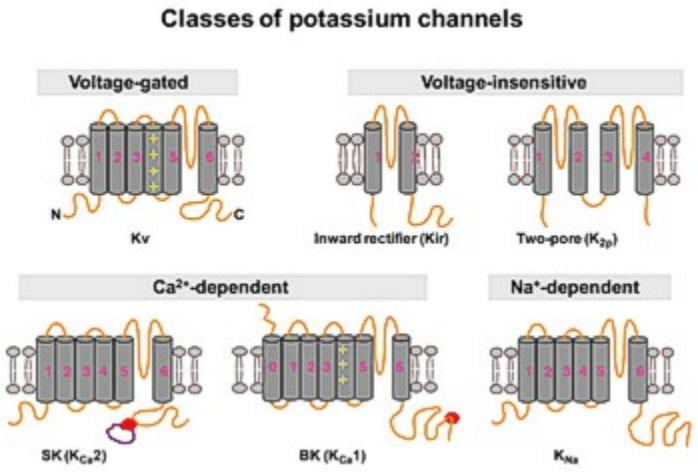
Haijun Chen Research Statement Details

Goal:

Ion channels are membrane proteins which allow ions across cell membranes in response to physical and/or chemical stimulations. They play a key role in electrical signaling of excitable cells such as neurons and cardiac myocytes. Dysfunction of ion channels could cause human neuronal, muscular, and cardiac disorders such as arrhythmia and epilepsy. Our goals are to understand how several subfamilies of potassium channels (Fig.1) are gated and regulated in physiological and pathological conditions.

Overview:



Background K+ channels in hypokalemia. Hypokalemia refers to lower-than-normal serum potassium (K+) concentrations. Moderate hypokalemia may cause muscular weakness, muscle cramps, cardiac arrhythmias. More severe hypokalemia may result in flaccid paralysis, cardiac arrest and paralysis of the lungs. According to Emergency Medicine, hypokalemia is clinically significant in as many as 0.8%-1% of hospitalized patients in USA. Several types of muscles can unexpectedly become depolarized in hypokalemia. Although this well-known phenomenon is the key to understand the pathological mechanism of hypokalemic periodic paralysis, the most frequent form of heritable periodic paralysis, its mechanism is not yet known. We attempt to study the function of background K+ channels in muscle cells and elucidate the molecular mechanism of paradoxical depolarization.

Na+-activated K+ channels in ischemia. Na+-activated K+ channels potassium channels highly express in the brain and heart, but its physiological role is not well understood. It was generally assumed that these channels protect neurons and cardiac cells from hypoxic injury during ischemia. We are interested in understanding molecular properties of these channels and how they contribute cardiac excitability and play an important role in cardio-protection.

Voltage-gated K+ channels in epilepsy. A novel protein was recently found to associate with inherited epilepsy, and it functions as a neurotransmitter. We are interested in elucidating molecular mechanisms how this protein regulates synaptic transmission and why its mutations can cause epilepsy. We hypothesize that this protein targets one accessory subunit of voltage-gated potassium channel complexes highly expressed in post-synapse, changes biophysical properties of these potassium channels, and then alters excitability of post-synapse. We will

examine this hypothesis in both the expression system and brain slices.

Approach:

We mainly use patch-clamp and two-electrode voltage-clamp techniques to record gating currents, single channel currents, macroscopic currents, whole-cell currents, resting potentials, and action potentials from the expression systems or native tissues, though we employ multidisciplinary approaches (molecular biology, protein biochemistry, immunocytochemical staining, fluorescence imaging, and knockout mouse strategy) to strengthen our research.