ClC-1 chloride channel - matching its properties to a role in skeletal muscle

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ClC-1 is a member of a large family of Cl^- channels. It is primarily expressed in skeletal muscle, and is essential for maintaining normal electrical excitability of the muscle. Mutations in the gene encoding ClC-1 have been shown to cause myotonia, an impairment of skeletal muscle relaxation after voluntary contraction. Myotonia results from an increase in muscle excitability that can be detected in electromyograms in the form of myotonic runs. In humans, there are two forms of this disease: autosomal recessive Becker-type myotonia congenita, and autosomal-dominant myotonia or Thomsen disease.

ClC-1, as the other members of this family, is a dimeric, double pored channel, with each monomer forming an individual conduction pathway. ClC-1, which has been studied extensively using electrophysiological techniques, shows a complex gating behaviour. It displays two types of gating — a faster gating process that opens and closes each protopore independently (the ‘fast’ or ‘single pore’ gates), and a slower gating process that closes both protopores simultaneously (the ‘slow’ or ‘common’ gate). Both types of gating depend on permeating anions, and intracellular and extracellular pH. Recent results show that gating of ClC-1 is also regulated by intracellular nucleotides.

Dependence of ClC-1 on pH and ATP makes it a likely contributor to a complex mechanism that regulates muscle contractility in exercise and fatigue. The exact role of ClC-1 in muscle physiology, however, is yet to be established.