Mechanism of Inactivation of Piezo Ion Channels

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Piezo proteins have been identified as key components of mechanosensitive ion channels in humans and other mammals. These channels are in the early stages of characterization; their mechanisms of inactivation—decrease in channel activity in the continued presence of a stimulus—remain unclear. Previous work shows that inactivation is faster for inward than outward Piezo1 currents. In the standard recording technique, two variables - voltage and direction of ion permeation - change in the transition from inward to outward currents. In this project, the concentration of permeable ions in the extracellular solution of the cell-attached method of patch-clamp electrophysiology was manipulated to shift the voltage at which ion permeation changed direction. Analysis of inactivation kinetics following this shift determined which variable was responsible for differing inactivation speeds. Distinguishing between the variables provides insight into the mechanism for inactivation of the Piezo1 ion channel; it was hypothesized that Piezo1 follows C-type inactivation, a mechanism characterized by a conformational change in the channel near the pore mouth and whose speed responds to permeable ion concentration. Data collected showed that permeable ion concentration did not significantly change inactivation kinetics, suggesting that C-type inactivation is not the mechanism of inactivation of this Piezo channel.

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