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Role of PIEZO channels in mechanotransduction

The recently discovered mechanically-gated ion channels PIEZO1 and PIEZO2 are involved in a variety of physiological functions essential to life. PIEZO1 plays a fundamental role in the development of the mouse vasculature as well as the lymphatic system. The PIEZO2 protein is found in sensory neurons of the dorsal root ganglia (DRG) and Merkel cells where its presence is essential for detecting tactile stimuli.

PIEZO channels are activated by mechanical stimulations such as shear stress, compression and stretch. Recently we discovered that PIEZO channels are also powerfully modulated by voltage and can even switch to a purely voltage gated mode of activation. This switch is particularly favored in mutant PIEZO channels that cause a vascular disease in humans (Xerocytosis).

In articular cartilage we also show that PIEZO1 acts together with TRPV4 to sense pressure stimuli and to maintain proper chondrocyte homeostasis.

Furthermore, analysis of older invertebrate (*Drosophila*) and vertebrate (*Zebrafish*) PIEZO proteins revealed remarkably different features from their mammalian orthologues resembling more closely voltage-gated ion channels. We conclude that the voltage sensitivity of mechanosensitive PIEZO channels is an ancient property co-opted to add a regulatory mechanism in mechanosensitive processes in widely different cellular contexts.