Cellular and molecular mechanisms involved in sensing mechanical stimuli

Hitoshi Tatsumi[1], Kimihide Hayakawa[2], and Masahiro Sokabe[1, 2]

[1] Dept. of Physiology, Nagoya University Graduate School of Medicine, Japan, [2] Cell Mechanosensing Project, ICORP/SORST, JST, Japan.

Mechanosensitive (MS) channels are expressed in a variety of cells. They are thought to play crucial roles not only in the mechanosensation by specialized mechanosensors such as hair cells and baroreceptors, but also in volume regulation and locomotion in ordinary cells. Elucidation of the molecular and biophysical mechanisms involved in the regulation of MS channel activities is a central interest in basic biology. It is controversial whether eukaryotic MS channels need accessory proteins – typically cytoskeletal structures – for activation, because MS channel activities are modulated by pharmacological treatments that affect the cytoskeleton. Here we demonstrate that direct mechanical stimulation (stretching) of an actin stress fiber using optical tweezers can activate MS channels in cultured human umbilical vein endothelial cells. By using high-speed total internal reflection microscopy, we visualized spots of Ca^{2+} influx across individual MS channels distributed near focal adhesions. This study provides the first direct evidence that the cytoskeleton works as a force-transmitting and force-focusing molecular device to activate MS channels in eukaryotic cells. Furthermore, our recent experiments on the interaction between the actin filament and cofilin, an actin severing protein, suggest that actin cytoskeleton also works as a force -sensing device. We will review the recent progress in this field.