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A Controlled Mechanical Stimulus Applied to Cells to Study Piezo2 Channel Activation

Giorgia Demontis [1], Fernanda De Castro Reis [2], Paul Heppenstall [2], Marco Lazzarino [3] , Laura Andolfi [3]

[1] Department of Physics, University of Trieste, Trieste, Italy [2] Scuola Superiore Studi Avanzati (SISSA), Trieste, Italy

[3] Istituto Officina dei Materiali-Consiglio Nazionale delle Ricerche (IOM-CNR), Basovizza-Trieste, Italy

The mechanosensitive PIEZO2 channel is essential for light touch and proprioception, with alterations linked to hypersensitivity and pain. While its gating is partly understood, modulation by mechanical stimuli remains unclear.

Combining Atomic Force Microscopy (AFM) or Fluidic Force Microscopy (FluidFM) with calcium imaging enables precise mechanical stimulation and real-time monitoring of PIEZO2 activity. HEK293 cells transfected with PIEZO2 were stimulated with a bead-modified AFM probe at 50nN for 0.5s and 10s. Cells responded efficiently to short stimuli, aligning with their role in light-touch. PIEZO2 activation also triggered calcium responses in neighboring cells, suggesting mechanosensitive communication. Bead-modified cantilever indentation can activate channels on both plasma and intracellular membranes.

To target plasma membrane channels, FluidFM was used on dorsal root ganglion neurons, which endogenously express PIEZO2. The microchanneled cantilever, brought in contact with the soma of the neuron, was used to apply positive/negative pressure. A differential response based on culture time, possibly reflecting changes in PIEZO2 expression/localization, was observed.

These findings highlight AFM and FluidFM's potential in studying PIEZO2 activity across different cellular compartments in intact whole cell. Supported by PRIN2020–Project TOAC.