Mechanoelectrical transduction at the membrane-matrix interface

K. Poole,[1,2] M.R. Servin Vences,[2] M. Moroni[2] and G.R. Lewin,[2] [1]Department of Physiology and EMBL Australia Node for Single Molecule Science, School of Medical Sciences, University of New South Wales, NSW 2052, Australia and [2]Department of Neurobiology, Max Delbruck Center for Molecular Medicine, Robert-Rossle Str 10, 13125 Berlin-Buch, Germany.

Mechanically-gated ion channels, such as PIEZO1, convert mechanical inputs into an electrical response, a signal transduction process known as mechanoelectrical transduction. A unique aspect of mechanical activation of ion channels is that the applied physical stimulus will be modulated by all of the physical elements in the pathway from the site of stimulus application to the channel itself. As such, it is important to understand how accessory proteins (both extracellular and intracellular) can locally regulate mechanosensitive channel activation, within transmembrane force-sensing domains. In order to quantitatively study mechanosensitive channel activity we are utilising a method to directly monitor mechanoelectrical transduction at defined regions of the cell-substrate interface. Namely, we culture cells on elastomeric arrays of cylindrical structures: stimuli are applied by deflecting an element of the array subjacent to a cell that is being monitored using whole-cell patch clamp. This approach enables us to precisely measure the stimulus applied to the cell. We have found that molecular-scale (approx. 13 nm) displacements are sufficient to gate mechanosensitive currents in mouse, touch-receptive neurons. Such sensitive responses are dependent on the membrane scaffolding protein, STOML3 and the underlying extracellular matrix. By manipulating the putative components of mechanoelectrical transduction complexes in a heterologous system we have been able to change the sensitivity and the kinetics of the mechanically-gated currents activated by substrate deflections. These data indicate that the varying mechanosensitivity of different cells and tissues might be regulated not only by the expression of unique channels but also by the modulation of channel activity by accessory proteins.