Disrupted Mechanotransduction, Elastic Modulus and Cell Tension in Actinin 1&4 Knockout Cells

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Actin is the most abundant intracellular protein in eukaryotic cells and is involved in multiple cell functions such as cell spreading, migration, transduction of mechanical forces and cell tension. A mesh of fine actin fibers provides the cell shape and stability, whereas thick fibers transduce intracellular forces and form together with myosin 2 contractile fibers for cell migration. Therefore, actin filaments are bundled to fibers with actin-crosslinker proteins. Most of the actin fibers are linked to focal adhesion proteins, that are crucial mediators for cell adhesion to the substratum. The non-muscle alpha actinins 1 and 4 (A1/A4) are high abundant F-actin binding proteins and play a crucial role in actin cytoskeleton organization [1]. To investigate the cellular function of A1/A4 in terms of mechanotransduction and intracellular tension we analyzed murine NIH3T3 fibroblasts where A1/A4 were knocked out using CRISPR/Cas9-mediated genome engineering [2]. Using atomic force microscope (AFM), we could show that the actin stress fibers are much thinner and deposited around the cell nucleus in A1/A4 KO cells, resulting in another distribution of the elastic modulus. In addition, A1/A4 KO cells largely lost their cell tension resulting in abnormal focal adhesion organization and migration behavior.

[1] Sjçblom et al.: Cellular and Molecular Life Science 65 (2008), 2688 – 2701

[2] Timper et al.: submitted manuscript