Force-associated changes in nuclear tension together with calcium waves orchestrate mechanical-stress dissipation at the tissue-scale level

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Abstract

It is for long accepted that biochemical signals and mechanical cues regulate cell fate and function. Cells are equipped with specific protein complexes to perceive mechanical stimuli at the cell-ECM and cell-cell junctions, and also at the nuclear envelope. Using these receptors tissues sense global changes in tension and through various mechanisms including cell intercalation, proliferation and apoptosis, actively respond to maintain tissue tensional-homeostasis. The exact molecular mechanisms, and specifically the role of calcium signaling in orchestrating tissue response to mechanical stress are only being uncovered. In our work, we used microfluidic system that enables local epithelial stretching and we precisely investigated the role of the triggered calcium waves in the regulation of the tissue response to mechanical stimulation. We showed, that local increase in tissue tension triggers calcium waves that together with the increase in nuclear envelope tension and activation of the cPLA2 phospholipase, orchestrate cellular contractility to actively and rapidly dissipate mechanical stress. We support our in vitro model, with the in vivo observations in drosophila and cricket’s embryos.

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