Cell Physics 2021

Title: A BIOMECHANICAL SWITCH REGULATES THE TRANSITION TOWARDS HOMEOSTASIS IN MOUSE ESOPHAGEAL EPITHELIUM.

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Abstract

Epithelial cells are highly dynamic and can rapidly adapt their behavior in response to tissue perturbations and increasing tissue demands. However, the processes that finely control these responses and, particularly, the mechanisms that ensure the correct switch to and from normal tissue homeostasis are largely unknown. Here we explore changes in cell behavior happening at the interface between postnatal development and homeostasis in the epithelium of the mouse esophagus, as a physiological model exemplifying a rapid but controlled tissue growth transition. Single cell RNA sequencing and histological analysis of the mouse esophagus reveal significant mechanical changes in the epithelium upon tissue maturation. Organ stretching experiments further indicate that tissue strain caused by the differential growth of the mouse esophagus relative to the entire body promotes the emergence of a defined committed population in the progenitor compartment as homeostasis is established. Our results point to a simple mechanism whereby the mechanical changes experienced at the whole tissue level are integrated with those “sensed” at the cellular level to control epithelial cell behavior and tissue maintenance.

Nat Cell Biol. 2021 May;23(5):511-525. doi: 10.1038/s41556-021-00679-w. Epub 2021 May 10.