MAR15-2014-020360

Abstract for an Invited Paper
for the MAR15 Meeting of
the American Physical Society

Unjamming phase transition in the asthmatic airway epithelium[1]

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In asthma, an aberrant injury-repair response of the airway epithelium is pivotal in disease initiation and progression. Although the mechanism remains unclear, classical understanding emphasizes inflammatory events together with delayed epithelial cell differentiation and maturation. Here we reveal a physical mechanism that is not anticipated by that classical picture but dominates dynamics of cells cultured from airway epithelia nonetheless. In the course of maturation of the pseudostratified epithelial layer comprising primary human bronchial epithelial cells from non-asthmatic donors, we show a striking collective cellular behavior in which an immature, hypermobile, unjammed, fluid-like phase undergoes a transition into a mature, quiescent, jammed, solid-like phase. But compressive stresses on the epithelial layer that mimic bronchospasm drive the solid-like phase back to the fluid-like phase. We show, further, that the uncompressed epithelial layer from asthmatic donors exhibit spontaneous collective migration behavior that is similarly striking to that observed in compressed normal cells. However, in this case the migration results from a delay in the innate tendency of the epithelial layer to transition from an unjammed phase into a jammed phase. Moreover, the unjammed state of asthmatic cells accompanies intensified adhesive forces transmitted across cell-cell junctions. We introduce a theory of critical scaling that predicts a priori the existence of the observed phase transition. Surprisingly, this theory predicts the transition to be governed by cell shape and cell-cell adhesive forces in a manner that is paradoxical, but is borne out by our direct experimental observations. Together, these findings establish an unanticipated but rigorous physical foundation for further classification and investigation of epithelial layer behavior in asthma, and likely in other processes in disease or development in which epithelial dynamics play a prominent role.

[1]National Science Foundation (R01HL102373, R01HL107561, P01HL120839)