On the mechanics between ERK wave, adhesion, and collective cell migration

Summary

The epithelial cells show ordered and directed migration in wound healing and morphogenesis. This collective cell migration is guided by solitary wave of activated ERK MAP kinase, and it is long believed that this collective guidance is distinct from chemotactic motility. Many studies have identified intercellular/intracellular pathway behind ERK wave-directed migration, but its physical mechanism is still elusive in spite of accumulated knowledge. To address this issue, we build continuum mechanical model by considering (1) the balance of forces, (2) the conservation of volume (absence of division), and (3) intercellular relaxation of ERK signal. We found that transient changes of cell adhesion and cell compression amplifies subtle drift by cell deformation into giant net motion of cells. Moreover, migration velocity shows frequency-dependence on the speed of ERK-wave. The interplay of slow mechanical relaxation and fast signaling decay explains the existence of optimum speed of ERK wave, which has been experimentally demonstrated by Aoki et al. Dev. Cell 2017. Our findings indicate that ERK wave can organize collective cell migration by mechanical coordination alone, which may impact on the current understanding of the relation between signaling and mechanics in epithelial cells.