M2 Systèmes Biologiques et Concepts PhysiquesResearch projects 2019-2020

Title

Contribution of myosin II motors and vimentin intermediary filaments to cells and tissues mechanics

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Project description :

(Description should give a brief presentation of the state of the art and project motivations, the main scientific and technical questions that will be addressed by the trainee, the type of work and of results that are expected and the team(s) with whom the trainee will work.)

The contractile and viscoelastic properties of cells are essential for embryogenesis, morphogenesis, and tissue repair. Actin fiber-associated Non-Muscle Myosins II (NMMII) are motors maintaining the cell cytoskeleton under tension, controlling cell shape, cell adhesion, cell migration and cell division. At the opposite, intermediary filaments are thought to be responsible of the mechanical resistance of cells and tissues to large strains. These filaments have a very long turn-over but display an amazing compliance. Thus, both acto-myosin and intermediary filaments may have very complementary contributions to the mechanics of cells and tissues, allowing cells to deform and migrate while maintaining their integrity.
In a very recent publication, we investigated the role of two isoforms of NMII (NMIIA and NMIIB) in intercellular junction biogenesis and remodeling in epithelial cells, an essential process for morphogenesis and tissue repair (https://elifesciences.org/articles/46599). We demonstrated that NMIIA and NMIIB had very different localizations and functions in cadherin-based intercellular junction biogenesis. NMIIA is responsible of the tugging force applied on the junction, eliciting its maintenance and maturation while NMIIB is responsible for the anchoring of adhesion complexes to the contractile NMIIA based actomyosin fibres.
Along this study, we unexpectedly found that NMIIB specifically associates to an intermediary filament network composed of vimentin. Vimentin is only expressed in epithelial cells after the initiation of the epithelial to mesenchymal transition at the border

of epithelial colonies. Given these observations and the very few reports on vimentin implication in cell and tissue biological and mechanical properties, we believe it is worse pursuing the study of the contribution of NMIIB-vimentin interaction to intercellular junction maintenance and more generally to cell and tissue biomechanics.
The PhD student, Gautham Sankara, who is one of the first authors of the eLife paper cited above has already engineered CRISPR-Cas9 epithelial cells Knocked Down (KO) for vimentin as well as cells in which NMIIA and NMIIB have been silenced using shRNAs. Under his supervision, using with cellular tools in hand, the trainee will combine the use of micro pattern-based cell confinement, high resolution live cell imaging, traction force measurement, and AFM-based cell rheology determination (in collaboration with F. Lafont , Institut pasteur Lille), to investigate the contribution of the viscoelastic properties of the actin-NMII-vimentin cytoskeleton to cell-cell contact mechanics.

Reference: Heuzé ML, Sankara Narayana GHN, D'Alessandro J, Cellerin V, Dang T, Williams DS, Van Hest JC, Marcq P, Mège RM, Ladoux B. Myosin II isoforms play distinct roles in adherens junction biogenesis. Elife. 2019 Sep 5;8. pii: e46599. doi: 10.7554/eLife.46599.