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Mechanical cues bridging from cancer to autophagy

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Cells sense and react to \textit{in vivo} mechanical cues generated by neighbouring cells, ECM or surrounding biological fluids. The actin cytoskeleton senses extracellular mechanical forces, is a scaffold for signalling, and acts as an effector of biological processes. Metastatic cells increase the formation of actin stress fibres in order to form filopodia (spike-like protrusions) and invapodia (actin-rich protrusions involved in extracellular matrix degradation) which facilitate the detachment from the primary tumour and the invasion of new tissues (reviewed in [1]). Additionally, actin dynamics regulate cell polarity; cell-polarity repression coincides with loss of cell-cell junctions and epithelial mesenchymal transition, cellular events that promote tumour initiation and growth. As cell-division is a polarized process within tissues, loss of cell-polarity also enables stemness and uncontrolled proliferation. Clearly, the actin cytoskeleton not only governs the cellular homeostasis, but also participates in disease pathogenesis (neurodegeneration and cancer).

The term “Macro-autophagy” coined a well-conserved process whereby lysosomes degrade cytoplasmic components which have been captured in double-membrane vesicles, named autophagosome. The physiological relevance of autophagy primarily comes from its role in maintaining the normal turnover of cellular components (homeostasis) and clearing intracellular pathogens, toxic damaged organelles, long-lived proteins and aggregates [2-4]. As actin regulation impacts on autophagy degradation, actin plays a major role in modulating the accumulation and aggregation of common autophagy substrates like mutant huntingtin, tau or p62. Understanding the role of actin-upstream and -downstream effectors in modulating autophagy would be a step forward in identifying new elements causing toxicity and disease progression [5].

References:

Solving large-scale optimization problems using the adjoint method

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Study of magnetization switching in systems of interacting macrospins

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# Conference Program

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