ACADEMY OF FINLAND

Molecular Regulatory Networks of Life

NUCLEOMECHANICAL REGULATION OF CELL STATES – FROM PLURIPOTENCY TO CANCER (NUCLEOMECH)

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Our organs are made out of cells that attach tightly to each other to produce tissues. In order to make and maintain a tissue with its specific architecture and function, cells divide, move, change their shape and differentiate to produce the necessary proteins for their specialized role. Embryonic development is initially driven by embryonic stem cells that actively shape their microenvironment and dynamically alter their own state to form organized tissue patterns. After organs have been generated, specialized tissue-resident stem cells are responsible for tissue maintenance. These tissue-resident stem cells have lost the fundamental property to actively shape tissue architecture and instead they remain stably in their committed, tissue-specific state guided by pre-existing tissue architecture.

Strikingly, cancer cells resemble embryonic stem cells in that they can dynamically alter their state, organize their local microenvironment during growth and invasion, and actively adapt to new tissue compositions during metastasis. Thus, it is of fundamental importance to understand a) which factors allow cancer to bypass the committed adult cell-state and tissue barriers, and b) is it possible to force these cancerous, stem-like states towards normal development to limit disease progression?

NucleoMech is a unique, multidisciplinary consortium of clinicians, engineers, and biologists aiming to identify such factors by analyzing the properties of cells in three interconnected states: induced pluripotent stem cells (modelling human embryonic stem cells), differentiated tissue-resident stem cells, and cancer cells. We will uncover pathways relaying mechanical information from the tissue environment into the nucleus that are central in regulating human cancer behavior. We will focus on upper airways malignancies (oral cavity, pharynx and larynx) – major killers with limited therapeutic options. NucleoMech will develop a cross-disciplinary program to decipher how tissue microenvironment mechanics impacts the genome and cell states, fundamentally influencing cancer onset and progression.

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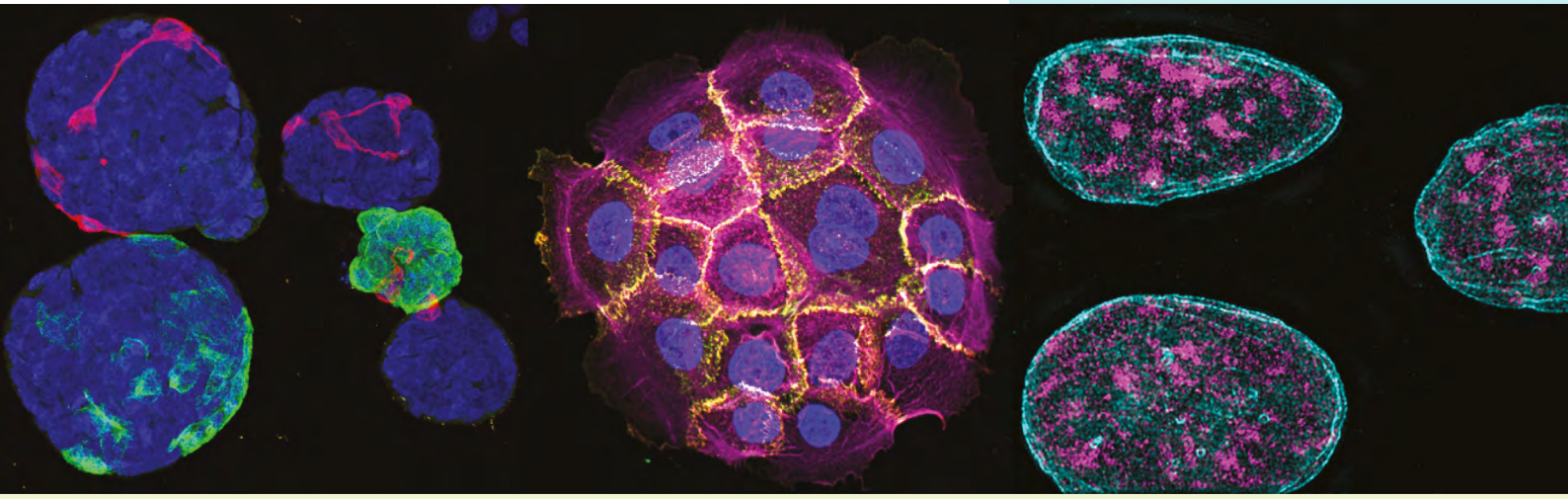

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