CCR – Impromptu Seminar

Friday, June 14th 2024, 14:30 PM

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Tracking the origin of cancer in space and time

Oncogenic mutations are abundant in tissues of healthy individuals, but rarely form tumours. Yet, how healthy tissue organization and dynamics may impact on the fate of these mutant cells remains unclear. Using the mammary gland as a model, we try to resolve these mechanisms. Making use of lineage tracing and (intravital) imaging approaches, we trace the fate of epithelial cells that acquire oncogenic mutations in their intact environment. We find that tissue hierarchy and dynamics, such as oestrous cycle driven remodelling, pregnancy and lactation, impact on mutant cell fate and behaviour. Interestingly, the impact of tissue remodelling is oncogene dependent, and may either be protective against or promoting mutant cell survival and spread. For example, in the context of Brca1-/-Trp53-/- cells, we find that rounds of local tissue remodelling, driven by the oestrous cycle leads to the stochastic and collective loss of mutant cells throughout the epithelium, and the elimination of the majority of mutant clones. However, it simultaneously enables a minority of mutant clones, that by chance survive, to geometrically expand. This expansion leads to cohesive fields of mutant cells spanning large parts of the mammary ducts. Eventually, this process of clone expansion becomes restrained by the one-dimensional geometry of the ducts, limiting uncontrolled colonization. Together, we reveal layers of protection that serve to eliminate mutant cells in healthy tissues, at the expense of the expansion of a minority of cells, which may spread, thereby predisposing the tissue to transformation.

Venue: Lecture Hall B2, Borschkegasse 4a
Time: June 14th 2024 – 14:30 PM
Host: Gergely Szakacs

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