



Life Sciences Seminar

Fine tuning of cell death during epithelial homeostasis: from local coordination to death commitment and cell extrusion

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While the signals regulating apoptosis during development are rather well known, what regulates the precise spatio-temporal distribution of cell death and the adjustment of cell elimination to local perturbations is not well understood. Using the *Drosophila* pupal notum (a single layer epithelium), we previously showed that cell extrusion and cell death could be modulated by cell deformations. We recently showed that this is mediated by the activation of the pro-survival signal EGFR/ERK by cell stretching. However, the exact contribution of the mechanical modulation of EGFR/ERK to normal development and morphogenesis was not known. By combining a live sensor of ERK, segmentation and tracking, we show that ERK is systematically activated for 1 hour in the first row of cells surrounding each extruding cell. This transient activation correlates with the transient stretching of the neighbouring cells and can be simulated by local ablation of a single cell. The pulse of ERK is sufficient to downregulate transiently caspase activation in the neighbouring cells. Using statistical analysis and simulations, we show that this feedback modulates the spatio-temporal distribution of cell death by generating a transient death-refractory zone around each dying cell. Finally, using a novel optogenetic tool to trigger caspase activation, we show that simultaneous extrusion of 3 cells is sufficient to perturb epithelial integrity. While such clusters are never observed in WT conditions, they start to appear upon perturbation of ERK feedback and are associated with transient loss of impermeability. Altogether, this work suggest that the global distribution of cell elimination is an emergent properties of local and transient feedbacks. In the second part, I will present our recent attempt to characterize the process of cell extrusion in the pupal notum and the contribution of caspase to cell extrusion.

Tuesday, February 11, 2020 04:15pm - 05:30pm

Mondi Seminar Room 3, Central Building



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