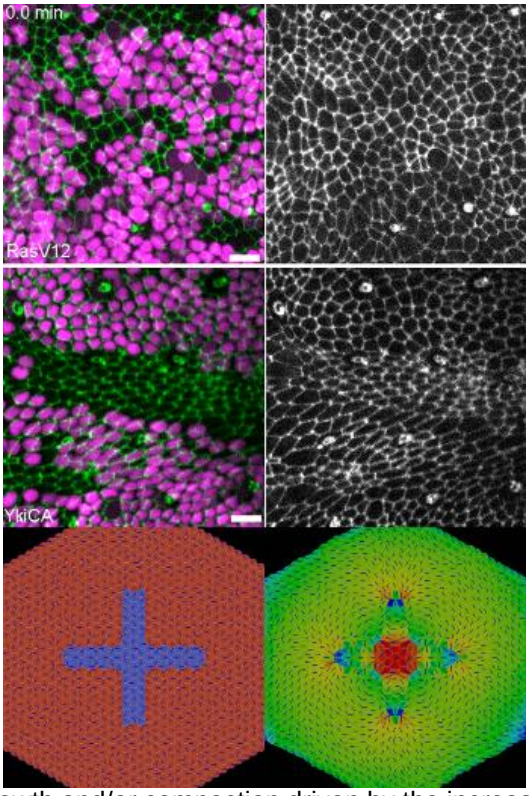
Characterisation of the role of tension at clonal interfaces during mechanical cell competition



The plasticity and robustness of living tissue is based on the capacity of every single cell to adjust its behavior to the modulations of its environment. This includes cell elimination through apoptosis. While this plasticity is required for tissue homeostasis and tissue morphogenesis, it can also be co-opted by a subset of cells to eliminate their neighbours and expand in the tissue. This is well illustrated by the concept of cell competition: a context-dependent cell elimination process that can drive the elimination of viable but suboptimal cells[1]. In this framework, supercompetitive cells can expand silently in the tissue by progressively eliminating neighbouring WT (wild type) cells by apoptosis. Several mechanisms have been proposed to participate to the preferential elimination of one cell population. Recently, we and others have shown that mechanical stress could drive preferential cell elimination through a process named mechanical cell competition[2-4]. Here, differential sensitivity to compaction lead to preferential elimination of one cell population. However, it is not clear how general is this process and whether different mechanisms can lead to cell compaction and cell elimination.

Recently, we characterized different oncogenes which can trigger compaction and elimination of neighbouring cells upon their activation in clones. More importantly, our preliminary results suggest that different mechanisms can promote the compaction and elimination of the WT cells: compaction driven by high clonal growth and/or compaction driven by the increase of tension at the clone interfaces. In this project, we would like to better characterise the mechanical properties of the interfaces between the clones and the WT cells and infer their impact on cell elimination.

The student will be using *Drosophila* pupal notum (a single layer epithelium) and the genetic tools of *Drosophila* to trigger conditional activation of oncogenes in clones. Using a combination of quantitative live imaging, laser ablation[5] and force inference methods[6], the student will characterise the relative changes of tension at the interfaces between the clones and the WT cells. These data will be integrated in a vertex model[7] to evaluate the impact of tension distribution on cell compaction and cell elimination. This project will lead to a better understanding of the mechanisms at play during mechanical cell competition, and in which conditions they can promote the expansion of pretumoural cells.

The internship will be performed under the supervision of two postdocs of the group (Léo Valon, biophysicist, Alexis Matamoro-Vidal, biologist) and the student will be fully integrated in the scientific activity of the lab (lab meeting, weekly seminars, workshop).

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