

Mechanisms driving symmetry-breaking in intestinal organoids

Symmetry-breaking events are fundamental biological processes for the formation of specialized tissues. In particular for intestinal organoids, symmetry-breaking is a paradoxical event: only a fraction of cells, part of a genetically identical population forming a cyst and immersed in unchanged medium, undergo differentiation. Although striking, the underlying mechanisms that drive symmetry-breaking are so far not known. In order to understand these mechanisms within a population of cells we need to be able to record with high spatiotemporal resolution the early growth of intestinal organoids as they form from single cells until around day 3, the usual time when symmetry-breaking has already occurred. This way we can extract important dynamical parameters such as cell distribution dynamics, synchronicity of cell divisions and cytoskeletal dynamics in order to answer the main causal relations needed for the appearance of the first differentiated cell. Such recordings are made possible by using a custom-built light-sheet microscope tailored for organoid imaging and developed in the lab. It not only allows the full recording of organoid formation with subcellular resolution but also gives potential to observe the tissues reaction to different perturbations in 3D over long periods of time, with the combination of e.g. a photoablation module. Furthermore, when combined with high content multivariate timecourse imaging, light-sheet microscopy allows the in-depth study of previously selected main mechanisms that might be driving symmetry-breaking in intestinal organoids.

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