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iPSZÜRICH

A Lecture Series Focused on Induced Pluripotent Stem Cells

FMI
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DYNAMICS AND PLASTICITY OF STEM CELLS IN THE REGENERATING HUMAN COLONIC EPITHELIUM

The human intestinal epithelium is a tissue with rapid turnover. Its complex regenerative process and differentiation trajectories have been challenging to study due to its inaccessibility and lack of temporal sampling. To this end, we developed a workflow to culture adult stem cell-derived human intestinal organoids from single cells to maturation. Extensive characterization of our model system indicated a transient regenerative response, followed by differentiation into all mature cell lineages. This switch is accompanied by a transition between two stem cell states. High-content screening and comparison to *in vivo* studies revealed that an initial fetal-like state is crucial for achieving successful regeneration, while the subsequent adult-like state is vital for maintaining a balance of cell lineages and continuous support of crypt-morphogenesis. Taken together, this study highlights the extensive plasticity of the intestinal epithelium and paves the way for further studies of human intestinal regeneration and its deregulation in pathologies.