CDB SEMINAR

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16:00~17:00 A7F Seminar Room

Establishment of intestinal stem cell culture system: from mouse to human

Summary

The intestinal epithelium is the most rapidly self-renewing tissue in adult mammals. Lineage tracing study demonstrated that Lgr5+ intestinal stem cells self-renew for long-term and produce all lineages of intestinal epithelial cells; enterocytes, goblet cells, enteroendocrine cells, Paneth cells. Recently, we developed a novel mouse intestinal stem cell culture system, in which Lgr5+ stem cells can form long-lived, self-organizing organoids under the presence of EGF, noggin and R-spondin1. R-spondin turned out to be a ligand for Lgr5 and activates canonical Wnt signal along with Wnt ligand. We found that Paneth cells, one of the daughter cells, express Wnt-3, EGF and Notch ligand, and function as stem cell niche in mouse small intestine.

As is the case for other adult human tissue stem cell culture system, the human intestinal stem cells are vulnerable to cellular senescence hindering long-term culture. We modified the mouse intestinal stem cells culture system by the addition of Wnt3A, Alk4/5/7 inhibitor, p38 inhibitor and nicotinamide, enabling single human intestinal stem cells to grow clonologically for long term (> 6 months). The technology was used to study metaplastic (Barrett epitlelium), inflammatory (inflammatory bowel disease), or neoplastic tissues (intestinal adenoma and cancer) from the human gastrointestinal tract. Furthermore, it was demonstrated that the organoids integrated into epithelial defect in mouse colitis model and accerelated intestinal mucosal healing.

Host:
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