

During gastrulation, three germ layers form: endoderm, mesoderm, and ectoderm, which determine tissue potential for organ formation depending on spatial location and signaling gradients. Generation of Organoids from PSCs and Adult Tissue PSC-derived organoids allow in vitro recapitulation of developmental processes. Adult tissue-derived organoids retain tissue identity and genetic stability over time. Endoderm-Derived Organoids Intestinal Organoids Require Wnt, Notch, FGF/EGF, and BMP/Nodal signaling. Derived from postnatal/adult epithelium or single intestinal stem cells. Cultured in 3D matrices (Matrigel) with EGF, Noggin, and R-spondin, allowing long-term expansion and differentiation. Gastric Organoids Derived from adult gastric stem cells or PSCs. Key signals: WNT3A, FGF4/10, Noggin, Retinoic acid. Main challenge: differentiation into mature parietal cells, requiring mesenchymal co-culture. Liver Organoids Contain hepatocytes and cholangiocytes (endodermal), plus mesenchymal cells (mesodermal). First long-term adult murine liver organoids developed in 2013 using HGF, EGF, FGF, and RSPO1. Single-cell-derived organoids retain hepatocyte function. Human liver organoids model diseases like A1AT deficiency, Alagille syndrome, polycystic liver disease, and cancer. Pancreatic Organoids Derived from embryonic pancreas progenitors or adult ductal cells. Culture with Matrigel, FGF10, Noggin, RSPO1, and EGF. Embryonic organoids produce endocrine/exocrine cells; adult-derived organoids mostly form ductal epithelium. Lung Organoids Include upper- and lower-airway organoids. PSC- or adult tissue-derived organoids require TGF $\beta$ /BMP inhibition, FGF4, Wnt, and Hedgehog activation. Contain basal, ciliated, club cells with mesenchymal support. Co-culture with neural or immune cells enhances growth and differentiation. Thyroid Organoids Generated from PSCs via forced expression of thyroid-specific transcription factors and BMP/FGF signaling. Form functional follicular structures in vitro, restoring thyroid hormone levels upon transplantation