

Supplementary Table 2. Methods for Organoid Engineering.

Method	Timeline of Organoids	Advantages	Disadvantages	Applications	Ref.
Bioprinting	Intestinal organoids (2021)	Controlled cell-matrix structures; Precise 3D biological geometries	Resolution of printed material; Density of the tissue; Organ functionality	Functional organ formation; Large-scale manufacture of artificial organs for transplantation and regenerative medicine	1,2
Droplet microfluidics	Cholangiocyte organoids (2021), Inter-organoid platform (2020), Lung organoids (2021)	Powerful platform for manipulating organoids; Establishment of complex organoids	Lacking control over the cell-to-cell ratios in the structures	Assessing intra-organoid heterogeneity; Fabricating homogenous organoids	3,4
Microwells	Intestinal organoids (2014), Kidney organoids (2018), Liver organoids (2018)	Controlled cell aggregation and growth patterns	Small scale	Live-cell manipulations; Direct quantitative analysis of organoids	5-7
Gel embedment	Intestinal organoids (2016-2017, 2021-2022);	Recapitulates the ECM components of tissue	Non-defined composition, lack of control over spatiotemporal cues	Increasing variability, decoupling stiffness, and enhancing the functionality of organoids	8-16
Surface tethering	Various organoids	Provides ECM support and signaling cues		Producing biomimetic scaffolds for organoid culture; Dissecting the	17,18

Scaffold anchoring	Intestinal organoids (2020)	Offers flexibility with specificity; Provide geometrical cues		stem cell niche Optimizing the combination of signals for modulating ASCs; Scale-up of organoids in a well-defined manner	19,20
Micro-fabricated cages/organ-on-chips	Liver organoids (2014), Pancreatic organoids (2019), Stomach organoids (2018), Kidney organoids (2019)	Can imitate key physiological and structural features of the organ	Absent of vascular structures	Drug screening; Disease modeling; Investigating cell-cell, cell-organ, and organ-organ interactions	7,21-28