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Primer

Organoids

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Supplementary Information

Supplementary Table 1: Soluble factors for organoids.

Cell Source	Matrix		Organoids	Soluble Factors
Tissue sampling (ASCs)	Growth factors Gel embedment		Intestine	Wnt, EGF, IGF, FGF, BMP, TGF
			Liver	Wnt, EGF, HGF, FGF, BMP, TGF, ROCK
			Gastro	Wnt, EGF, FGF, BMP, TGF
			Lung	Wnt, FGF, BMP, TGF, ROCK, MAPK
			Pancreas	Wnt, EGF, FGF, BMP, TGF
			Prostate	Wnt, EGF, FGF, BMP, TGF
			Endometrium	Wnt, EGF, HGF, FGF, BMP, TGF
			Tongue	Wnt, EGF, FGF, BMP, TGF
Genetic engineering (iPSCs)	BMP 4	Neuroectoderm	Brain	Wnt
			Eye	Wnt, IGF, FGF
	Activin-A/BMP4	Mesoderm	Vessel	Wnt, FGF, VEGF, BMP
			Kidney	Wnt, FGF
	Activin-A	Endoderm	Intestine	Wnt, EGF, FGF, BMP
			Gastro	Wnt, EGF, FGF, BMP
			Liver	FGF, BMP
			Lung	Wnt, FGF, BMP, TGF
			Thyroid	Wnt, EGF, FGF, BMP

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

				stem cell niche	
Scaffold anchoring	Intestinal organoids (2020)	Offers flexibility with specificity; Provide geometrical cues		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

Supplementary Table 3: List of repositories with data formats (data deposition)

Repository	Type	Status	Data formats	Link
PDMR: Patient-derived models' repository	Human cancer organoid repository, as part of bigger cancer material repository	Data-requests and specimen-request only, organoid request in development, no data or material deposition	patient diagnosis data, originating patient material, PDX, PDC and CAF, PDO, sequencing data (whole exome and RNAseq)	https://pdmr.cancer.gov
HCA|Organoid: Human Cell Atlas Organoid	Human organoids, both tissue-derived and iPSC-derived	Pilot – preformed on brain organoids (iPSC) and colon organoids (tissue), no data or material deposition	single-cell transcriptomics, single-cell epigenomics and time-series imaging, matched to primary tissue	https://hca-organoid.eu
Gene Expression Omnibus (GEO)	Transcriptomics-related data	Data deposition for all transcriptomics, not limited to organoids	gene expression, non-coding RNA, ChIP, genome methylation, high-throughput RT-PCR, SNP arrays, SAGE, protein arrays	https://www.ncbi.nlm.nih.gov/geo/
GitHub	Code-sharing platform	Code deposition, not limited to organoids	code for analysis in variety of software	https://github.com

*PDX – patient-derived xenograft, PDC – patient-derived cell line, CAF – cancer-associated fibroblast, PDO – patient-derived organoids, iPSC – induced pluripotent stem cells, ChIP – chromatin immunoprecipitation, SAGE – serial analysis of gene expression

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