Supplementary tables

Supplementary Table S1. Complete overview of studies applying metabolomics and/or lipidomics to organoid-based models included in this review. For each study, the organoid type, biological origin, omics strategy, analytical platform, and primary biological context are reported.

Author (Year)	Journal	Organoid type	Species / origin	Omics approach	Analytical platform	Biological context
Bonanini et al. (2024)	Exp Cell Res	Hepatic organoids	Human, adult donor-derived	Targeted lipidomics	HILIC-MS/MS (Exion LC AD + QTRAP 6500+)	Energy metabolism and glucose production
Braun et al. (2020)	Cancers	Pancreatic PDOs	Human, patient-derived	Untargeted metabolomics	GC-MS	Cancer recurrence mechanisms
Cappuccio et al. (2023)	Front Mol Biosci	Brain organoids	Human dorsal forebrain	Spatial metabolomics & lipidomics	HR-MALDI-MSI + Orbitrap FTMS	Human brain development
Chen L. et al. (2022)	J Chromatogr B	Colorectal PDOs	Human, patient-derived	Untargeted metabolomics	UPLC-QTOF-MS	Metabolic response to curcumin
Chen J. et al. (2023)	Bioact Mater	Biliary ductal organoids	Human-derived	Untargeted metabolomics	LC-MS (dansylation labeling)	Biliary tree regeneration
Chen L. et al. (2025)	Biosci Rep	Colon PDOs	Human, patient-derived	Metabolomics + transcriptomics	HPLC-Orbitrap MS/MS	PHGDH inhibition, serine metabolism
Cheng et al. (2025)	Environ Res	Hepatic organoids	Human hESC-derived	Metabolomics + transcriptomics	UHPLC-OE-MS	Aged microplastic toxicity
Druso et al. (2025)	BMC Mol Cell	Tracheospheres	Mouse	Targeted metabolomics +	UHPLC-Q Exactive	Differentiation media effects

	Biol			transcriptomics	MS	
Duivenvoorden et al. (2023)	Anal Chem	Intestinal organoids	Human small intestine	Lipidomics + MSI	MALDI-MSI + Orbitrap MS	Spatial lipid phenotyping
Eckenstein et al. (2025)	Metabolites	RCC tumoroids	Human, patient-derived	Metabolomics + proteomics	RPLC-Orbitrap Q Exactive HF	Mitochondrial translation inhibition
Ene et al. (2025)	Stem Cell Res Ther	Blood vessel organoids	Human iPSC-derived	Targeted lipidomics	UPLC-Triple Quad 6500 (MRM)	Extracellular vesicle biomanufacturing
Fan et al. (2025)	J Biol Chem	Breast cancer PD-OTCs	Human, patient-derived	SIRM (dual tracers)	IC-UHR-FTMS + NMR	Metabolic reprogramming, therapy
Feng et al. (2025)	Food Res Int	Hepatic polyspheres	Human HepG2-derived	Untargeted metabolomics	LC-MS	DBP-induced toxicity
Gadara et al. (2024)	Anal Chem	Cerebral organoids	Human hiPSC-derived	Targeted lipidomics	Microbore LC-MS/MS (Triple Quad 6495)	APOE-related lipid phenotypes
Kes et al. (2025)	Cell Rep Med	Kidney tumoroids	Human, pediatric	Metabolomics + isotope tracing	Q Exactive HF / Exactive MS	Nucleotide synthesis vulnerability
Koc et al. (2025)	BMC Ophthalmol	Corneal organoids	Human hiPSC-derived	Untargeted metabolomics	GC-MS	Aniridia-associated keratopathy
Krauß et al. (2025)	EMBO Mol Med	AKP colorectal organoids	Mouse-derived	Metabolomics + transcriptomics	UHPLC-Q Exactive Orbitrap	EGFR-driven metabolic rewiring
La Gioia et al. (2025)	Anal Bioanal Chem	Colorectal PDOs	Human, patient-derived	Untargeted metabolomics	Micro-UHPLC-Orbitrap Exploris 120	Low-input sensitivity enhancement

Li X. et al. (2025)	Toxicol Appl Pharmacol	Lung organoids	Mouse AT2-derived	Untargeted metabolomics	GC-MS	Anti-tuberculosis drug toxicity
Li Y. et al. (2023)	Cell Rep Med	PDAC PDOs	Human, patient-derived	Targeted metabolomics + lipidomics	LC-MS + GC-MS + UHPLC-QTOF	Chemotherapy resistance
Liu X. et al. (2022)	Sci Total Environ	Brain organoids	Human hiPSC-derived	Lipidomics + transcriptomics	UPLC-Orbitrap MS	Graphene oxide toxicity
Liu Q. et al. (2024)	Adv Sci	Cochlear organoids	Mouse-derived	Metabolomics + transcriptomics	LC-MS/MS (Triple TOF 5600)	Hair cell differentiation
Neef et al. (2020)	Metabolites	Colorectal PDOs	Human, patient-derived	Metabolomics + lipidomics	LC-QTOF-MS (HILIC + RPLC)	5-FU metabolic response
Notaras et al. (2021)	Mol Psychiatry	Forebrain organoids	Human-derived	Metabolomics + proteomics	Hybrid MS	Neuropsychiatric risk
Ochima et al. (2025)	Front Bioeng Biotechnol	Kidney-related 3D cultures	Human HEK293T	Untargeted metabolomics	400 MHz ^{1}H-NMR	Cell adhesion mechanisms
Rodrigues et al. (2021)	Arch Toxicol	Intestinal organoids	Human colon & SI	Metabolomics + transcriptomics	FI-MS (Q Exactive)	5-FU intestinal toxicity
Romeo et al. (2023)	Nat Commun	Blood vessel organoids	Human iPSC-derived	Metabolomics + proteomics	LC-MS/MS Q-TOF	Microvascular integrity
Sekhar et al. (2023)	Front Endocrinol	Parathyroid PDOs	Human, benign	Untargeted metabolomics	UHPLC-MS/MS Q Exactive HF	Hyperparathyroidism
Taylor et al. (2020)	Sci Rep	Adipose organoids	Mouse-derived	Shotgun lipidomics	Q Exactive Plus	Immune–adipocyte crosstalk

Toyoda et al. (2024)	Cancer Sci	Pancreatic organoids	Mouse-derived	Metabolomics + proteomics	SWATH-MS + CE-TOFMS	TP53-related vulnerabilities
van der Kemp et al. (2023)	NMR Biomed	CRC tumoroids	Human-derived	Targeted metabolomics	HR-MAS MRS + solution NMR	Tumor progression
Wang G. et al. (2022)	Cell Stem Cell	Kidney organoids	Human fetal / hiPSC	Metabolomics + transcriptomics	MALDI-MSI + NMR	Metabolic fate trajectories
Wang Q. et al. (2021)	Front Genet	Kidney organoids	Human hiPSC-derived	Metabolomics + transcriptomics	UHPLC-Orbitrap MS	Differentiation dynamics
Wang X. et al. (2024)	Food Res Int	Intestinal organoids	Human-derived	Metabolomics + transcriptomics	Triple TOF 6600	Breast milk vs formula
Wang X. et al. (2025)	Mol Nutr Food Res	Intestinal organoids	Human-derived	Multistage metabolomics	Triple TOF 6600	Nutritional effects
Wang X. et al. (2024)	Nutrients	Intestinal organoids	Human-derived	Multi-omics	LC-QTOF-MS	ECM and junctional biology
Xuan et al. (2024)	Sci Total Environ	Intestinal organoids	Mouse-derived	Untargeted metabolomics	LC-MS/MS	Nanoplastic safety
Xuan et al. (2025)	Ecotoxicol Environ Saf	Lung organoids	Mouse-derived	Metabolomics + transcriptomics	LC-MS	Radiation toxicity
Zhou et al. (2025)	Acta Pharmacol Sin	CRC PDOs	Human paired primary/metastatic	Targeted metabolomics	GC-TOFMS + UPLC-MS/MS	Histone lactylation in metastasis

Supplementary Table S2. Detailed technical characteristics of analytical platforms used in organoid-based metabolomics and lipidomics studies.

Platform category	MS analyzer	Chromatography / acquisition	Quantification	Typical metabolome coverage	Representative studies
Untargeted LC–MS	Orbitrap, Q-TOF	UHPLC (RPLC/HILIC), ESI ±	Relative (TIC, peak sum, z-score)	10^2–10^3 features	Braun 2020; Chen 2022; Wang X 2025
Targeted LC–MS	Triple quad, Orbitrap	UHPLC–MS/MS (MRM/PRM)	Absolute / semi-absolute	10^1–10^2 metabolites	Krauß 2025; Druso 2025
Lipidomics (LC/MS)	Orbitrap, triple quad	HILIC-MS/MS, shotgun	Relative / absolute	10^2–10^3 lipids	Bonanini 2024; Gadara 2024
Microbore LC–MS	Triple quad, Orbitrap	1.0 mm i.d. UHPLC	Relative	10^2–10^3 features	Gadara 2024; La Gioia 2025
GC–MS	Single quad, TOF	EI-GC-MS + derivatization	Relative	10^1–10^2 metabolites	Braun 2020; Koc 2025
MSI	TOF, Orbitrap, FTICR	MALDI-MSI	Relative (pixel-based)	10^2 m/z features	Cappuccio 2023; Wang G 2022
NMR	400–800 MHz	HR-MAS / solution ^{1}H-NMR	Relative (AUC)	~10–50 metabolites	van der Kemp 2023
Multi-platform / SIRM	Orbitrap, Q-TOF, NMR	LC–MS + GC–MS ± tracers	Absolute / enrichment	Pathway-resolved	Fan 2025; Kes 2025