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LC-MS, Organoids and Organ-on-Chip

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*DiMasi et al. 2016, Journal of Health Economics **Franzen et al, 2019, Drug discovery today

Why animal research?



Human systemic

- Biological similarity to humans
 - 85% of mice genes are analogue in humans
- Complexity of a full organism
- Understanding disease mechanisms
- Regulatory need
- Scientific necessity



Human systemic

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Mouse Genome Sequencing Consortium, *Nature* 2002 Stanford University, 2025 Harvard Medical School, 2025

Issues with animal models

1/3 of drugs tested in animals reach clinical trials

Of that 1/3, <8% pass phase I

85% failure rate from pre-clinic to clinic

- 46% toxicity
- 35% lack of efficacy

50% of drugs that pass phase III make it to market

5% of animal tested drugs obtain approval

UNIVERSITY OF OSLO Hackam et al. *JAMA*FDA, Report, 2004 Ledford et al. *Nature*Ineichen et al. *PLOS Biology*





What are organoids and organ-on-chip?

- Differentiated from e.g. iPSC or patients
- Developmental biology
- Self-organizing
- Recapitulate organ-specific functions
- Microfluidic devices
- Based on Lab-on-chip devices
- Lined with cells or tissues



Aizenshtadt et al. Advanced Healtcare Materials 2024



What's the point?

"Top 10 emerging technologies to change human lives"

- World Economic Forum (2016)

"Organoids named technology of the year"

- Nature Methods (2017)

"Emulate - 10 most innovated biotech companies"

- Fast Company (2022)

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Science

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FDA no longer needs to require animal tests before human drug trials

New law welcomed by animal welfare groups, but others say change won't happen fast

JAN 2023 • 5:30 PM • BY MEREDITH WADMAN

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Convincing data that demonstrates the advantages of human organ chips over animal models will be needed before pharmaceutical companies accept this new technology into their laboratories.

- Ingber et al. in Nature Reviews Genetics (2022)

Liquid chromatography – Mass Spectrometry

• How much sugar is in this cake?



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Conventional HPLC-MS for drug metabolism



Page 10

Harrison et al. Experimental & Molecular Medicine 2023

Organ-in-a-Column



Page 11

Key take away

 Direct coupling of LC-MS to OoC-like devices is possible

Limitations

- Only semi-quantitative
- Poor separative power (5 cm C4 column)
- Low robustness
- Increased MS-maintenance



Kogler et al. Analytical Chemistry 2022

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Medium complexity



William's E Medium

Amine Aside	Vitemine	In expensio Celto
Amino Acids	Ivitamins	inorganic Saits
L-Alanine	Ascorbic Acid • Na	Calcium Chloride
L-Arginine (free base)	D-Biotin	Calcium Nitrate • 4H2O
L-Asparagine • H2O	Calciferol	Cupric Sulfate • 5H2O
L-Aspartic Acid	Choline Chloride	Ferric Nitrate • 9H2O
L-Cysteine (free acid)	Folic Acid	Magnesium Chloride • 4H2O
L-Cystine	myo-Inositol	Magnesium Sulfate (anhydrous)
L-Glutamic Acid	Menadione (sodium bisulfite)	Potassium Chloride
L-Glutamine	Niacinamide	Sodium Bicarbonate
Glycine	D-Pantothenic Acid (hemicalcium)	Sodium Chloride
L-Histidine (free base)	Pyridoxal • HCl	Sodium Phosphate Monobasic (anhydrous)
L-Isoleucine	Retinol Acetate	Zinc Sulfate • 7H2O
L-Leucine	Riboflavin	
L-Lysine • HCl	Thiamine • HCl	
L-Methionine	DL-α-Tocopherol Phosphate • Na	
L-Phenylalanine	Vitamin B12	
L-Proline	Other	
L-Serine	D-Glucose	
L-Threonine	Glutathione (reduced)	
L-Tryptophan	Methyl Linoleate	
L-Tyrosine • 2Na • 2H2O	Pyruvic Acid • Na	
L-Valine		

+ biomolecules from Organoids

Additivos	
Automotes	
10/ EDC	
1/0103	
1% ΝΕΔΔ	
1% GlutaMAX	
2/0 01010111 01	
0.1% ITS	
0.1% Pen-strep	

Page 13

Kogler et al. Analytical Chemistry 2024

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Determination of tolbutamide and 4-hydroxy tolbutamide



Kogler et al. Analytical Chemistry 2024

Validated method for OoC samples

- C18 column
 Robust (>1000 injections)
 Simultaneous and accurate determination
 Minimal off-line sample preparation
 Validated for selectivity, matrix interference, accuracy, precision, linearity, range, LLOD/LLOQ and carryover.
 - Compliant with FDA and ICH guidelines

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Chip system



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Page 16

Busek et al. Lab on a chip 2023

Organoid and Chip Samples



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Electromembrane extraction of cell culture media



Unacidified

SDS-PAGE of samples and extracts



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Page 19

NMR to evaluate small molecules

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Page 20



Organoids exposed to diltiazem



Kogler et al. Analytical Chemistry 2025

Page 21



Cellspace is an innovation project from the Hybrid Technology Hub at the University of Oslo and Oslo University Hospital.

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Thank you for your attention!

Bioanalytical Chemistry Hybrid Technology Hub

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