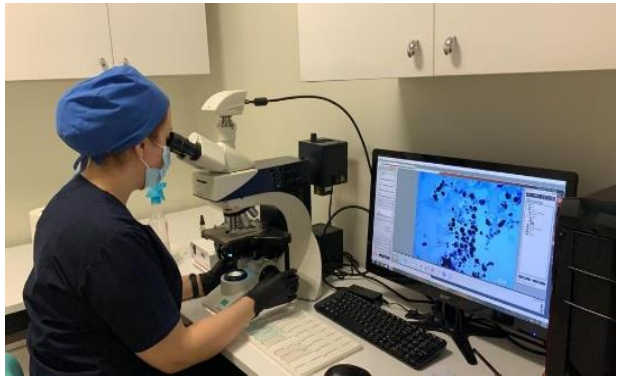
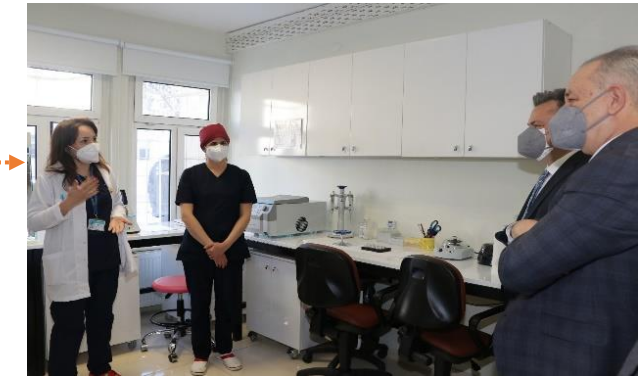
MicroStemTissue.com

Cellular Therapy and Stem Cell Production

Cell Culture Rooms



Immunohistochemistry Lab



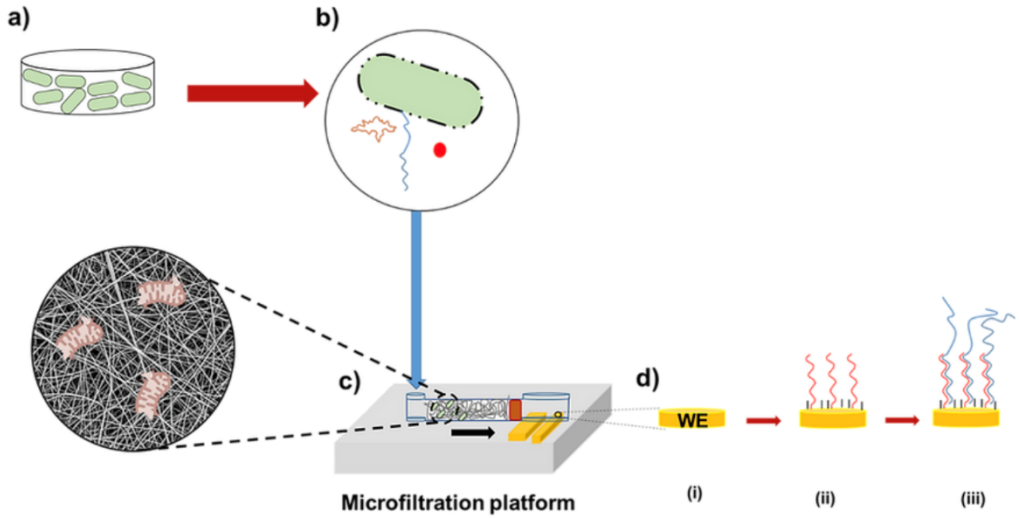
Molecular Biology Labs

Flow Cytometry & Immunophenotyping Labs

Tissue Engineering & MEMS

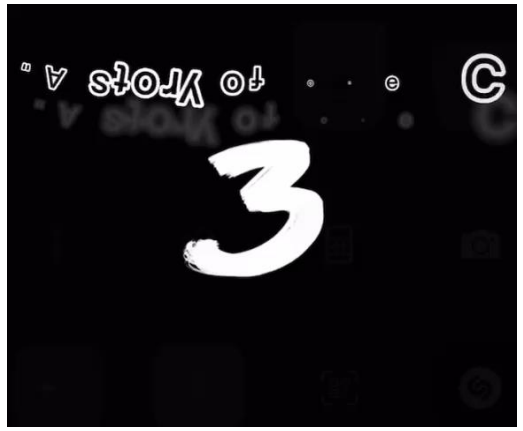
Metallurgy and Materials Engineering
Biomaterials Research and Development Laboratory

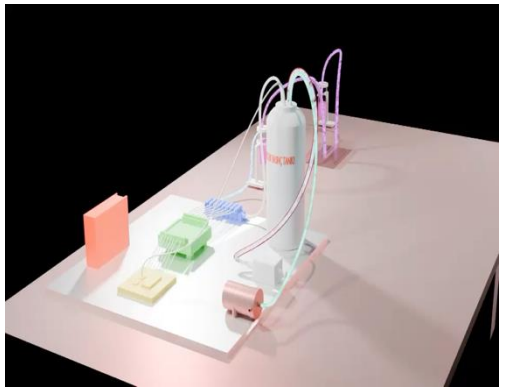
- Nanolif uretimi
- Filtrasyon uygulamalari
- Kontrollu ilac salinimi

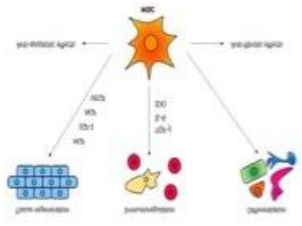


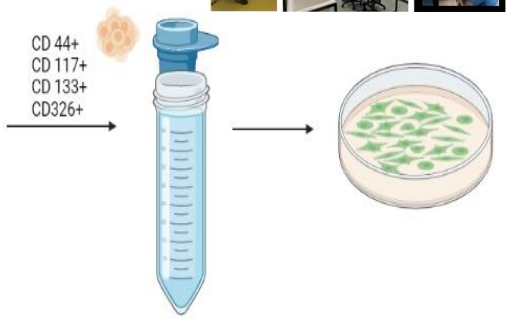
Currently;

- More than 13 MSc (8 international)
- 17 PhDs (4 international)
- 5 Postdocs
- 4 Visiting Scholars





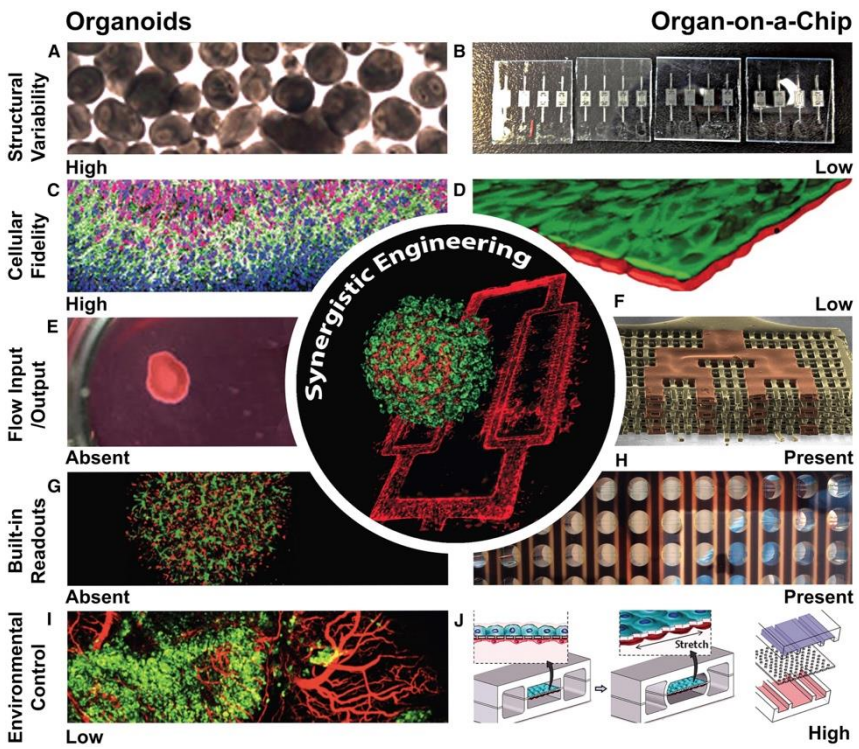


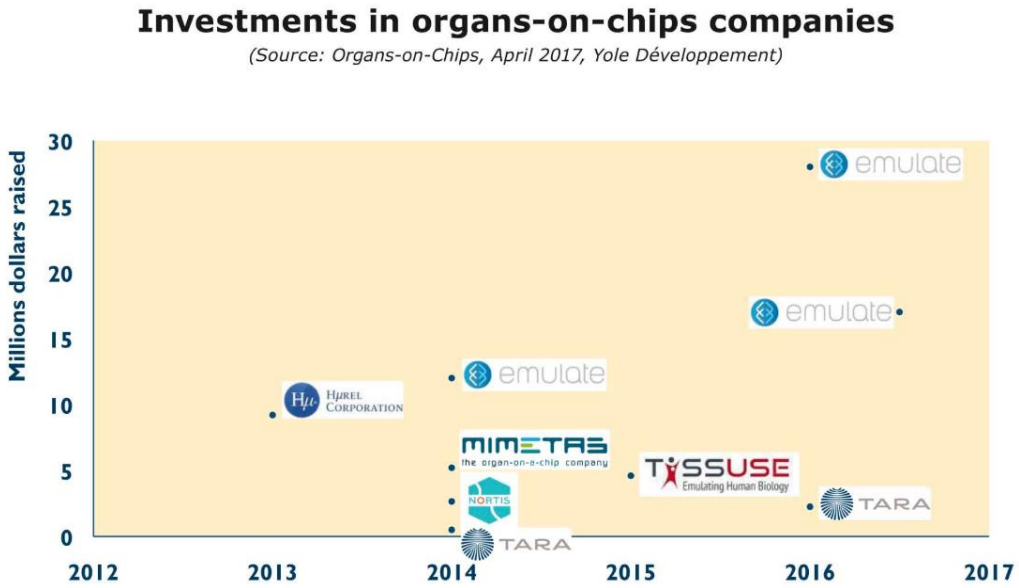


At present;

- 1 International, 5 TUBITAK, 1 TUSEB supported projects
- 6 Scientific Research Foundation (Eskisehir Osmangazi University)

A promising platform: Organ on a Chip





https://bisresearch.com/industry-report/organ-on-chip-market.html

*https://www.sciencedirect.com/science/article/pii/S193459091730334X

DRUG DEVELOPMENT PROCESS

Out of every 10,000-15,000 new compounds identified during discovery, **five are considered safe for testing** in human volunteers. **Only one of these compounds** is typically approved **as a marketed drug.**

10,000-15,000 Compounds → 250 Compounds → 5 Compounds → 1 FDA-Approved Drug

3-6 YEARS	6-7 YEARS	0.5-2 YEARS
Drug Discovery	Clinical Trials	FDA Review
Pre-clinical	Phase I: 20-100 Volunteers	Manufacturing
	Phase II: 100-500 Volunteers	Phase IV Post-Approval
	Phase III: 1,000-5,000 Volunteers	
Pre-discovery	IND Submitted	NDA Submitted

AVERAGE COST: $3 billion+ DURATION: 10-15 years*

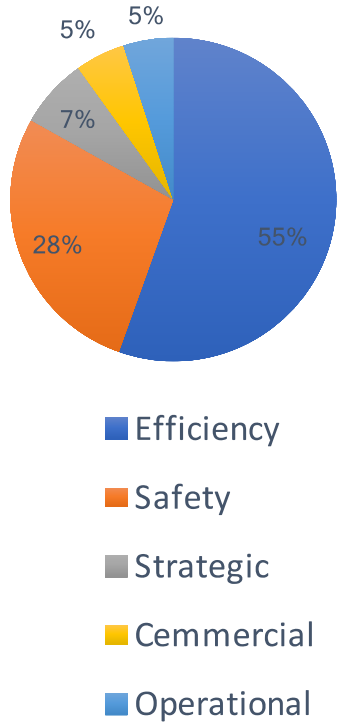
PPD

*Source: ACRO

ppdi.com

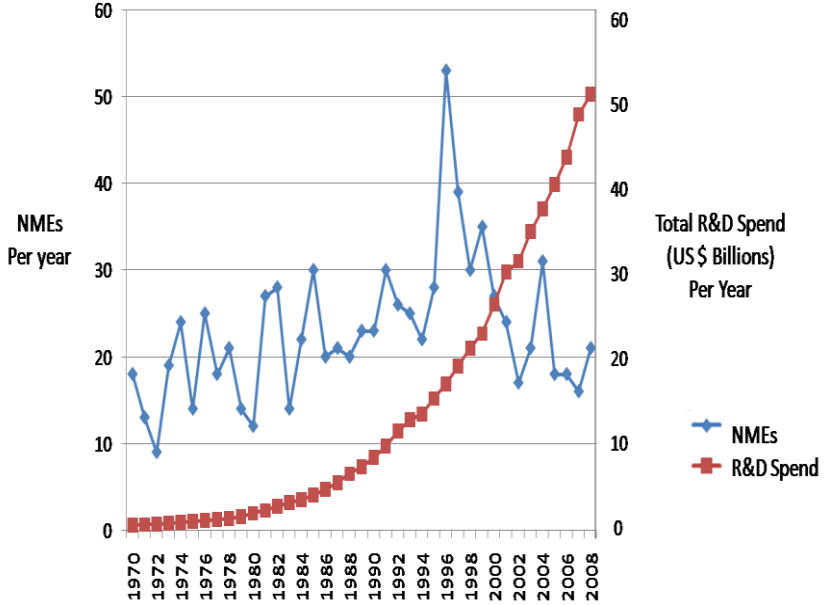
$9.1 billion R&D

Cause to failure

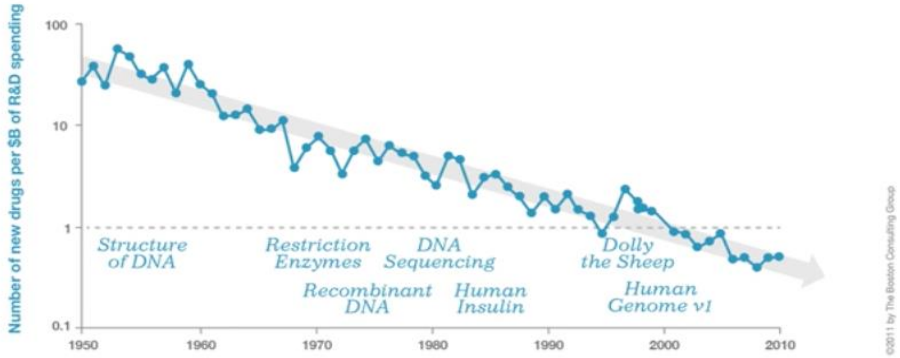


Nature Reviews | Drug Discovery

More money less drugs :(



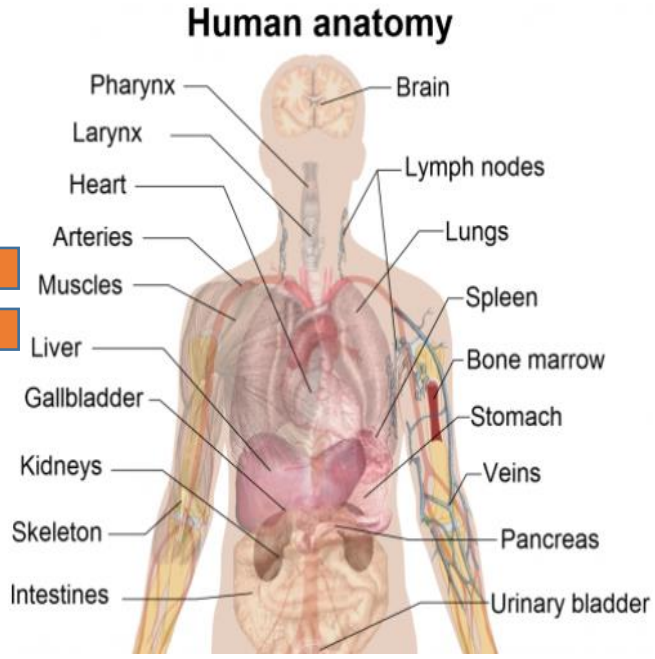
R&D productivity is on the decline



Two main tools...

Static planar cell cultures

Animal models



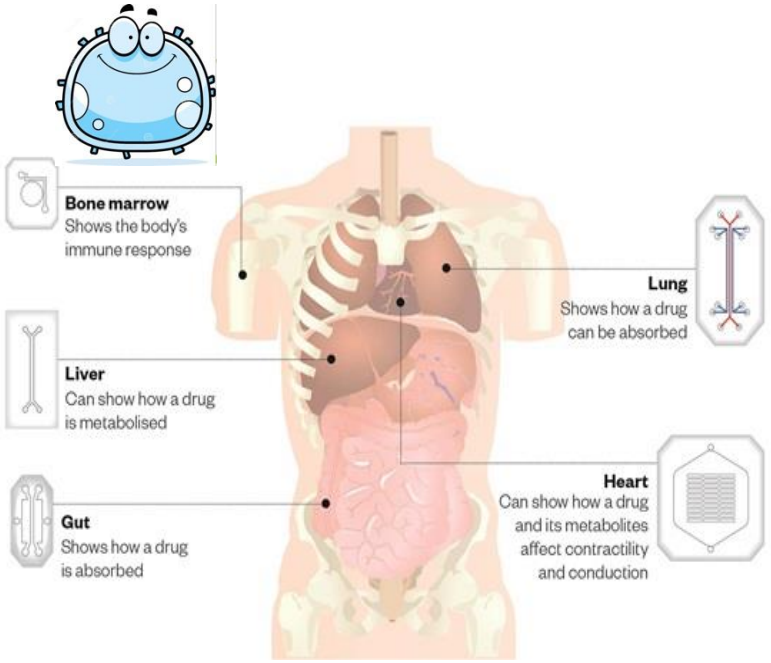
Nature Reviews | Drug Discovery

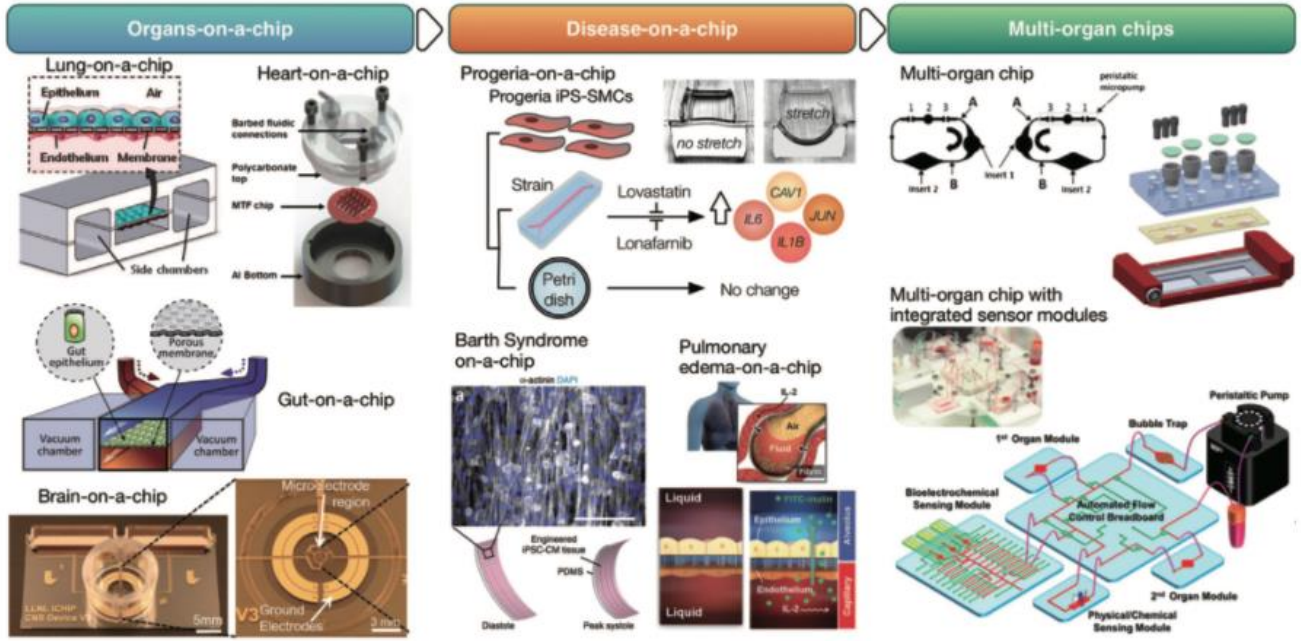
Exciting new avenues for drug discovery and development:

Organs-on-chips

- Organ-on-a-chip systems are miniaturized microfluidic 3D human tissue and organ models designed to recapitulate the **important biological and physiological parameters** of their *in vivo* counterparts.
  - High-resolution, real-time imaging and *in vitro* analysis of biochemical, genetic and metabolic activities of living cells in a functional tissue and organ context.

- These *in vitro* models, featuring biomimetic compositions, architectures, and functions, are expected to replace the conventional planar, static cell cultures and bridge the gap between the currently used preclinical animal models and the human body.

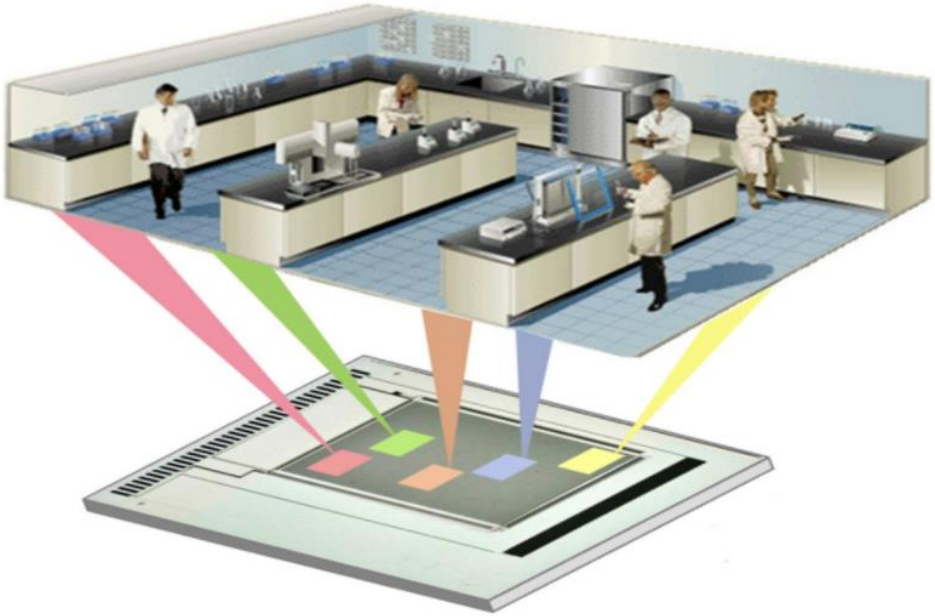




~7000 rare disease

Ribas et al., 2018

LoCs can provide advantages!



- Sample savings – nL of enzyme, not mL
- Faster analyses – online monitoring, real-time imaging, can heat, cool small volumes quickly
- Integration – combine lots of steps onto a single device
- Labor-free testing reducing human errors
- Long-term monitoring

tissue development, organ physiology and disease etiology

Forbes

Jan 11, 2022, 05:00am EST | 102,578 views

Moral Progress Denied By FDA Leadership: New 'OOC' Technology Could Have Allowed The FDA To Abandon Its Cruel Animal Testing Requirements.

Dr. David Gortler | FDA Drug Safety & Investigational Medicine News
Contributor ⓘ
Healthcare
Former FDA Medical Officer and Senior Advisor to the FDA Commissioner

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KYIV, UKRAINE - 2021/09/05: An animal protection activist holds a placard reading "Animal Lives ... [+] SOPA IMAGES/LIGHTROCKET VIA GETTY IMAGES

the #FDAModernizationAct 2.0, which would update drug-testing regulatory standards for the first time in nearly 100 years.

https://www.forbes.com/sites/davidgortler/2022/01/11/moral-progress-denied-new-ooc-technology-could-have-allowed-the-fda-to-abandon-its-cruel-animal-testing-requirements/?sh=3bb017f2323c

Science

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

10 JAN 2023 · 5:30 PM · BY MEREDITH WADMAN

New medicines need not be tested in animals to receive U.S. Food and Drug Administration (FDA) approval, according to legislation signed by President Joe Biden in late December 2022. The change—long sought by animal welfare organizations—could signal a major shift away from animal use after more than 80 years of drug safety regulation.

"This is huge," says Tamara Drake, director of research and regulatory policy at the Center for a Humane Economy, a nonprofit animal welfare organization and key driver of the legislation. "It's a win for industry. It's a win for patients in need of cures."

In place of the 1938 stipulation that potential drugs be tested for safety and efficacy in animals, the law allows FDA to promote a drug or biologic—a larger molecule such as an antibody—to human trials after either animal or nonanimal tests. Drake's group and the nonprofit Animal Wellness Action, among others that pushed for changes, argue that in clearing drugs for human trials the agency should rely more heavily on computer modeling, "organ chips," and other nonanimal methods that have been developed over the past 10 to 15 years.

Tens of thousands of rodents are used by companies for drug toxicity testing each year. IEVGEN CHABANOV/ALAMY

A version of this story appeared in Science, Vol 379, Issue 6628.

Science

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

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past 10 to 15

U.S. FOOD & DRUG ADMINISTRATION

Search Menu

Home / Drugs / Drug Safety and Availability / FDA's ISTAND Pilot Program accepts a submission of first organ-on-a-chip technology designed to predict human drug-induced liver injury (DILI)

FDA's ISTAND Pilot Program accepts a submission of first organ-on-a-chip technology designed to predict human drug-induced liver injury (DILI)

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Drug Safety and Availability

Drug Alerts and Statements

[9/24/2024] FDA's Center for Drug Evaluation and Research (CDER) has accepted the first letter of intent (LOI) into the Innovative Science and Technology Approaches for New Drugs (ISTAND) Pilot Program for an organ-on-a-chip technology, a type of micro-physiological system (MPS), to study drug-induced liver injury (DILI) for certain drug candidates.

Content current as of:
09/24/2024

Regulated Product(s)
Drugs

A version of this story appeared in Science, Vol 379, Issue 6628.

Got a tip for Science's news department?
CONNECT

Global MPS Day
March 9, 2023

https://www.science.org/content/article/fda-no-longer-needs-require-animal-tests-human-drug-trials

HIGHLIGHT

feature

Features • PERSPECTIVE

Impact of organ-on-a-chip technology on pharmaceutical R&D costs

Nora Franzen[1,2], Wim H. van Harten[1,2], Valesca P. Retèl[1,2], Peter Loskill[3,4], Janny van den Eijnden-van Raaij[5] and Maarten IJzerman[2,6], m.j.ijzerman@utwente.nl

Healthcare systems are faced with the challenge of providing innovative treatments, while shouldering high drug costs that pharmaceutical companies justify by the high costs of R&D. An emergent technology that could transform R&D efficiency is organ-on-a-chip. The technology bridges the gap between preclinical testing and human trials through better predictive models, significantly impacting R&D costs. Here, we present an expert survey on the future role of organ-on-a-chip in drug discovery and its potential quantitative impact. We find that the technology has the potential to reduce R&D costs significantly, driven by changes in direct costs, success rates and the length of the R&D process. Finally, we discuss regulatory challenges to efficiency improvements.

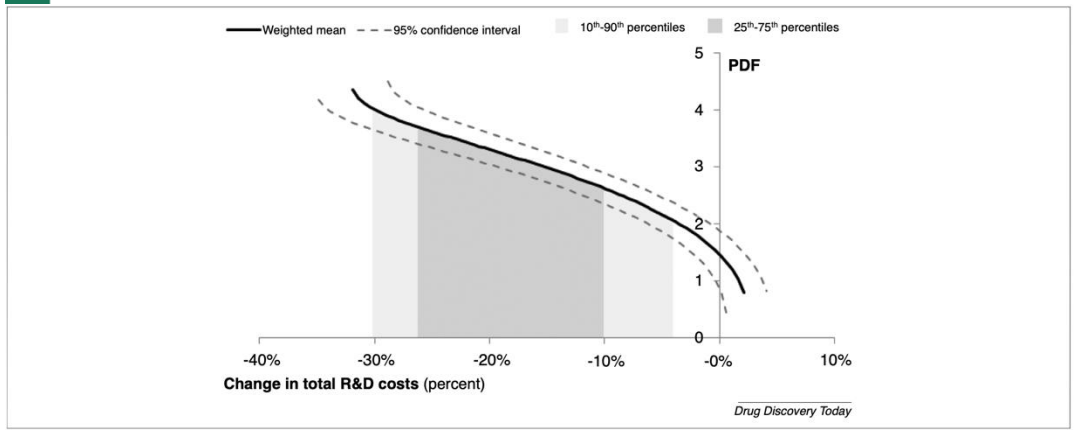

FIGURE 1

Relative likelihood of organ-on-a-chip-induced change in total R&D costs: probability density function (PDF) of the beta distribution. Analysis of the relative likelihood of the change in total R&D costs owing to organ-on-a-chip in 5 years. The probability density function (y axis) is plotted as a function of the from the experts' survey probable change in total R&D costs (x axis). The dashed lines represent the 95th confidence interval of all values. The shaded area represents the area under the curve: 50% of all values show a reduction in total R&D costs of 10–26% (dark gray). Eighty percent of the values show a reduction in total R&D costs of 4–30% (light gray).

communications medicine

ARTICLE

https://doi.org/10.1038/s43856-022-00209-1 OPEN

Performance assessment and economic analysis of a human Liver-Chip for predictive toxicology

Lorna Ewart[1✉], Athanasia Apostolou[1], Skyler A. Briggs[1], Christopher V. Carman[1], Jake T. Chaff[1], Anthony R. Heng[1], Sushma Jadalannagari[1], Jeshina Janardhanan[1], Kyung-Jin Jang[1], Sannidhi R. Joshipura[1], Mahika M. Kadam[1], Marianne Kanellias[1], Ville J. Kujala[1], Gauri Kulkarni[1], Christopher Y. Le[1], Carolina Lucchesi[1], Dimitris V. Manatakis[1], Kairav K. Maniar[1], Meaghan E. Quinn[1], Joseph S. Ravan[1], Ann Catherine Rizos[1], John F. K. Sauld[1], Josiah D. Sliz[1], William Tien-Street[1], Dennis Ramos Trinidad[1], James Velez[1], Max Wendell[1], Onyi Irrechukwu[2], Prathap Kumar Mahalingaiah[3], Donald E. Ingber[4,5,6], Jack W. Scannell[7] & Daniel Levner[1]

Results Here, we show that the Liver-Chip met the qualification guidelines across a blinded set of 27 known hepatotoxic and non-toxic drugs with a sensitivity of 87% and a specificity of 100%. We also show that this level of performance could generate over $3 billion annually for the pharmaceutical industry through increased small-molecule R&D productivity.

COMMUNICATIONS MEDICINE | (2022)2:154 | https://doi.org/10.1038/s43856-022-00209-1 | www.nature.com/commsmed

HIGHLIGHT

feature

Features • PERSPECTIVE

Impact of organ-on-a-on pharmaceutical R&

Nora Franzen[1,2], Wim H. van Harten[1,2], Valesca P. Retèl
Janny van den Eijnden-van Raaij[5] and Maarten IJzerma

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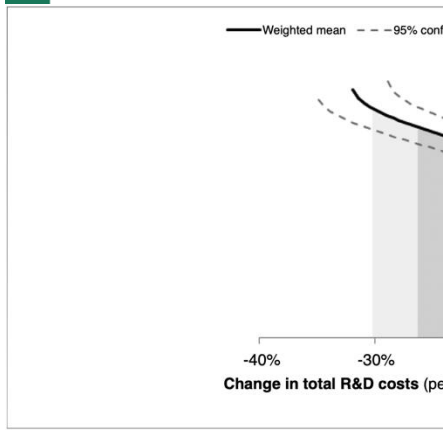

FIGURE 1
Relative likelihood of organ-on-a-chip-induced change in total R
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experts' survey probable change in total R&D costs (x axis). The da
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costs of 4–30% (light gray).

Contents lists available at ScienceDirect

Toxicology Letters

journal homepage: www.journals.elsevier.com/toxicology-letters

National reflection on organs-on-chip for drug development: New regulatory challenges

Sonia Gomes Teixeira [a], Paul Houeto [a,*], Florence Gattacceca [b], Nicole Petitcollot [b], Danièle Debruyne [b], Michel Guerbet [b], Joël Guillemain [b], Isabelle Fabre [a], Gaelle Louin [a], Valérie Salomon [a]

[a] *French National Agency for Medicines and Health Products Safety (ANSM), 143/147 Boulevard Anatole France, 93285 Saint-Denis, France*
[b] *External Experts of Permanent Scientific Committee (PSC) of French National Agency for Medicines and Health Products Safety (ANSM), 143/147 Boulevard Anatole France, 93285 Saint-Denis, France*

ARTICLE INFO

Editor: Dr. Angela Mally

Keywords:
Organs-on-chip (OoC)
Microphysiological systems (MPS)
Liver-on-a-chip
Drug development
Preclinical models
Regulatory criteria

ABSTRACT

Organs-on-chip (OoC) are innovative and promising *in vitro* models, particularly in the process of developing new drugs, to improve predictivity of preclinical studies in humans. However, a lack of regulatory consensus on acceptance criteria and standards around these technologies currently hinders their adoption and implementation by end-users. A reflection has been conducted at the National Agency for Medicines and Health products safety (ANSM) in order to address this issue, which has gained momentum at the international level in recent years. If the subject of OoC is of international interest, France is also in the process of structuring an OoC network, in order to best support the emergence of this new technological innovation. Focusing on liver-on-a-chip, the authors drafted a first list of regulatory requirements to help standardize these devices and their use. Technological and biological relevance of liver-on-a-chip was also evaluated, in comparison with current *in vitro* and *in vivo* models, based on the available literature. The authors offer an analysis of the current scientific and regulatory situation, highlighting the key regulatory issues for the future.

Check for updates

ıic analysis of
:icology

ı[1], Jake T. Chaff[1],
ıg[1], Sannidhi R. Joshipura[1],
:opher Y. Le[1],
)uinn[1], Joseph S. Ravan[1],
ıis Ramos Trinidad[1],
, Donald E. Ingber[4,5,6],

ıidelines across a blinded
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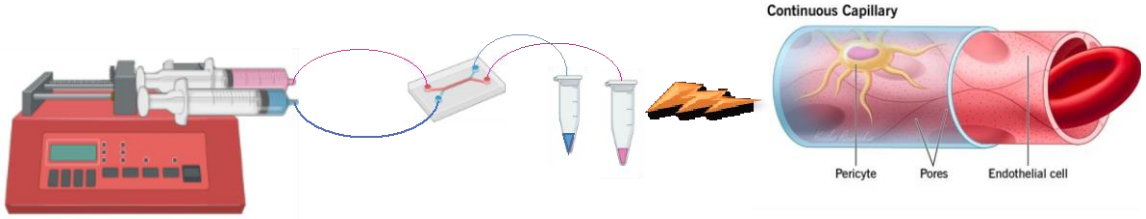
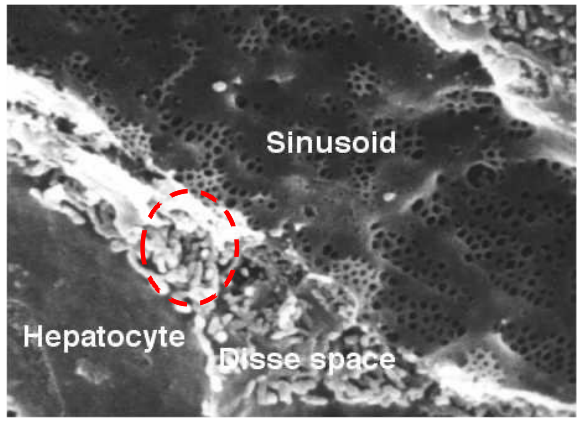
ver $3 billion annually for
) productivity.

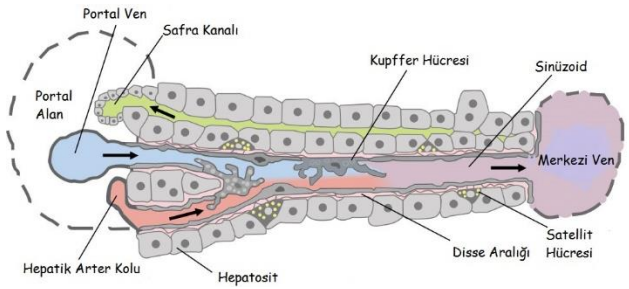
TÜBİTAK

Mimic the dynamic and micro-environment!

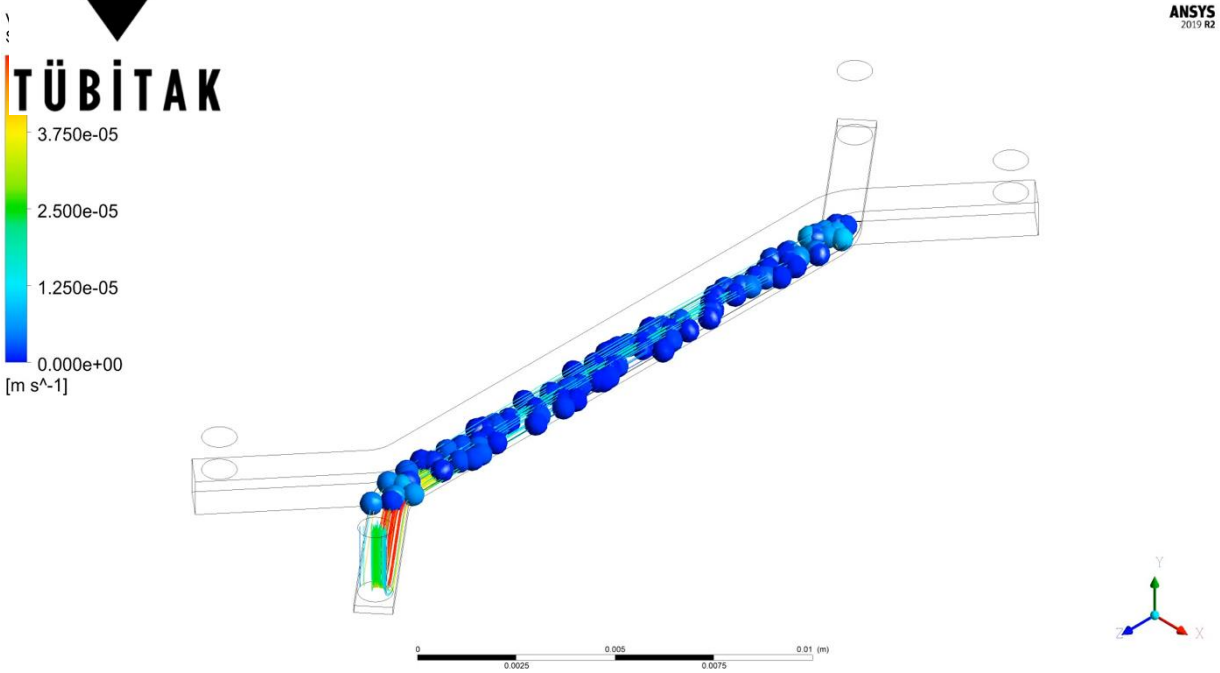
Ongoing Projects

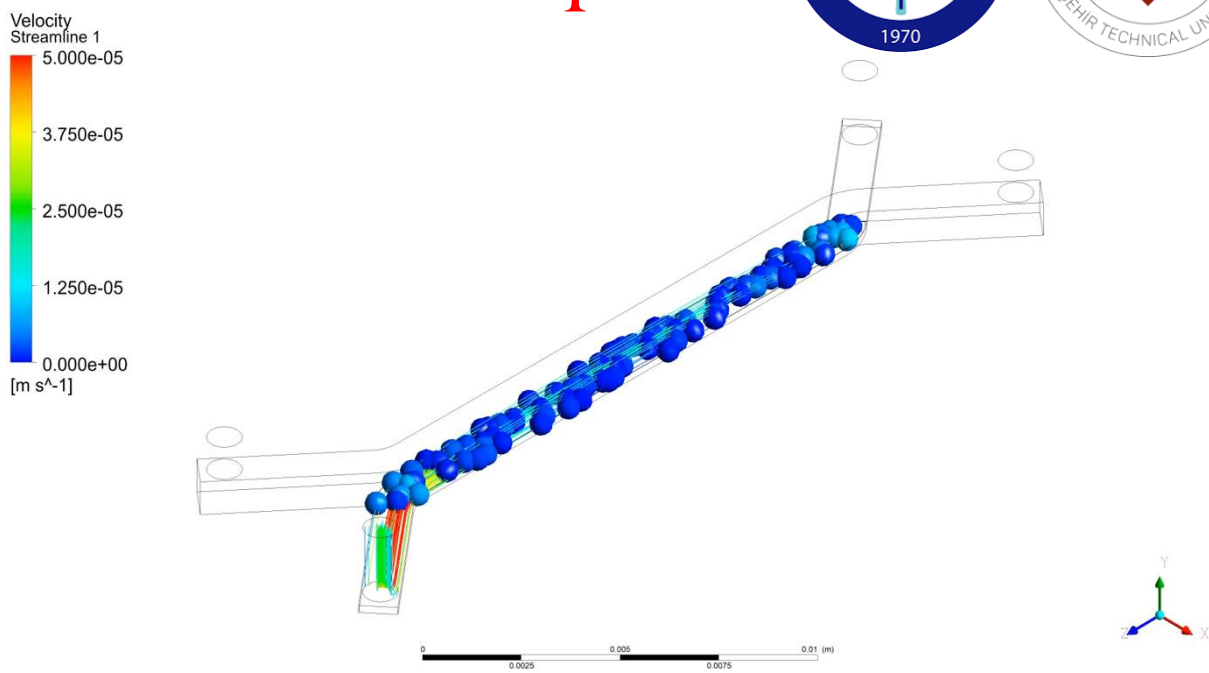


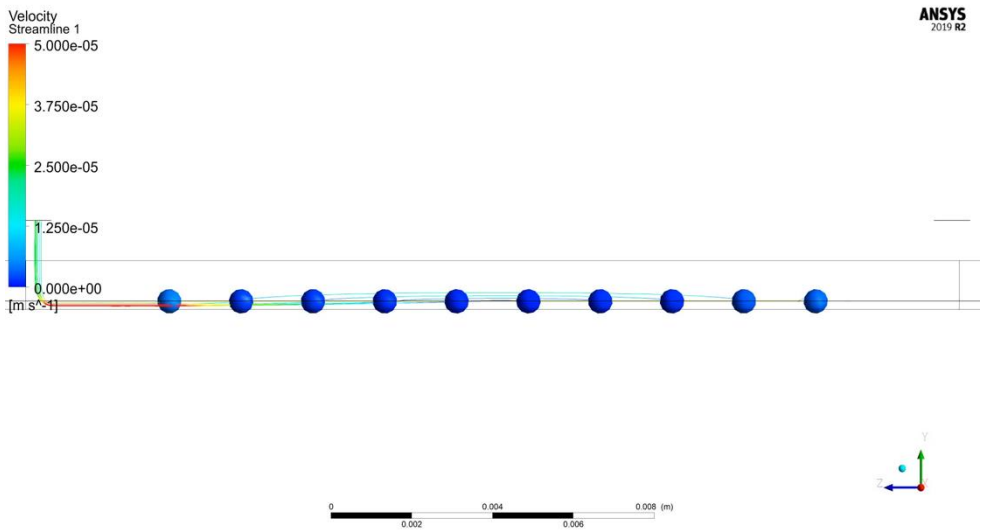




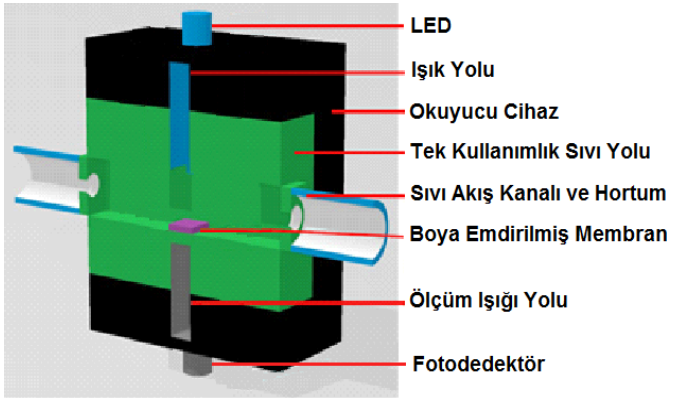
Simulation of Microfluidic Chip

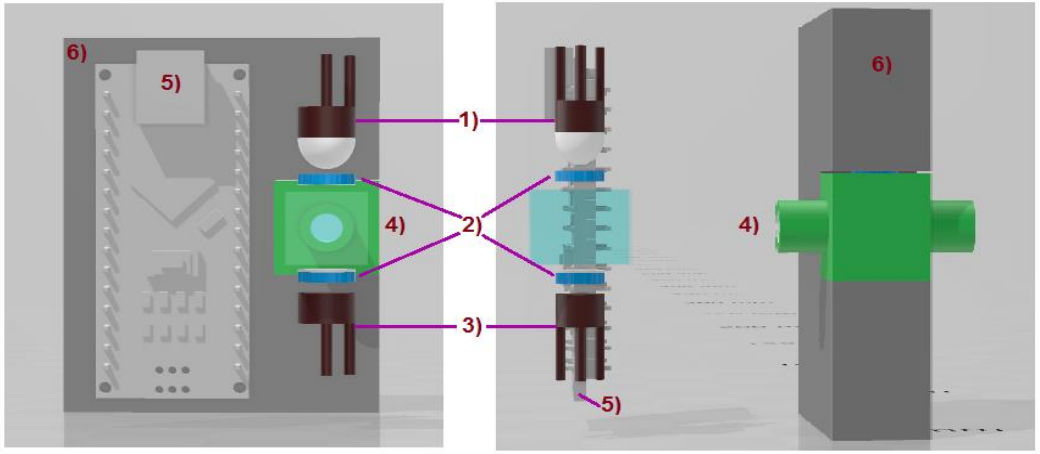


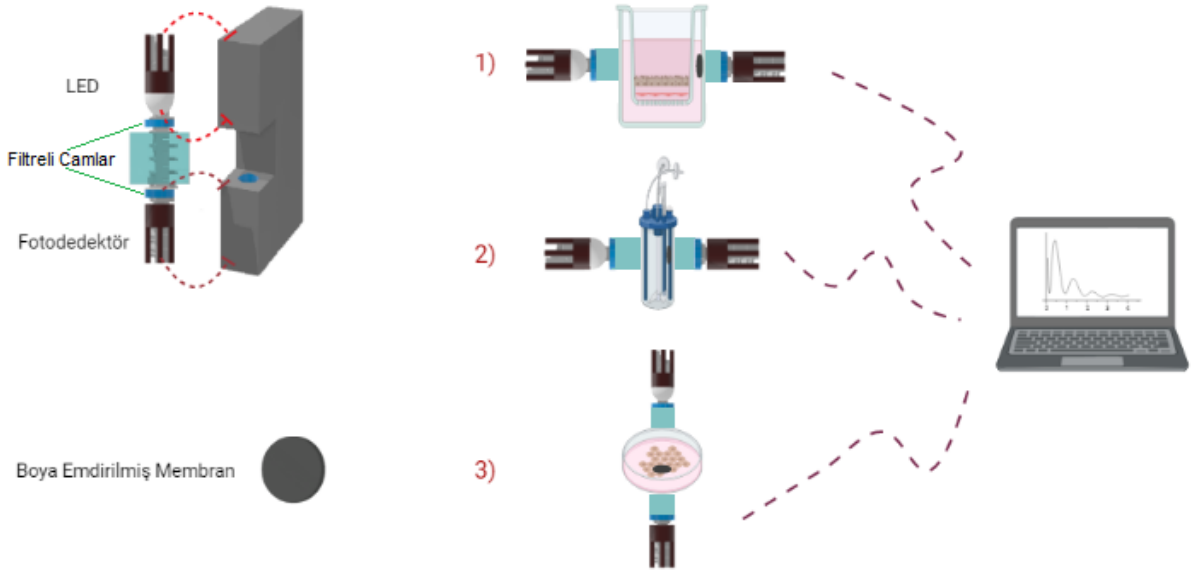


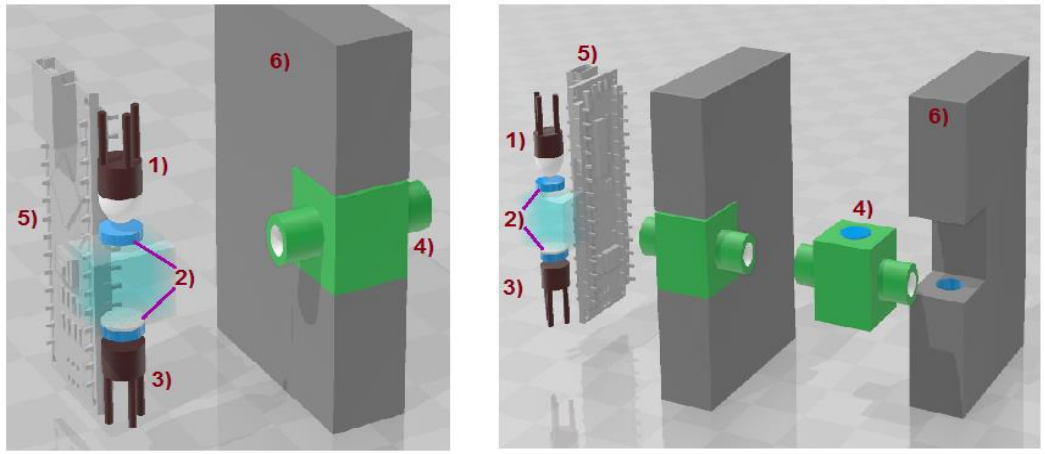


Optical Based pH Sensor for Continuous and High Sensitivity pH Measurement in Different Cell Media Environments



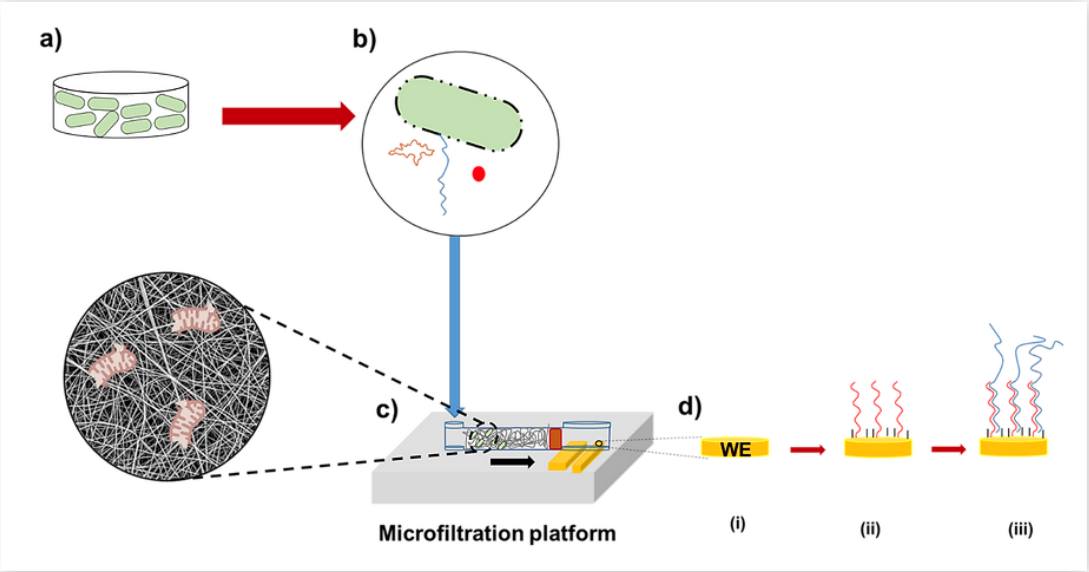






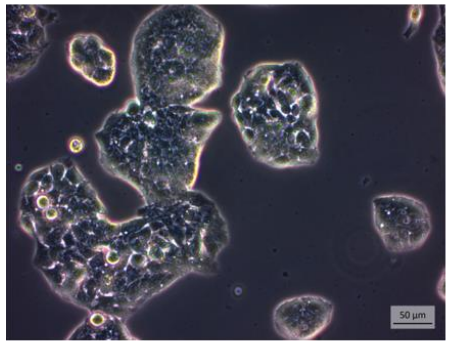
Nanofiber in a Microfluidic Chip: Development of a Microfiltration Platform for Bacterial Wall Removal

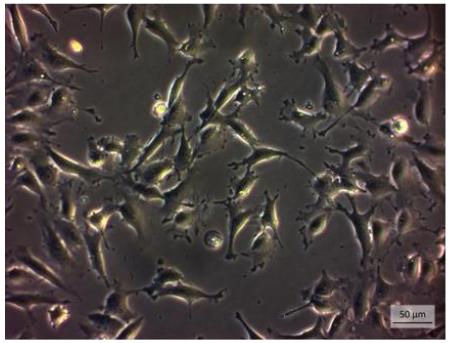
Highly efficient and cost-effective microfiltration platforms

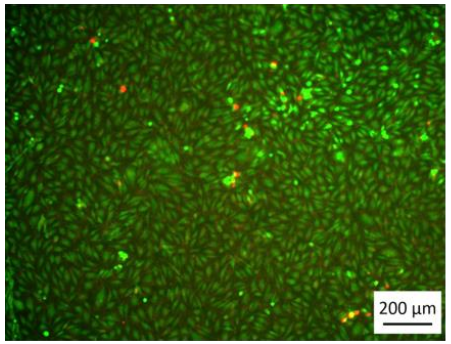


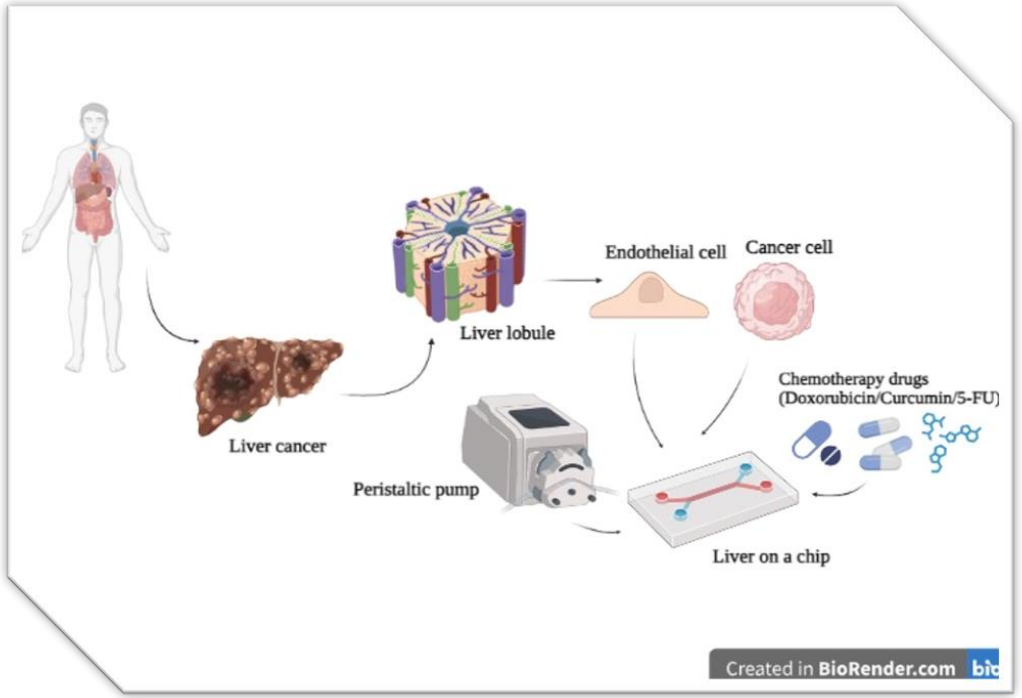
Developing microfluidic chip-based microfiltration platforms for the selective removal, elimination, and filtration of biological target molecules of great interest for various disciplines. The microfiltration platform can be highly effective in removing biological and chemical contaminants, such as bacteria, viruses, dyes, and toxic heavy metal ions. In our novel studies, the suggested platform incorporates nanofiber technology for the filtration of biological target molecules in which an inexpensive, simple, and high-performance filtration capabilities is aimed.

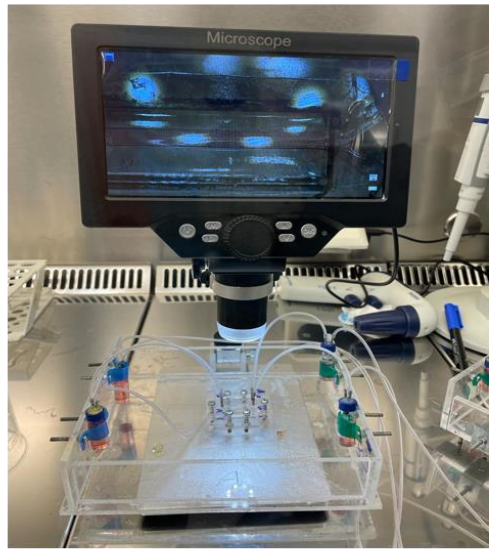
Biomimetic Cancer on a Chip Models for Advancement of Therapy

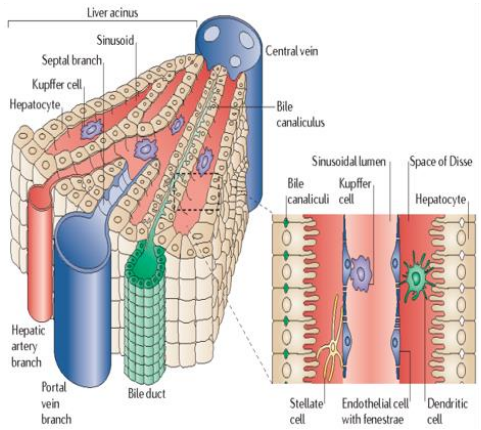


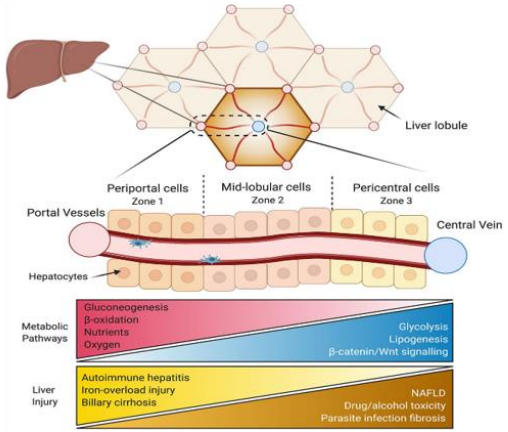


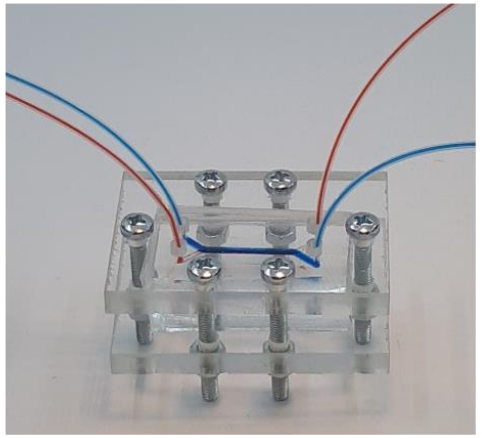






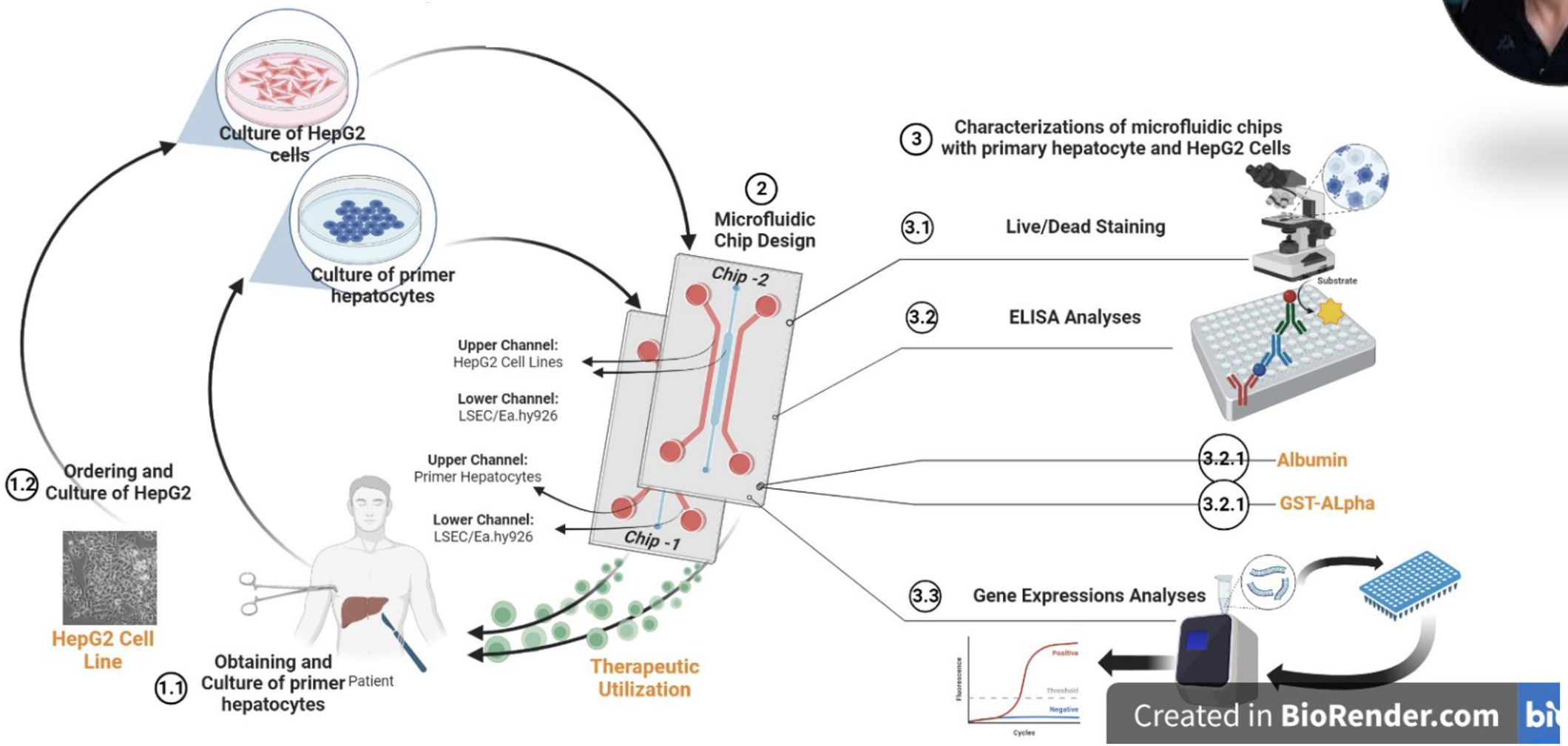




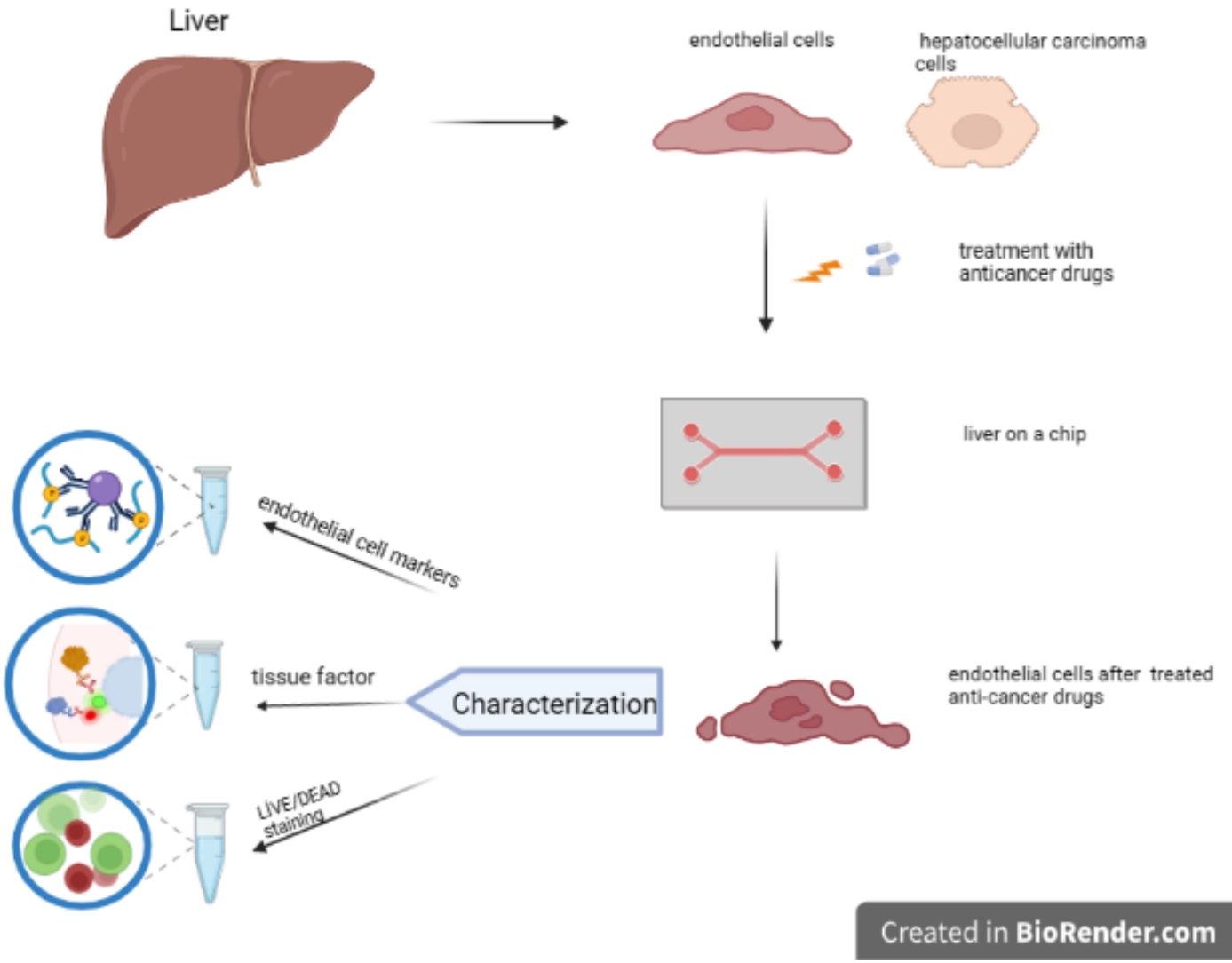


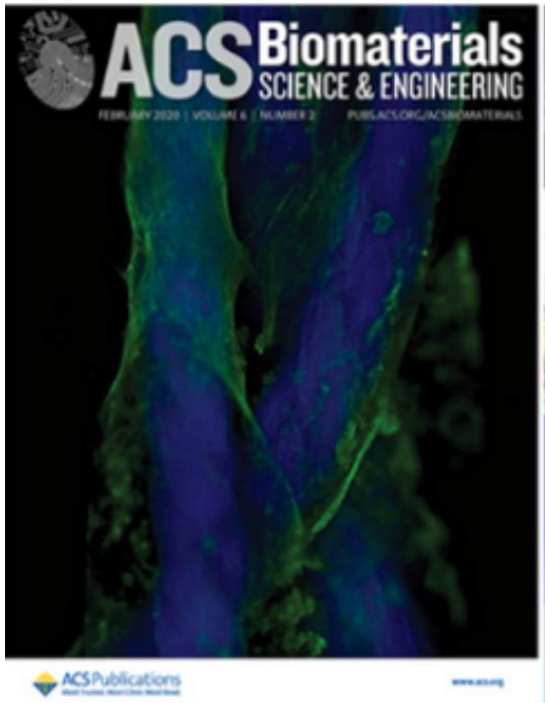
TÜBİTAK

Evaluation of Hepatocytes In Liver on a Chip



Investigation of Drug-induced Endothelial Damage in Liver Cancer Platform

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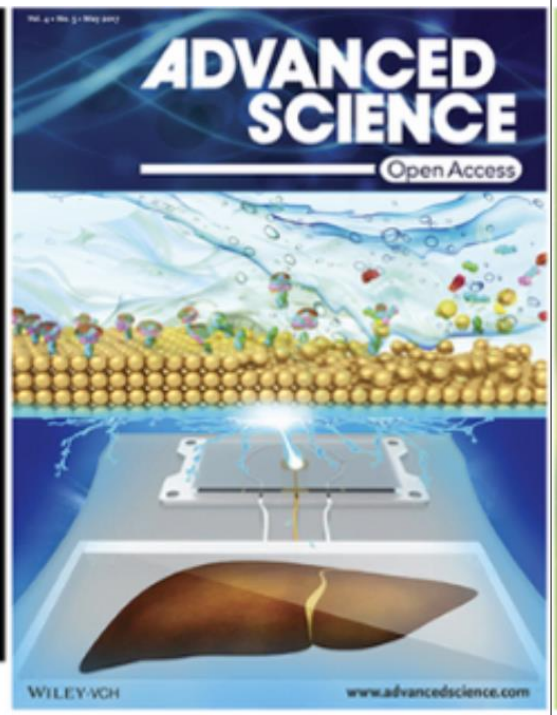
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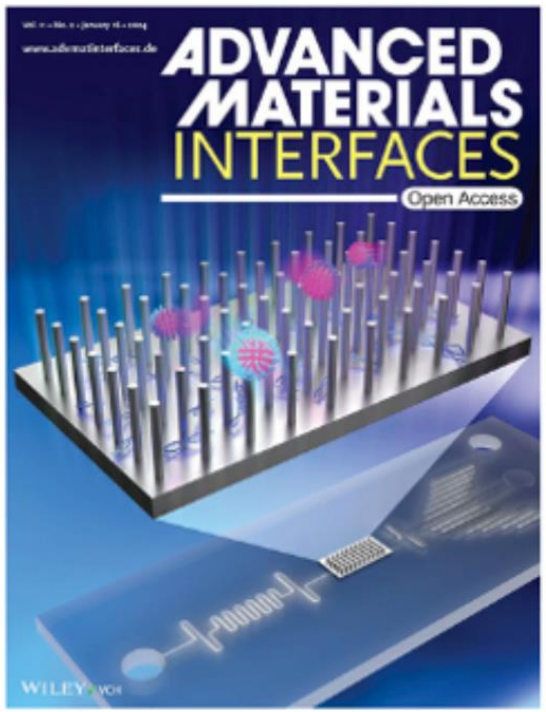
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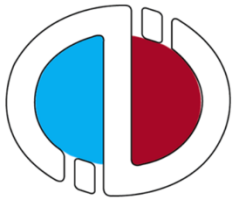

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