

# Johns Hopkins Engineering

## Immunoengineering

Immunoengineering - Immunoprofiling

Immune Organ-on-a-chip



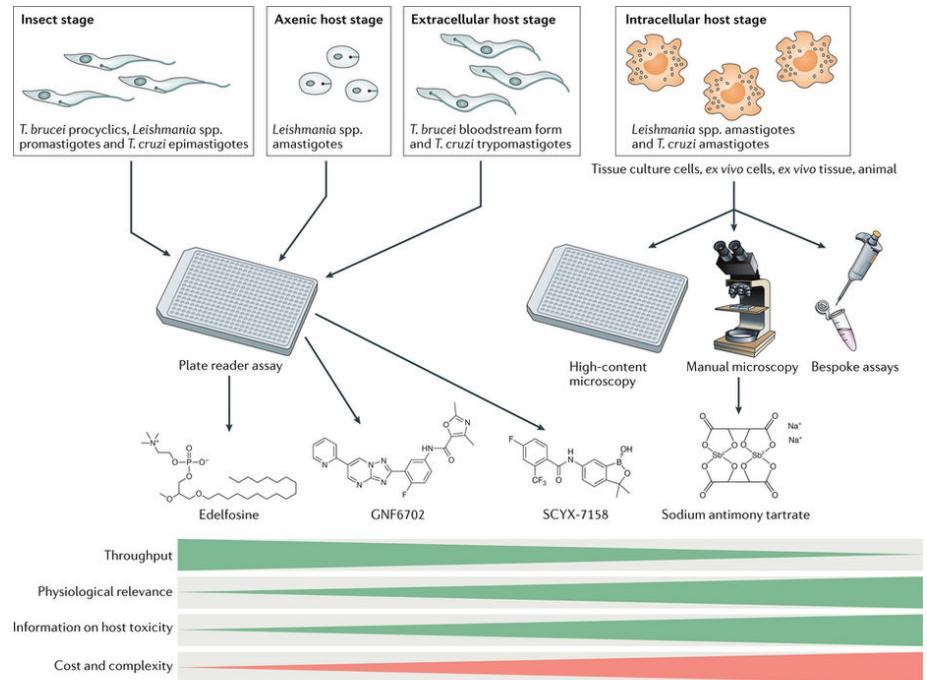
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# Outline

- Introduction to organs-on-a-chip
- Applications within immunology

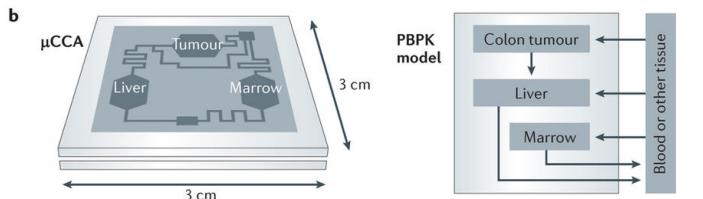
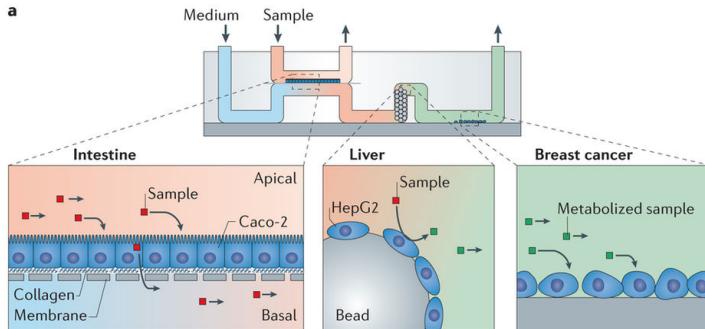
# Establishing Relevant In Vitro Models

- For therapeutic discovery and understanding biologic function
- Lower cost than studying things *in vivo*
- Less complex than *in vivo* system enabling mechanistic dissection
- Physiological relevance can be lost

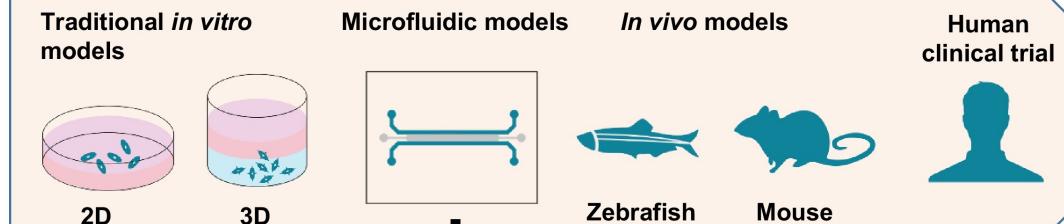


Nature Reviews | Microbiology

# Organs-on-a-chip an Intermediate



Nature Reviews | Drug Discovery



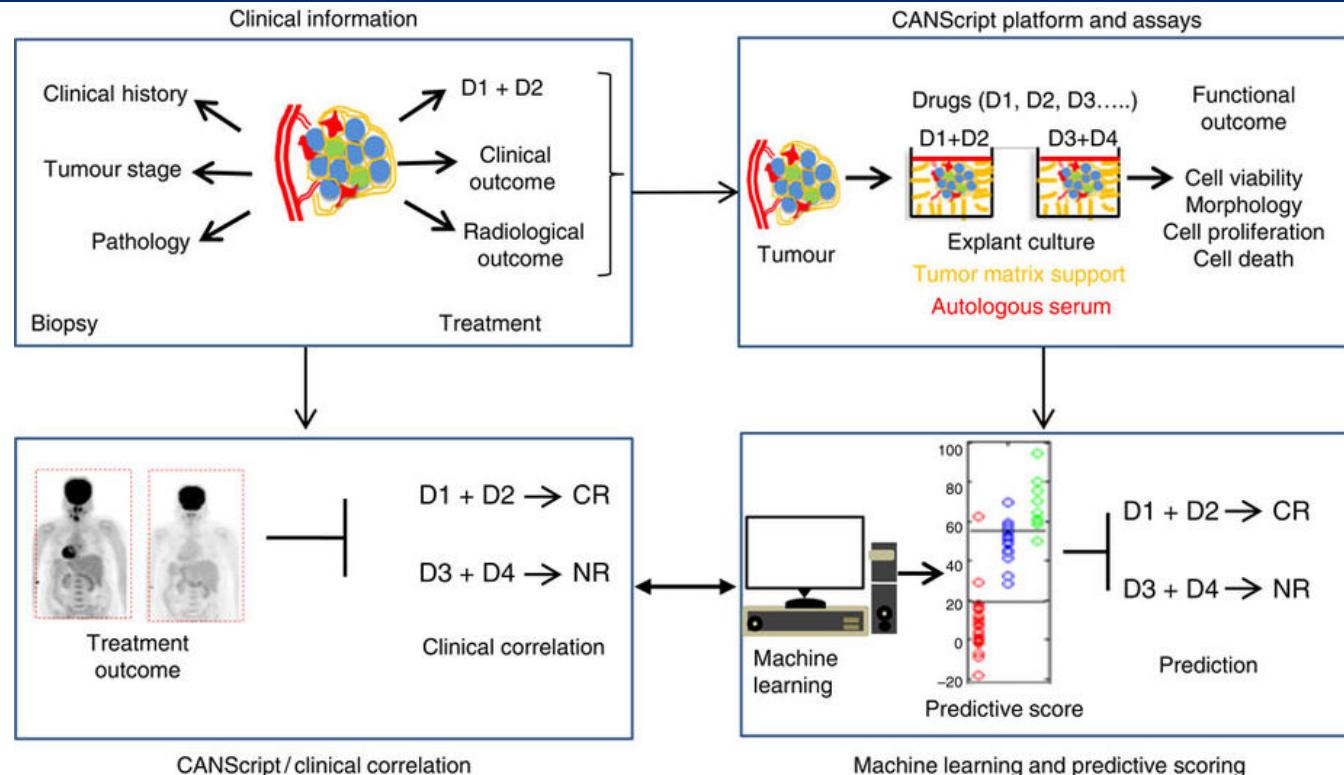
## Advantages of microfluidic models over:

Traditional <i>in vitro</i>	Traditional <i>in vitro</i> and <i>in vivo</i> models	<i>In vivo</i> models
-Ability to directly perfuse vascularized structures	-Increased control of microenvironment -Improved imaging capabilities -Fewer cells and less drug needed	-Use of cells exclusively of human origin

Trends in Cancer

Boussommier-Calleja, Alexandra, et al. "Microfluidics: a new tool for modeling cancer-immune interactions." *Trends in cancer* 2.1 (2016): 6-19.  
Esch, Eric W., Anthony Bahinski, and Dongeun Huh. "Organs-on-chips at the frontiers of drug discovery." *Nature reviews Drug discovery* 14.4 (2015): 248.

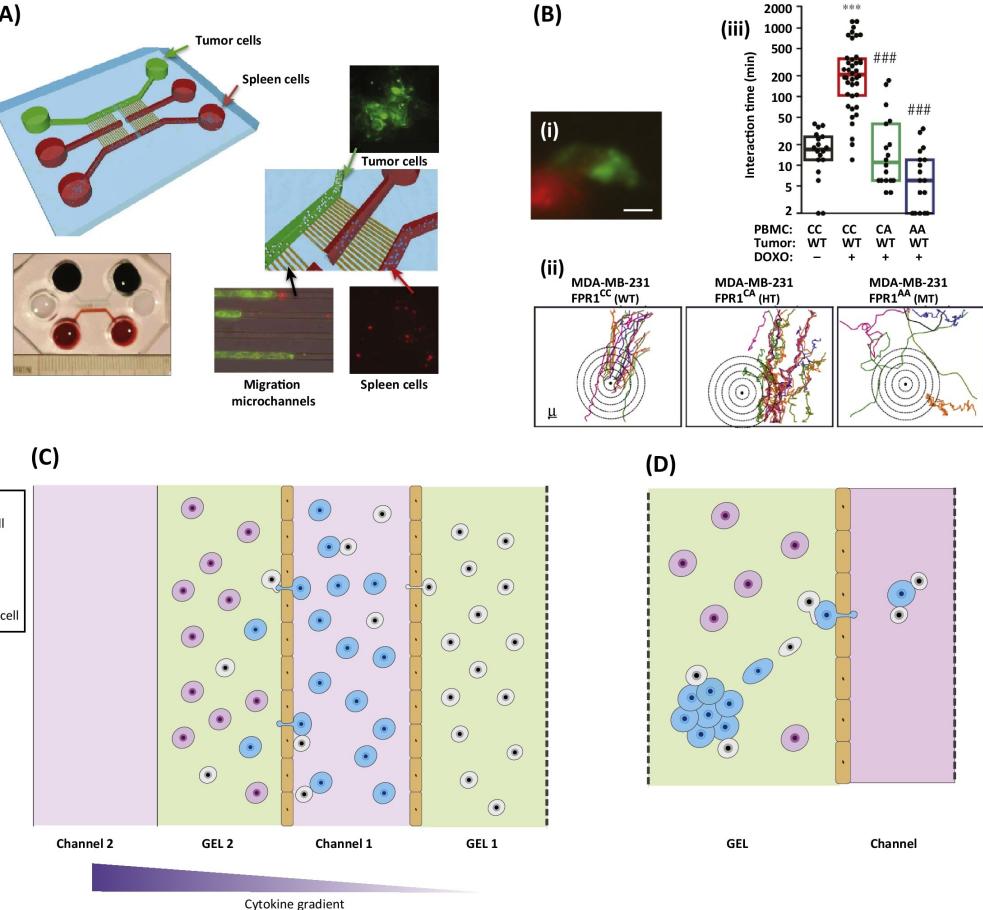
# Fitting Into Personalized Medicine



Majumder, Biswanath, et al. "Predicting clinical response to anticancer drugs using an ex vivo platform that captures tumour heterogeneity." *Nature communications* 6 (2015): 6169.

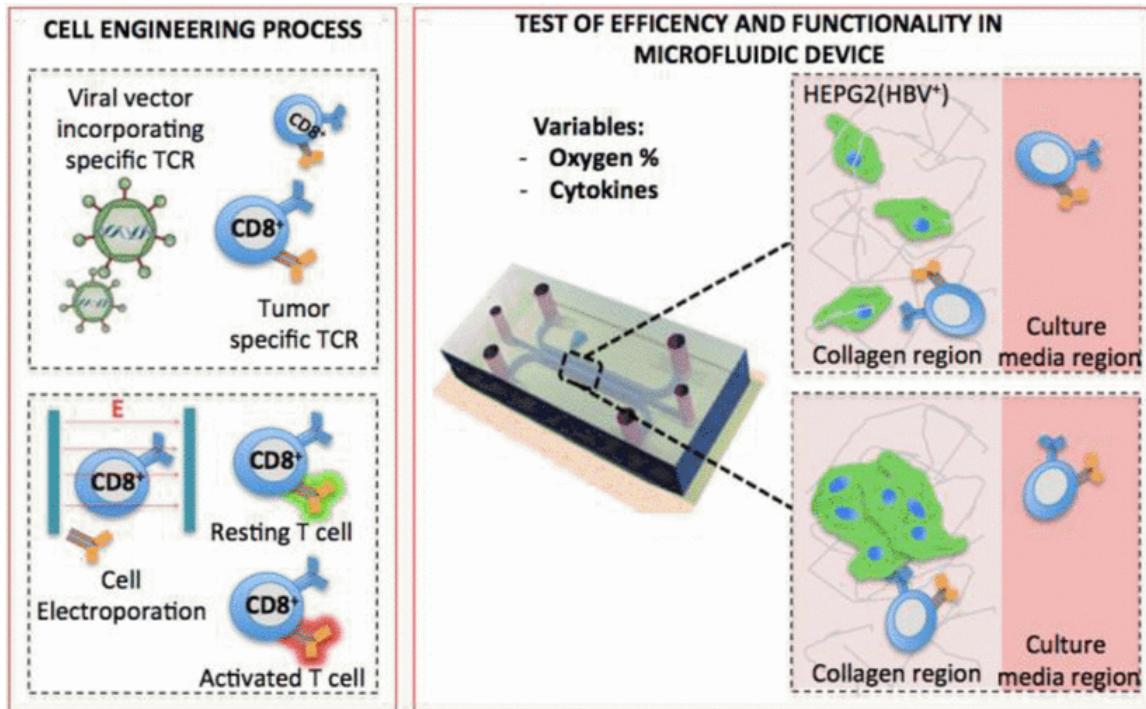
# Cancer-Immune Interactions

- 3D and 2D tumor biology different (HLA+ TAA)
- Migration of immune cells to tumor
- Design:
  - Gels to use
  - Media/Cytokines
  - Size of channels
  - Cell concentration
  - Cell source and types



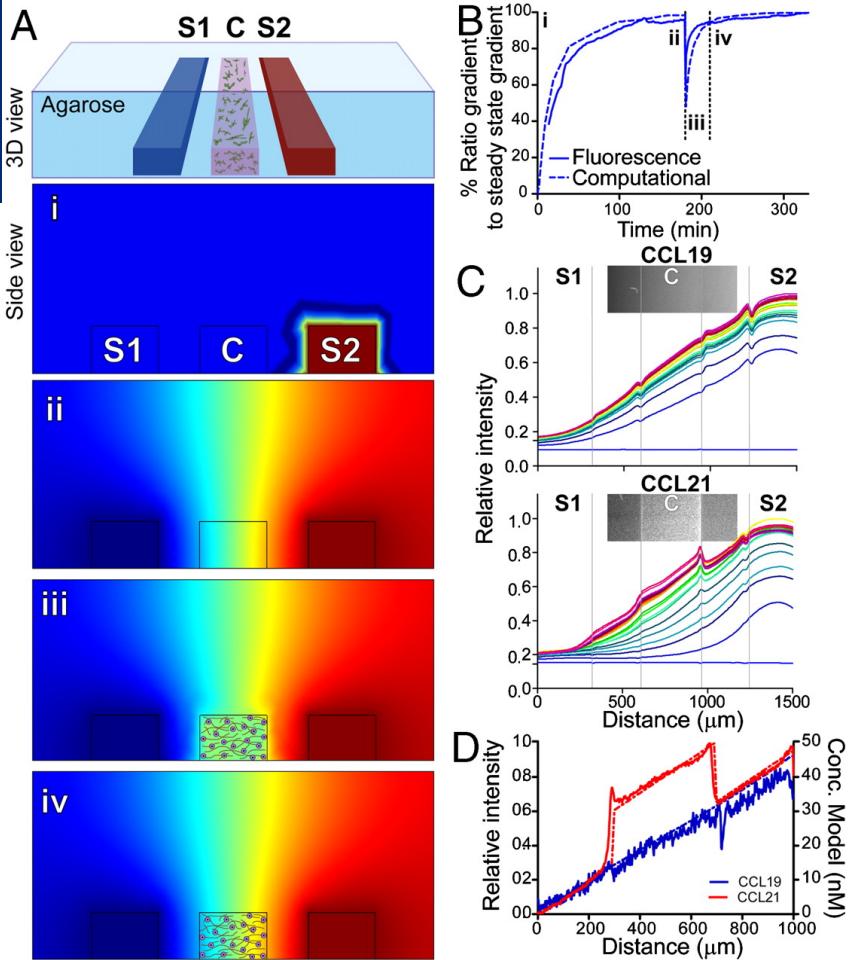
# Migration and Cancer Interaction

- Analyze CAR T cell killing of tumor cells
- Design:
  - Did not compare to 2D
  - Oxygen availability
  - Cell viability



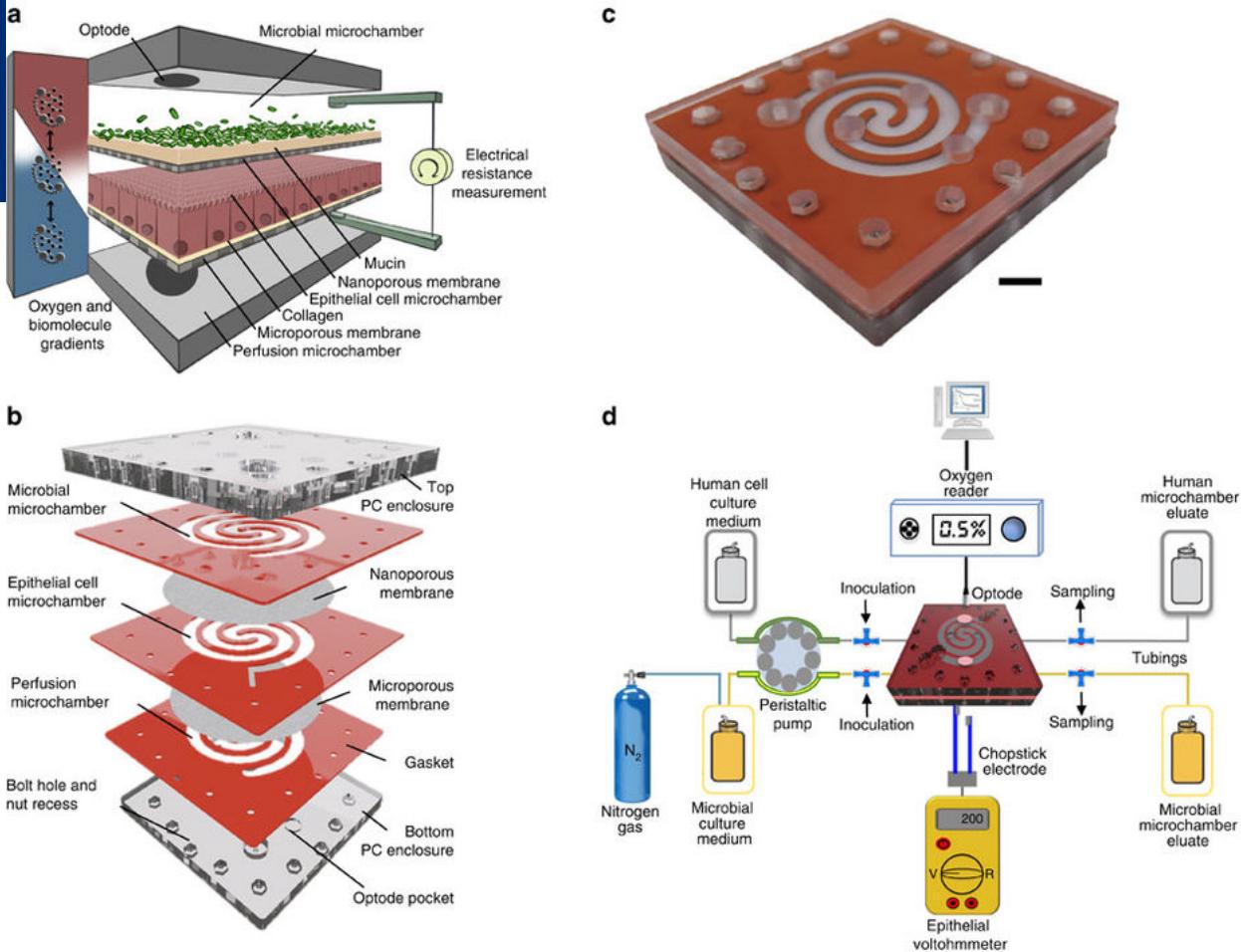
# For Migration

- Analyze DC migration to lymph node based on chemokines
- Chemotaxis usually done in 2D
- Design:
  - Gels
  - Established measurable gradients
  - Modeling
  - Consistency



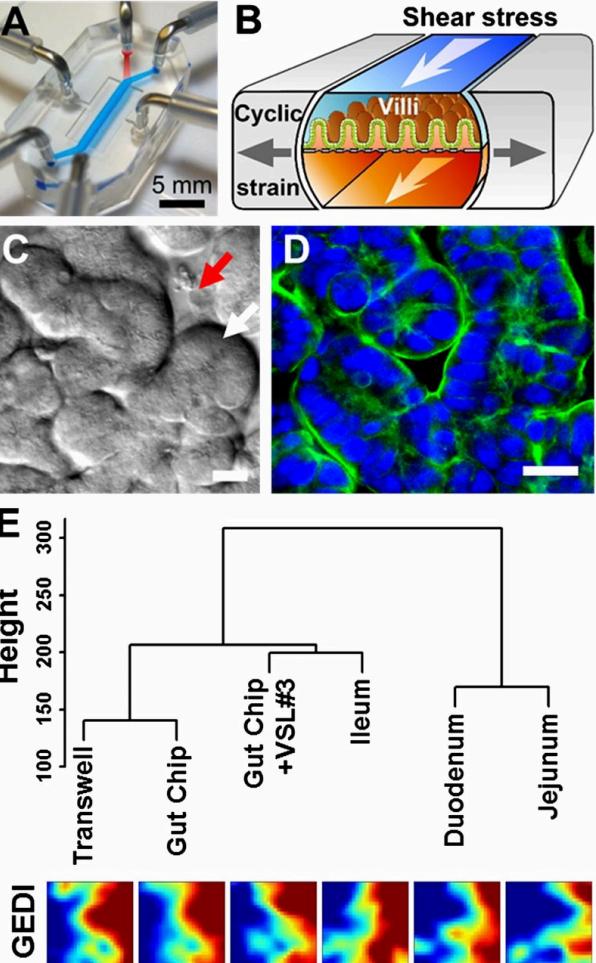
# Human Gut Microbe Interface

- Incorporate both bacteria and human cells
- Animal models not representative
- Design:
  - Compare to *in vivo* transcriptional, metabolic, and immune responses
  - Aerobic growth
  - Nutrient source location
  - Method for cell seeding
  - Measure TEER
  - Protocol for co-culture



# Gut Microbiome on Chip

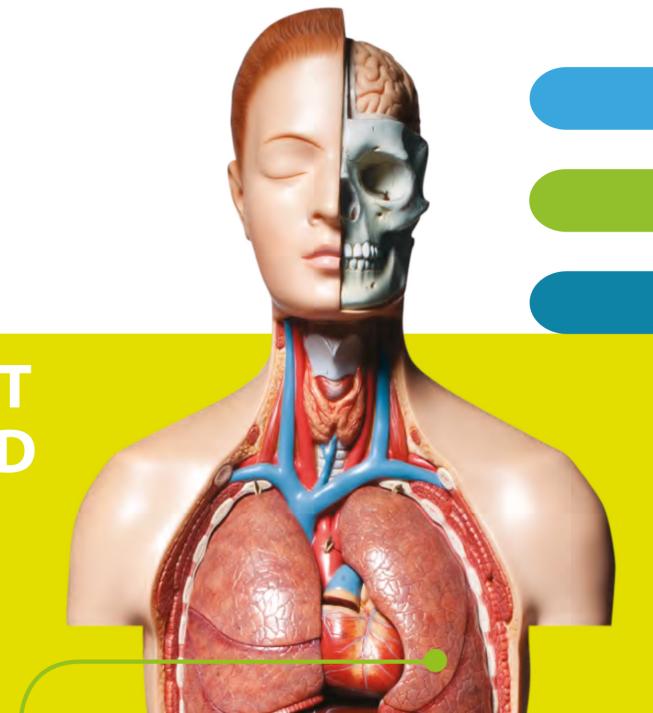
- Incorporate bacteria, human intestinal epithelial cells, immune cells
- Animal models not representative
- Design:
  - Shear stress/strain
  - Differentiation of cells
  - Length of culture in vitro
  - Model for antibiotic, inflammation, and probiotic



# Already reaching industry

**MIMETAS**  
the organ-on-a-chip company

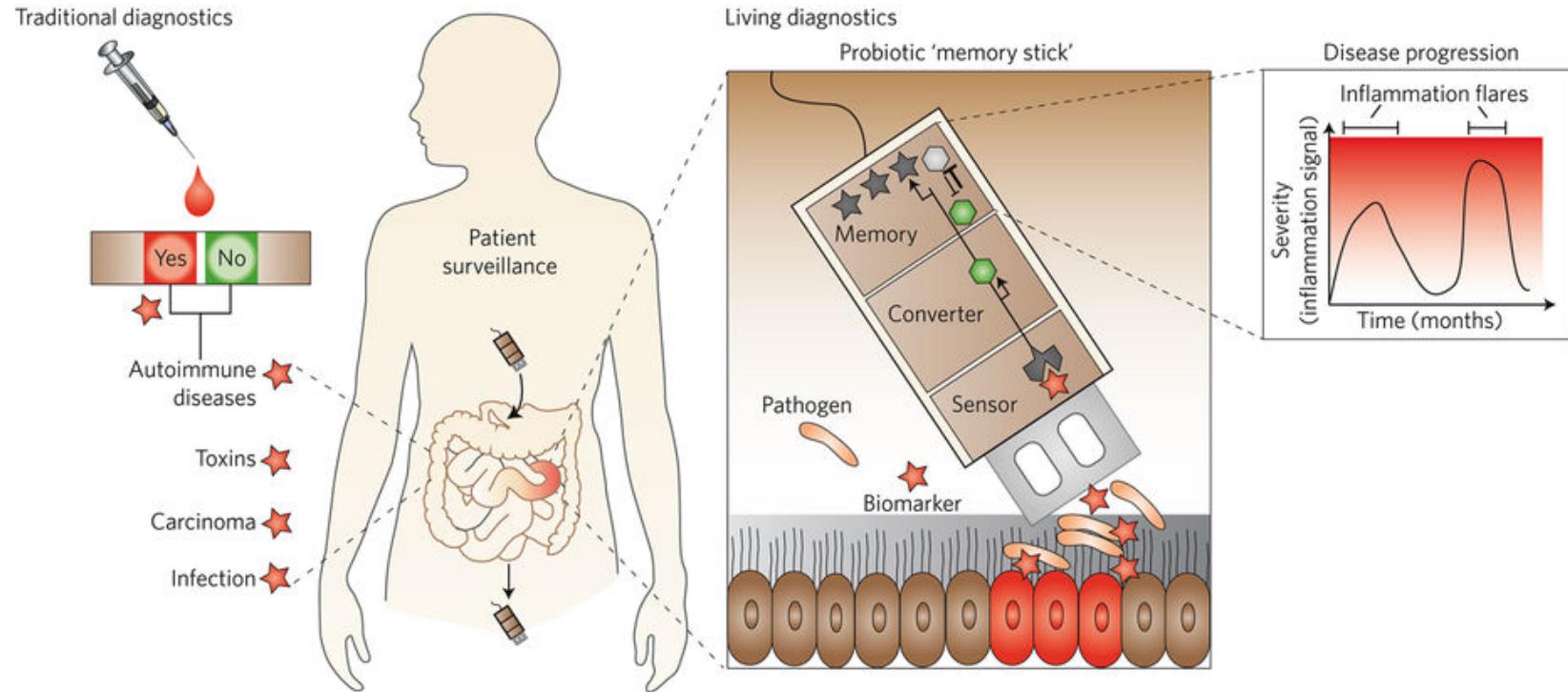
**HIGH-THROUGHPUT  
HUMAN TISSUE AND  
DISEASE MODELS**



# Challenges and Opportunities for Organs-on-a-chip

- Limited data – need validation of model with *in vivo* findings
- Depend on high-resolution imaging
- Cumbersome data analysis
- Manufacturability and scalability
- Still Chips-in-a-lab (require equipment)
- Lack of multidisciplinary approach (incorporation of biologists)

# Another approach: Getting more information *in vivo*



Sedlmayer, Ferdinand, and Martin Fussenegger. "Synthetic biology: A probiotic probe for inflammation." *Nature Biomedical Engineering* 1.7 (2017): 0097.



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