Scientific Discoveries Made Using Non-Animal Methods (NAMs)

Organ-on-a-Chip / Micro-physiological Systems

Lung-on-a-chip replicates human lung disease and drug responses

- Team: Donald Ingber and colleagues, Wyss Institute, Harvard University
- Country: USA
- Significance: Demonstrated that microfluidic chips lined with human lung cells could model pulmonary edema, COPD, and drug toxicity more accurately than animal models. Led to FDA recognition of organ-chips as a valid testing platform.
- Key refs: Huh et al., Science 2010; Huh et al., Science Translational Medicine 2012

Liver-on-a-chip identifies drug toxicity missed by animal testing

- Team: Multiple groups including Emulate Inc. and CN Bio Innovations
- Countries: USA, UK
- Significance: Human liver chips detected drug-induced liver injury (DILI) for compounds that had passed animal safety testing but later failed in humans. Demonstrated superior predictive value over animal models for hepatotoxicity.

FDA Modernization Act 2.0 (2022) — regulatory milestone

- Country: USA
- Significance: Removed the legal mandate requiring animal testing for drug approval, explicitly allowing organ-chips, organoids, and computational models as alternatives. A direct result of accumulated NAM evidence.

Human Organoids

Intestinal organoids reveal stem cell biology and disease mechanisms

- Team: Hans Clevers and colleagues, Hubrecht Institute
- Country: Netherlands
- Significance: Developed the first human intestinal organoids from adult stem cells, enabling study of gut disease, cancer, and drug responses in human tissue without animals. This technology has since been extended to liver, kidney, brain, and retinal organoids worldwide.
- Key ref: Sato et al., Nature 2009

Brain organoids model microcephaly caused by Zika virus

- Team: Multiple groups, notably Guo-li Ming and Hongjun Song, Johns Hopkins; and Paola Arlotta, Harvard
- Country: USA
- Significance: Human brain organoids demonstrated that Zika virus preferentially infects neural progenitor cells and causes microcephaly-like features — a finding that could not be adequately modeled in mice due to species differences.
- Key refs: Qian et al., Cell 2016; Garcez et al., Science 2016 (Brazil/USA collaboration)

Tumor organoids used for personalized cancer treatment

- Teams: Multiple, including Hans Clevers group; Institute of Cancer Research, London
- Countries: Netherlands, UK, USA, and others
- Significance: Patient-derived tumor organoids ("living biobanks") used to screen chemotherapy drugs for individual patients, improving treatment selection. Several clinical trials now incorporate organoid-guided therapy.

In Vitro Skin and Tissue Models

Reconstructed human skin models replace animal testing for cosmetics and chemicals

- Developers: MatTek (EpiDerm), Episkin (L'Oréal), Henkel
- Countries: USA, France, Germany
- Significance: Validated by OECD and regulatory agencies as replacements for the Draize rabbit skin irritation test. Now standard in the EU (where cosmetics animal testing has been banned since 2013) and increasingly adopted globally.

Corneal and eye irritation models

- Developers: EpiOcular (MatTek), SkinEthic HCE (Episkin)
- Countries: USA, France
- Significance: Validated alternatives to the Draize rabbit eye test for assessing eye irritation potential of chemicals and consumer products.

Computational and In Silico Methods

AlphaFold predicts protein structures without animal-derived data

- Team: DeepMind
- Country: UK
- Significance: AI-based prediction of protein 3D structures from amino acid sequences alone. Has transformed structural biology and drug target identification, providing data that previously required years of laboratory work. Open-access database covers over 200 million predicted structures.
- Key ref: Jumper et al., Nature 2021

Quantitative Systems Pharmacology (QSP) models predict drug outcomes

- Multiple teams and companies globally

- Countries: USA, UK, Germany, and others
- Significance: Computational models of human physiology used to predict drug efficacy, dosing, and toxicity. Increasingly accepted by FDA and EMA as supporting evidence in drug submissions, reducing reliance on animal pharmacokinetic studies.

Virtual clinical trials and digital twins

- Notable efforts: Unilever (safety assessment), Sanofi, Novartis
- Countries: UK, France, Switzerland, USA
- Significance: Computer simulations of human physiology used to predict clinical outcomes, optimize trial design, and in some cases reduce or replace early-phase human and animal studies.

Human Cell-Based and iPSC Models

iPSC-derived cardiomyocytes detect cardiac drug toxicity

- Teams: Multiple, including the CiPA initiative (Comprehensive in Vitro Proarrhythmia Assay), Yamanaka lab (original iPSC derivation)
- Countries: Japan (iPSC technology), USA, international (CiPA)
- Significance: Human induced pluripotent stem cell-derived heart cells now used to screen drugs for cardiac toxicity (arrhythmia risk), addressing a major cause of drug withdrawals that animal models frequently missed. CiPA is now integrated into FDA regulatory guidance.
- Key ref (iPSCs): Takahashi and Yamanaka, Cell 2006 (Nobel Prize 2012)

Human cell-based models of neurodegenerative disease

- Teams: Multiple, including work at Harvard, NIH, UCL
- Countries: USA, UK
- Significance: iPSC-derived neurons from patients with Alzheimer's, Parkinson's, and ALS used to study disease mechanisms and screen drugs in human cells, overcoming well-documented failures of animal models to predict treatment outcomes in these diseases.

Bioengineering and Advanced In Vitro Systems

3D bioprinted human tissues for drug testing

- Developers: Organovo, Aspect Biosystems (Vancouver)
- Countries: USA, Canada
- Significance: 3D bioprinted liver and kidney tissues used for drug toxicity screening. Aspect Biosystems (Vancouver, BC) has developed bioprinted human tissue therapeutics and tissue models, representing notable Canadian NAM innovation.

Canadian Contributions

Aspect Biosystems — 3D bioprinting platform

- Location: Vancouver, BC
- Significance: Developing bioprinted human tissue models as alternatives to animal testing for drug development. One of Canada's most prominent NAM-related companies.

Canadian Centre for Alternatives to Animal Methods (CCAAM)

- Location: University of Windsor, Ontario

- Significance: Canada's first dedicated academic centre for NAM research, established 2017. Conducts and promotes research using human-relevant, non-animal approaches.

Tan et al., and related research

Human skin-lymphoreticular model-on-chip for inflammatory skin diseases

- Team: Zheng (Maomao) Tan, Partho Protim Adhikary, D. Wörz, and Sarah Hedtrich, University of British Columbia
- Country: Canada
- NAM used: Human-based organ-on-a-chip
- Significance: Developed a human-based skin-lymphoreticular model-on-chip that emulates inflammatory skin conditions, eliminating the need for animal models of atopic dermatitis and related diseases. This represents a fully human in vitro system that captures immune-skin interactions on a chip platform.
- Ref: Tan et al., Advanced Healthcare Materials, 2026, e03170

Disrupting TSLP signaling as a treatment for atopic diseases

- Team: Partho Protim Adhikary, T. Idowu, Zheng Tan, C. Hoang, S. Shanta, M. Dumbani et al., University of British Columbia / Renaissance Bioscience Corp.
- Country: Canada
- NAM used: In vitro human cell-based drug screening
- Significance: Identified putative small molecule inhibitors that disrupt TSLP–TSLP receptor interactions, yielding a novel treatment option for atopic diseases. Discovery made using human cell-based assays rather than animal disease models.

- Ref: Adhikary, Idowu, Tan et al., EMBO Molecular Medicine 16(7), 2024