Advisory Committee to the Director, NIH Recommendations on Catalyzing the Development and Use of New Approach Methods (NAMs) to Advance Biomedical Research

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SACATM
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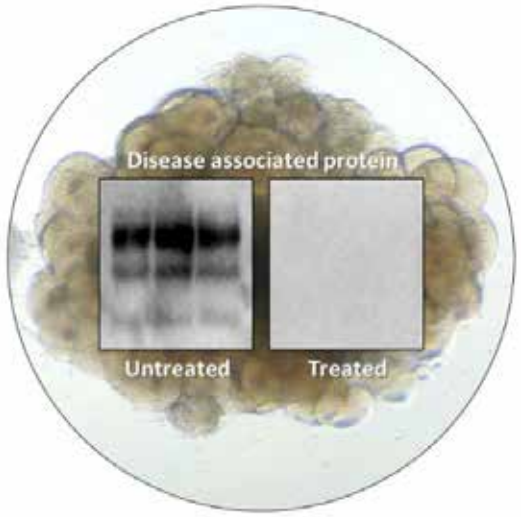
IMPETUS FOR EFFORT

TECHNOLOGY DRIVES OPPORTUNITY

Media Advisory Tuesday, March 9, 2021

NIH scientists use human cerebral organoid to test drug for deadly brain disease

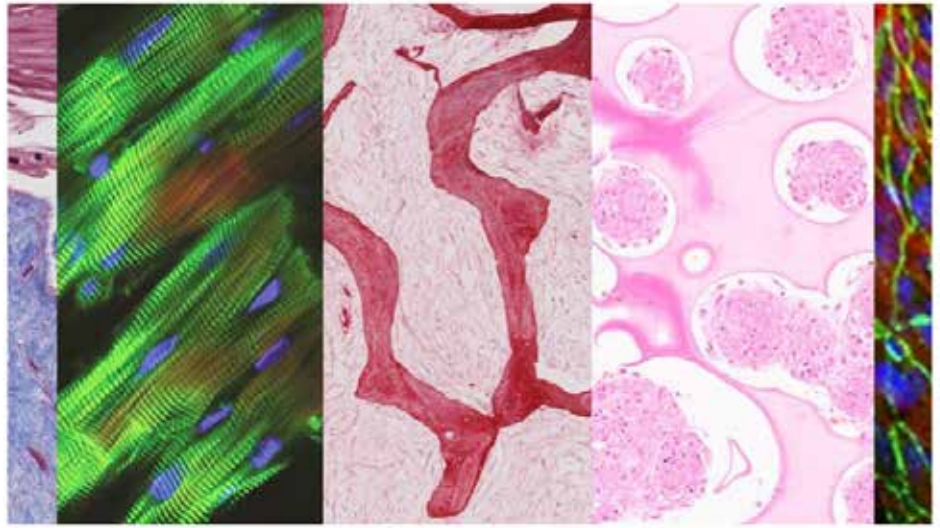


A cerebral organoid shown overlaid with test results from prion infected organoids that were left untreated or treated with PPS. The results show that treatment reduces disease-associated protein. *NIAID*

Plug-and-Play Organ-on-a-Chip Can Be Customized to the Patient

Major advance from Columbia Engineering team demonstrates first multi-organ chip made of engineered human tissues linked by vascular flow for improved modeling of systemic diseases like cancer

APR 27 2022 | BY HOLLY EVARTS



Tissues cultured in the multi-organ chip (from left to right: skin, heart, bone, liver, and endothelial barrier) maintained their tissue-specific structure and function after being linked by vascular flow. Photo credit: Kacey Ronaldson-Bouchard/Columbia Engineering

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HUMAN RELEVANCE IN MIND

DEFINING NEW APPROACH METHODS & IDENTIFYING OUR SCOPE

in Chemico

- Cell-free methods
- Epigenetics
- Biochemical pathways
- Chemical genetics

in Vitro

- Cultured cell methods
- Induced Pluripotent Stem Cells (iPSC)
- Microphysiological Systems (MPS)

in Silico

- Computational methods
- Artificial intelligence, deep learning, machine learning
- Mathematical modeling and simulations

Extremely Valuable For:

- **Conducting basic research**
- **Uncovering human patho/physiological mechanisms**
- **Translating knowledge into products or practice**

THE POWER OF NEW APPROACH METHODS

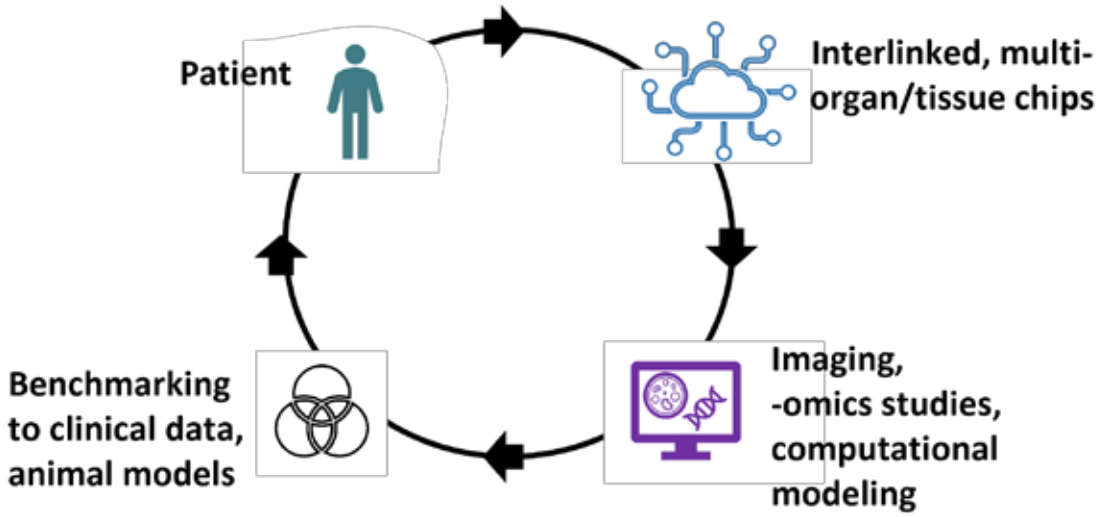
CANCER METASTASIS EXEMPLAR

Current Challenges

- Difficult to study metastasis and how cancer cells move to distant organs
- Current models are poor predictors of stages and progression of cancer in humans

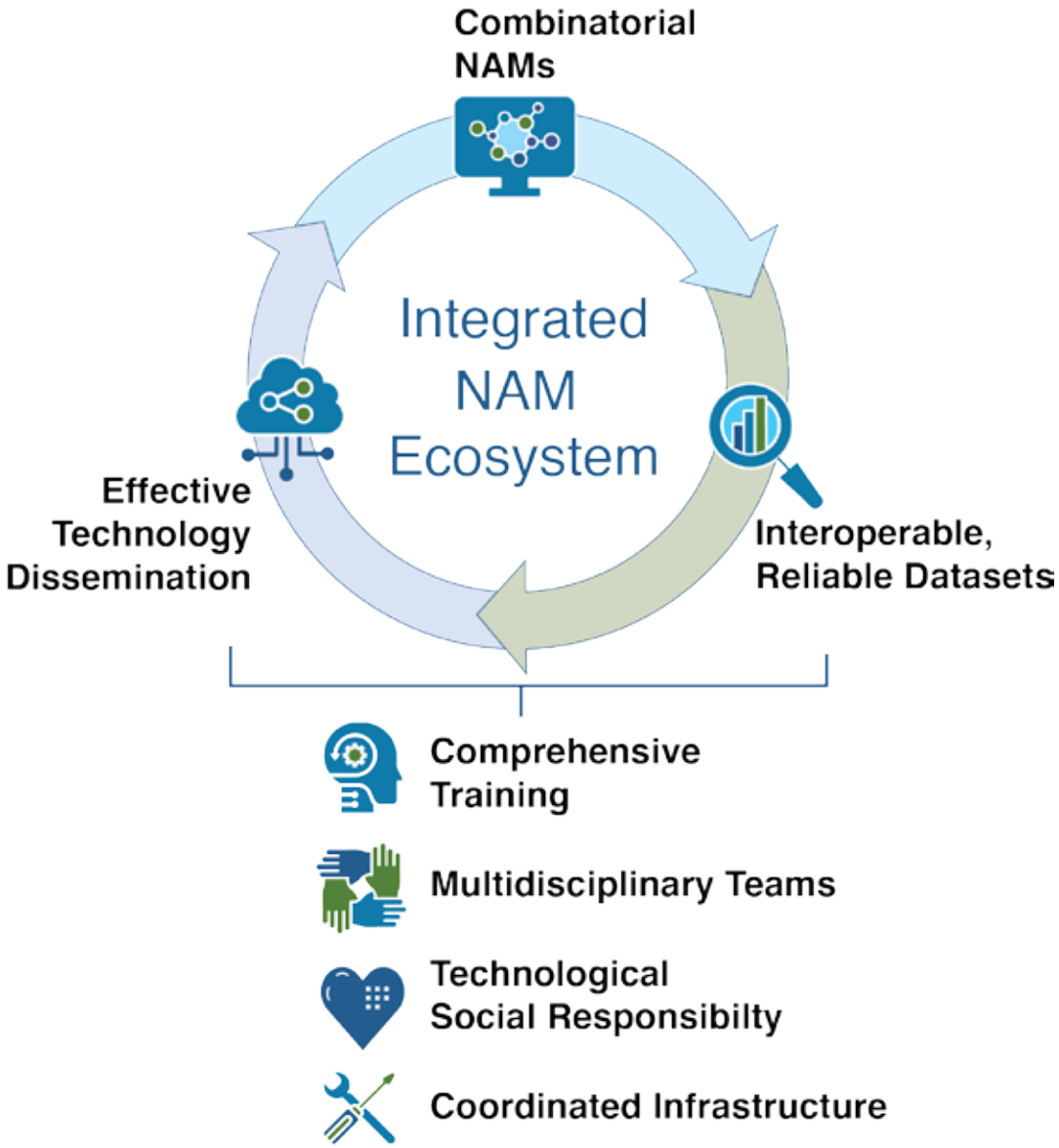
The Vision

Patient-specific NAMs and integrated approaches



WG & NIH VISION

AN INTEGRATED ECOSYSTEM TO CATALYZE SCIENTIFIC DISCOVERY



RECOMMENDATIONS—Accepted by ACD & NIH Director; Implementation Underway

1.	Prioritize the development and use of **combinatorial NAMs**
2.	Establish **resources, infrastructure, and collaborations** to promote the use of interoperable, reliable, and well curated/high quality datasets produced from research using NAMs
3.	Promote effective **dissemination and interconnection** of NAMs technologies
4.	Invest in comprehensive **training** to bolster continuous advances in NAMs development and use
5.	Facilitate **multidisciplinary teams** with expertise across technologies and the lifecycle of NAMs development and use
6.	Promote **social responsibility** in both the creation and deployment of NAMs across the research lifecycle
7.	Support and maintain **coordinated infrastructure** to catalyze effective and responsible NAMs development and use

RECOMMENDATION 1

PRIORITIZE THE DEVELOPMENT AND USE OF COMBINATORIAL NAMs

1.1. Establish benchmarks and standards for individual NAMs and combinatorial NAMs to foster technology integration efforts and demonstrate impact of combinatorial effect

1.2. Support research comparing and benchmarking relevant animal, NAMs and human models to validate translational potential, reduce reliance on singular methods, reduce costs, and identify integration frameworks and strengths and weaknesses in model approach

RECOMMENDATION 2

ESTABLISH RESOURCES/INFRASTRUCTURE/COLLABORATIONS TO PROMOTE INTEROPERABLE/RELIABLE AND WELL CURATED/HIGH QUALITY DATASETS

2.3. Identify or establish a designated repository for NAM data sharing, consistent with FAIR principles, privacy protections, and security practices, with sufficient metadata requirements to promote equitable reuse of high quality NAMs data

2.4 Create alliances and collaborations for collecting, managing, sharing, and publishing high-quality NAMs data, including increasing access to hard-to-access data such as:

- Industry data, focusing on the pre-competitive space and regulatory approval submissions
- Unpublished data, particularly from failed studies (in an effort to address survival bias)*

RECOMMENDATION 3

PROMOTE EFFECTIVE DISSEMINATION AND INTERCONNECTION OF NAMs TECHNOLOGIES

3.1. Establish mechanisms to support testing, validation, qualification, and benchmarking of integrated systems to maximize uptake of these systems by the community, including frameworks for describing which stakeholder should advance which component

3.2. Create accessible and reliable sources and repositories for disseminating validated NAMs.

- Integrate strategies for deploying technologies broadly and equitably, including to under-resourced organizations and research areas*

RECOMMENDATION 4

INVEST IN COMPREHENSIVE TRAINING TO BOLSTER CONTINUOUS ADVANCES IN NAMs DEVELOPMENT AND USE

4.3. Invest in training across the research to implementation pipeline, including addressing hurdles in bringing technologies to fruition, such as regulatory and policy requirements, patient care, etc. For example:

- **Embed academic researchers** in industry, regulatory, national laboratories, and policy not-for-profits*
- **Create collaborations between researchers and clinicians** to incorporate patient perspectives in NAMs development*
- **Foster entrepreneurship training***

4.4. Promote awareness and understanding of NAMs through publicly available educational course modules and workshops covering the lifecycle of NAMs, from conceptualization to dissemination, use, and commercialization*

RECOMMENDATION 5

FACILITATE MULTIDISCIPLINARY TEAMS WITH EXPERTISE ACROSS TECHNOLOGIES AND THE LIFECYCLE OF NAMs DEVELOPMENT AND USE

5.1. Develop funding opportunities to support multi-disciplinary teams, considering potential scientific, technological, and engineering needs; **regulatory or policy requirements***; ethical considerations; and patient/public adoption

RECOMMENDATION 6

PROMOTE SOCIAL RESPONSIBILITY IN BOTH THE CREATION AND DEPLOYMENT OF NAMs ACROSS THE RESEARCH LIFECYCLE

6.1. Foster equitable development and use of NAMs for research and public benefit. For example:

- **Support research to characterize individual differences, method biases, etc**. to understand, minimize, and correct for variability and biases
- **Promulgate guidance for considering sources of tissues, cells, and data/metadata** to source ethically and/or represent population diversity
- Promote **open sharing of technology and data** when possible

6.2. Strengthen interagency partnerships to develop a coordinated federal approach to NAMs that enables science to advance efficiently, safely, and ethically while minimizing administrative and regulatory burden

RECOMMENDATION 7

SUPPORT AND MAINTAIN COORDINATED INFRASTRUCTURE TO CATALYZE EFFECTIVE AND RESPONSIBLE NAM DEVELOPMENT AND USE

7.1. Create mechanisms for disseminating NAMs resources, technologies, and expertise efficiently, equitably, and reliably across researchers and institutions. For example:

- **Protocols** for technology development and use, qualification of reagents and equipment, tracking of materials and experimental details, and standard operating procedures for teams
- **Clearing houses and repositories** for easy, reliable, and inexpensive access to specialty reagents and custom syntheses
- **Knowledge-bases for tracking** NAMs, how they are used, for what purposes, and how in combination with what other models*

7.2. Promote or establish consortia and venues for sharing established best practices, standards, definitions, frameworks, and harmonized approaches for NAMs*

7.4. Identify opportunities to build upon existing efforts both nationally and internationally to **link resources and identify a clear source of coordination** for NAMs resources

OUTLOOK

Implementation & Continued Engagement

The NIH Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) is leading implementation of the recommendations.

- Conducted a prioritization and feasibility analysis of all recommendations
- Identified and engaged lead NIH ICOs
- NIH-wide data call for relevant activities
- Ongoing communication with key offices and programs, including ICCVAM

DPCPSI welcomes ongoing discussion with ICCVAM!