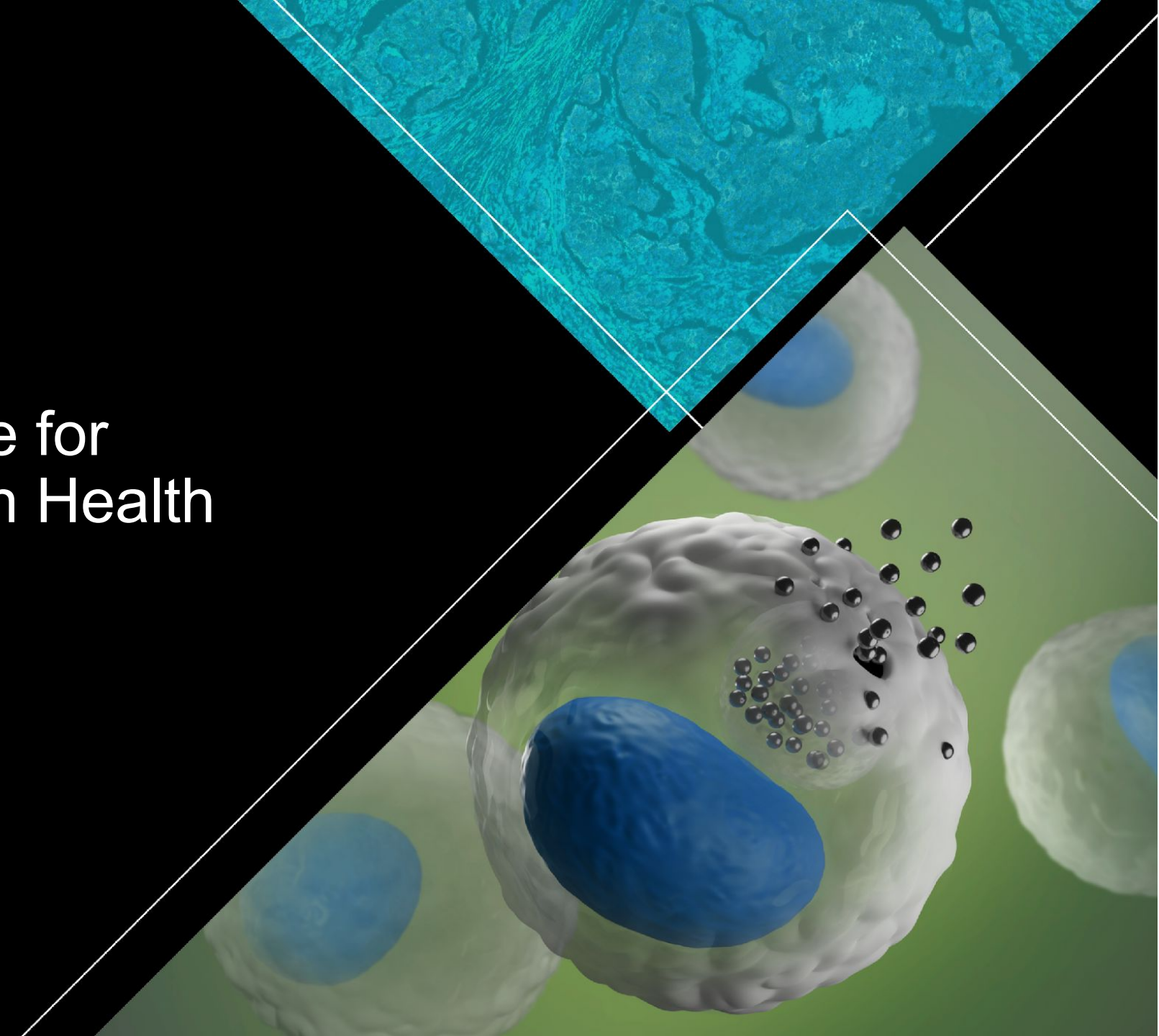
Frederick National Laboratory for Cancer Research

Around the Corner: Peering into the Future for Personalized Precision Health



Eric Stahlberg, PhD

BigCARE Lecture Series

July 23, 2024

University of California, Irvine

Contact: Eric.Stahlberg@nih.gov

SPONSORED BY THE NATIONAL CANCER INSTITUTE

Acknowledgements

- **The number of individuals who have contributed to this presentation, both directly and indirectly, represents a large and rapidly growing community.**
- **Acknowledging specific groups who have contributed**
  - **Lead Organizations**
    - NCI, DOE, FNLCR, LLNL, ORNL, ANL, BNL, LANL, PNNL Many universities
  - **Collaborative Teams**
    - ATOM Team
    - JDACS4C Team
    - NCI-DOE Collaborations Team
    - Cancer Data Science Initiatives Team
    - NCI-DOE Digital Twin Teams
    - IMPECCABLE Team
    - FDA PrecisionFDA Team
    - Open Health Systems Laboratory
    - Many more…

Funding provided by the Cancer Moonshot[SM]

The many conversations along throughout the journey, personally, at multiple workshops, meetings and events such as this along the way

Frederick National Laboratory for Cancer Research

FNL's mission: *To provide a unique national resource for the rapid development of new technologies to address some of the most urgent and demanding problems in the biomedical sciences, including cancer, ongoing unmet challenges in HIV/AIDS, and threats of emerging infectious diseases.*

FNLCR is the only Federally-Funded Research and Development Center (FFRDC) dedicated exclusively to biomedical research

- Operated in the public interest by Leidos Biomedical Research, Inc. on behalf of the National Cancer Institute

Two major campuses in Frederick, MD-- located at Fort Detrick and the ATRF

- Frederick National Laboratory employees co-located with NCI researchers and other contractors
- Additional Frederick National Laboratory scientists at Bethesda and Rockville sites

The Global Nature of Health and Precision Medicine

- Health concerns are both geographically local and global
- Diseases have a global impact, e.g. cancer, infectious diseases

- Fundamental human biology is conserved across the globe
- Local conditions influence, disease insights are shared globally

- Use all available treatment options to restore health
- Treating the patient as a whole

- Collaboration across disciplines and organizations

- ***Medical and biological digital twins foster global collaboration***

Topics

- *Technology and information are advancing rapidly and opening exciting new pathways to probe and understand the huge complexities of human biology.*
- *Approaches to wellness, disease, and long-term health are being transformed globally, with many new insights leading the way to a new future for precision medicine and personal health.*
- *Explore many changes taking place as the fusion of health information, biology and technology are realized.*

Disclaimer: Comments and thoughts shared are my own and do not reflect any official position.

Biomedical Digital Twins

Challenges in Medicine Today

- **Clinicians are overloaded**
  - Too many patients, too much information, not enough insight
- **Patients are disconnected**
  - Access to care challenges, information fragmentation
- **Increasing diagnostic and treatment options**
  - Innovation, AI and technology advances
- **Treatments are increasingly expensive**
  - Balancing broad use and precision medicine
- **Outside patient factors**
  - Behavior, nutrition, compliance, overall wellness
  - Exposure factors
  - Social Determinants of Health
- **Education**
  - Keeping up with it all

How do we improve the health of everyone, including the medical system?

Cancer

- **Cancer is both common and unique**
  - There are commonalities among cancers
  - Yet, everyone's cancer is different
  - Cancer impacts different parts of the body differently
- **Cancer impacts broadly**
  - Cancer cell is initially local
  - Tumor and tumor micro environment
  - Metastasis, recurrence, treatment, side-effects
  - Patients, populations and beyond

Figure 1. Estimated New Cancer Cases* and Deaths Worldwide for Leading Cancer Sites by Human Development Index, 2018

WORLD

Cases

Males		Females	
All sites	8,818,700	All sites	8,218,200
Lung, bronchus & trachea	1,368,500	Breast	2,088,800
Prostate	1,276,100	Colon, rectum & anus	823,300
Colon, rectum & anus	1,026,200	Lung, bronchus & trachea	725,400
Stomach	683,800	Uterine cervix	569,800
Liver	596,600	Thyroid	436,300
Urinary bladder	424,100	Uterine corpus	382,100
Esophagus	399,700	Stomach	349,900
Non-Hodgkin lymphoma	284,700	Ovary	295,400
Kidney	254,500	Liver	244,500
Leukemia	249,500	Non-Hodgkin lymphoma	224,900

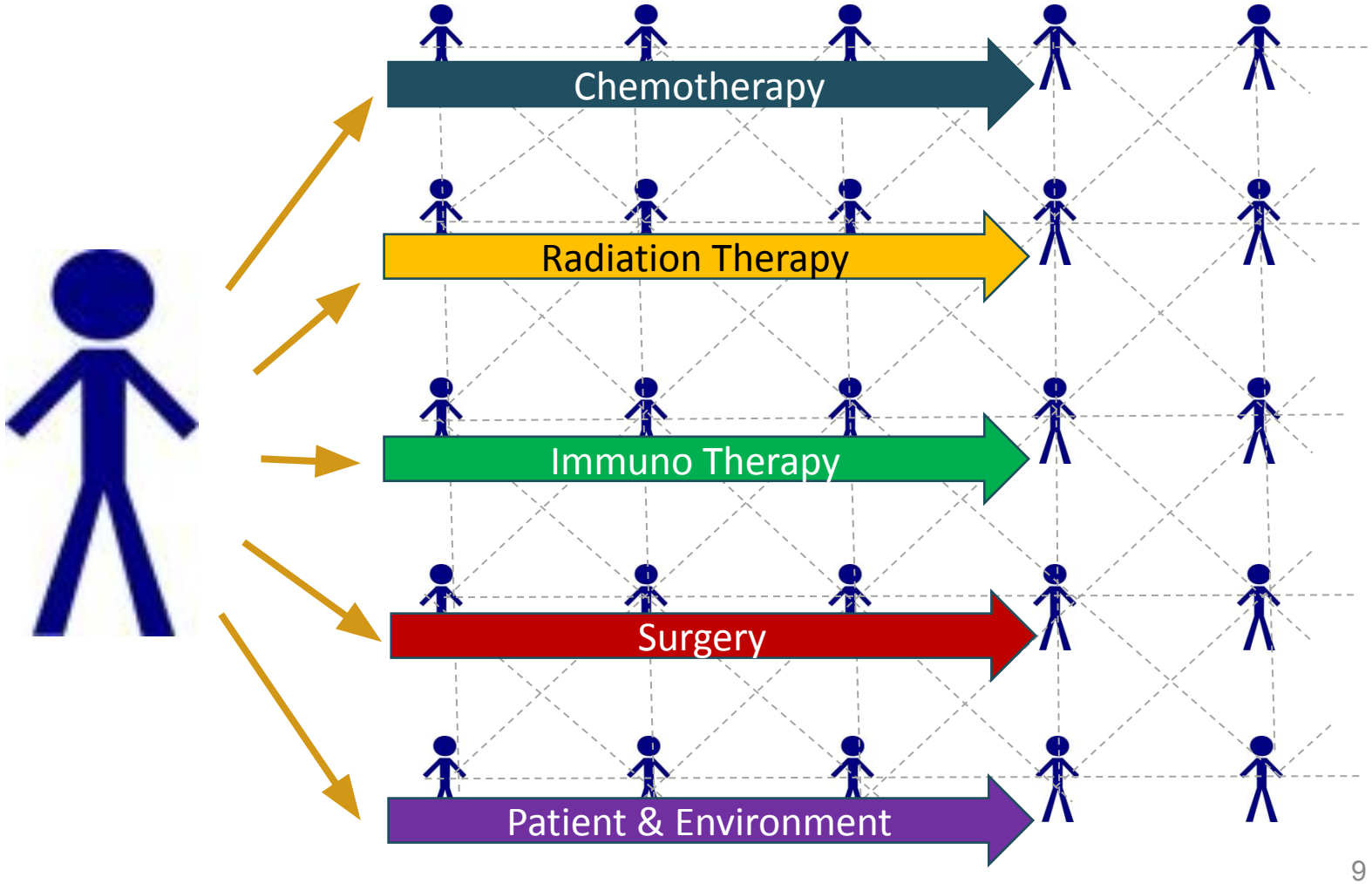
Deaths

Males		Females	
All sites	5,347,300	All sites	4,142,600
Lung, bronchus & trachea	1,184,900	Breast	626,700
Liver	548,400	Lung, bronchus & trachea	576,100
Stomach	513,600	Colon, rectum & anus	396,600
Colon, rectum & anus	484,200	Uterine cervix	311,400
Prostate	359,000	Stomach	269,100
Esophagus	357,200	Liver	233,300
Pancreas	226,900	Pancreas	205,300
Leukemia	179,500	Ovary	184,800
Urinary bladder	148,300	Esophagus	151,400
Non-Hodgkin lymphoma	146,000	Leukemia	129,500

Global Cancer Facts & Figures, 4th edition. Atlanta: American Cancer Society, Inc. 2022

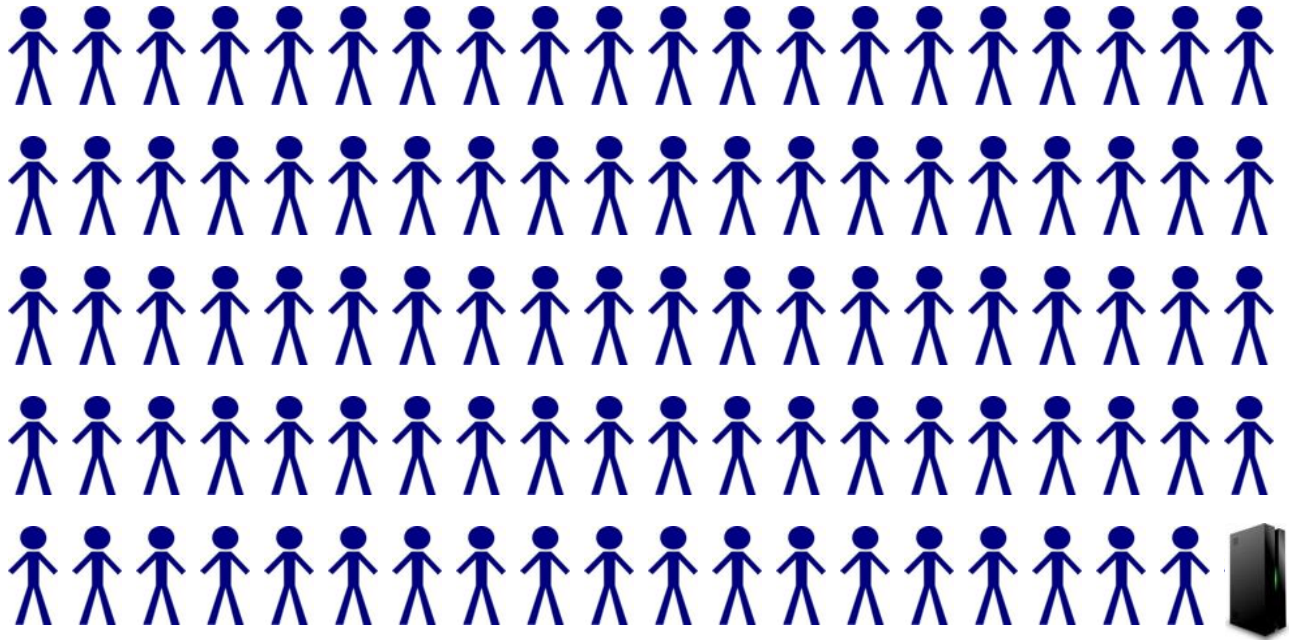
Challenge: Treating Cancer Requires *Integrated* Predictions and Personalization

- **Predictive modeling needed across treatment approaches**
- **Integrated predictive modeling to support effective decisions**
- **Which, what, when, how, how much?**
- **How do we monitor?**
- **Early detection of efficacy**
- **Prevention and early detection of potential confounding or adverse events**



Why the Digital Twin in Medicine

- Traditional approaches rely on many individuals to develop general predictions
- Results take time to achieve
- Imprecise conditions
- Explorations limited by available physical models, samples, data



(diverse population and selected to be similar)

Adapted from slide given at SC11 Personalized Healthcare Challenges for High Performance Computing
https://sc11.supercomputing.org/schedule/event_detail.php-evid=bof169.html

“The Digital Twin Approach”

- Digital twin brings predictive analytics to the forefront
- Explore possible treatments
- Pursue and refine hypotheses
- Explore conditions and scenarios
- Progressively iterate and integrate understanding and insights

(identical population with directed variability)

Goal: Provide critical insights for the individual patient

Adapted from slide given at SC11 Personalized Healthcare Challenges for High Performance Computing
https://sc11.supercomputing.org/schedule/event_detail.php-evid=bof169.html

National Academies of Science, Engineering and Medicine: 2023 Report on Digital Twins

- US National Academies of Science, Engineering and Medicine Report released December 2023
- Emphasized Research Gaps and Future Directions

Download:
https://www.nationalacademies.org/our-work/foundational-research-gaps-and-future-directions-for-digital-twins

"A digital twin is a set of virtual information constructs that mimics the structure, context, and behavior of a natural, engineered, or social system (or system-of-systems), is dynamically updated with data from its physical twin, has a predictive capability, and informs decisions that realize value. The bidirectional interaction between the virtual and the physical is central to the digital twin."

Use cases for digital twins

- **Transportation**
  - Planes, trains and automobiles
- **Manufacturing**
  - Supply chain, production lines, reactors
- **Systems**
  - Patient flow, water systems, treatment systems, power plants, traffic, finance
- **Defense, aerospace**
- **Life science**

Cancer Patient Digital Twins

- Digital twin brings predictive analytics to the forefront
- Explore possible treatments
- Pursue and refine hypotheses
- Explore conditions and scenarios
- Progressively iterate and integrate understanding and insights

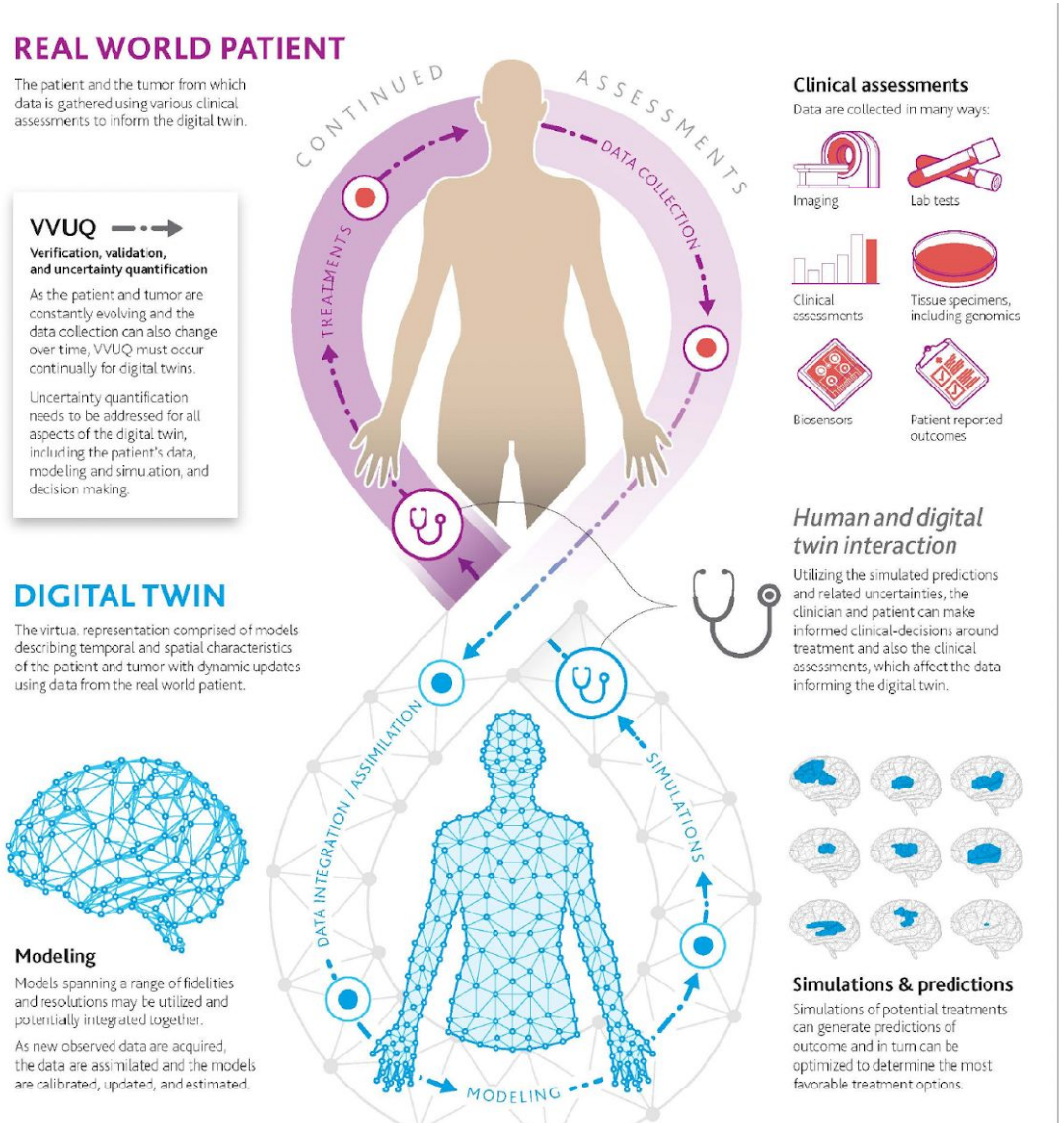
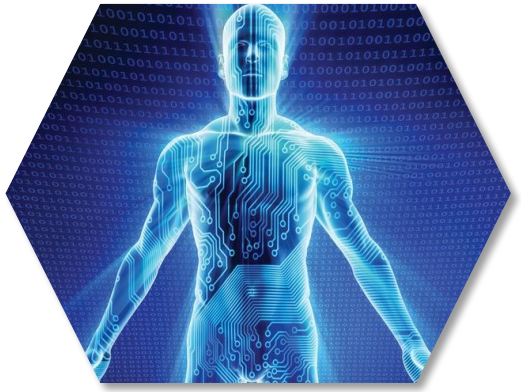
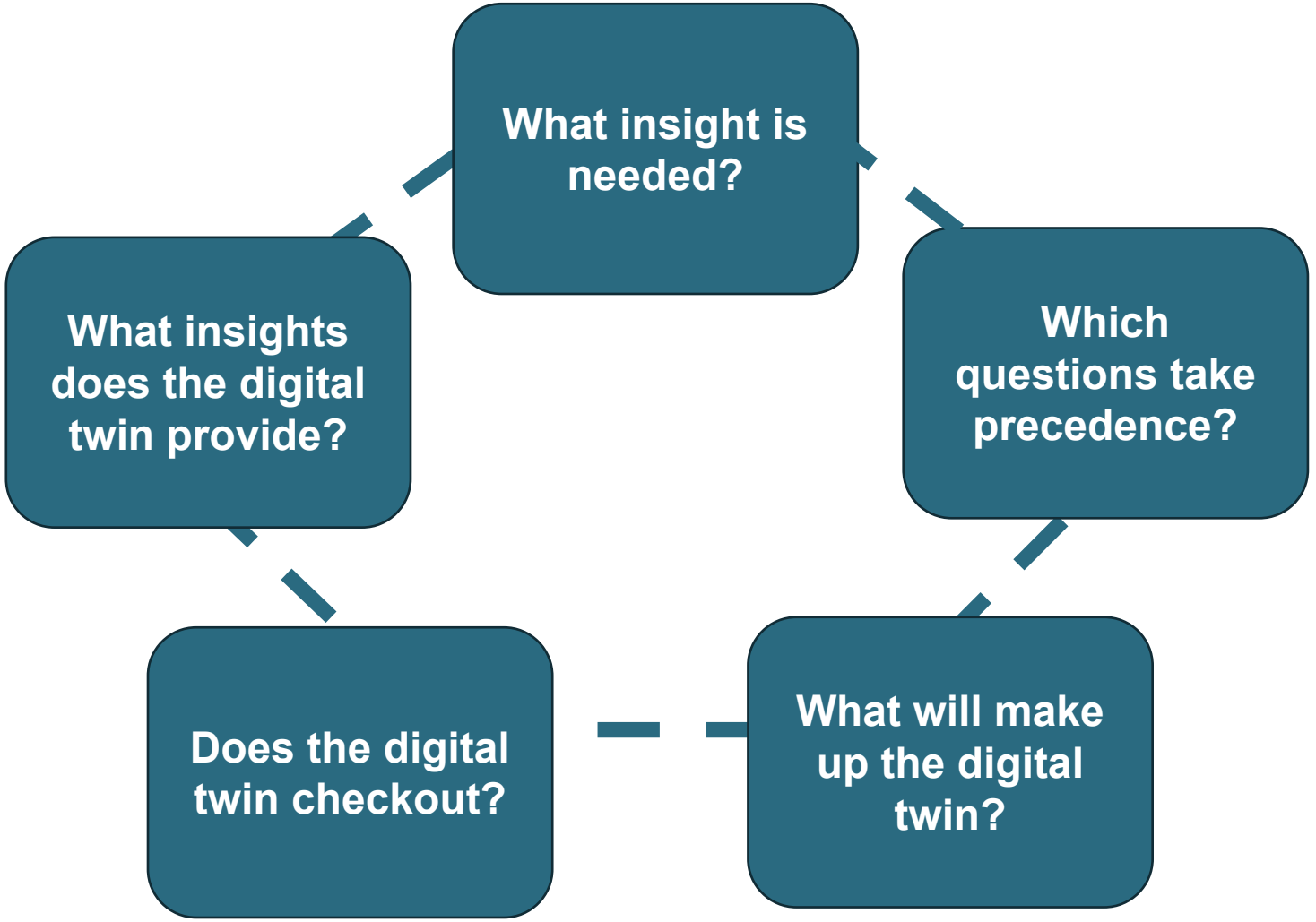


Image source: National Academies Sciences, Engineering, Medicine
Foundational Research Gaps and Future Directions for Digital Twins (2023)

Composing a Digital Twin

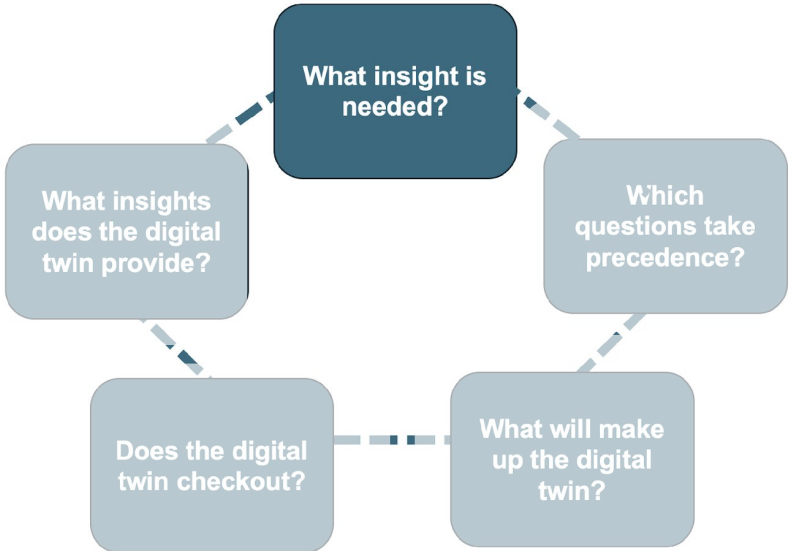
"Building a digital twin is driven by needed answers and insights"





What insights are needed?

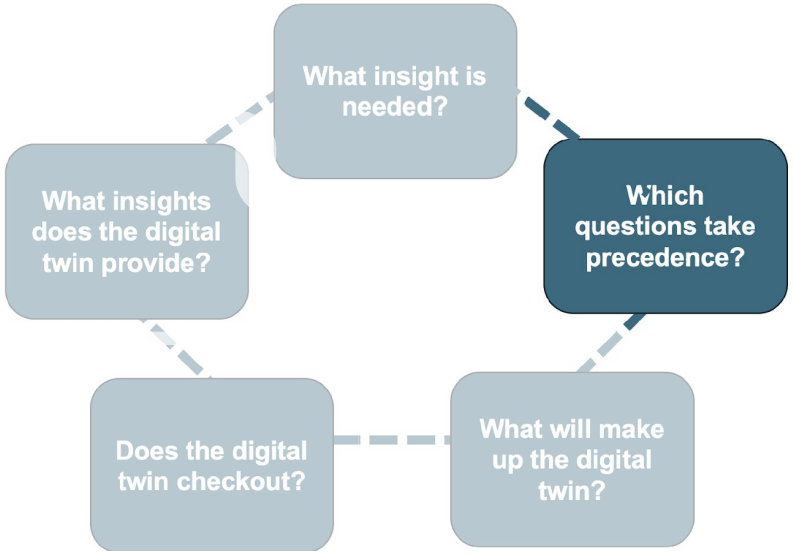
- **Need to know questions to be answered and decisions to be supported**
- **Many questions**
- **Opportunity to learn**



- **Summary points**
  - *Starting the conversation on desired questions to be answered and decisions fosters a collaborative discussion around the medical digital twin*
  - *There are many questions to be answered, so there are many potential digital twins*

What questions take priority?

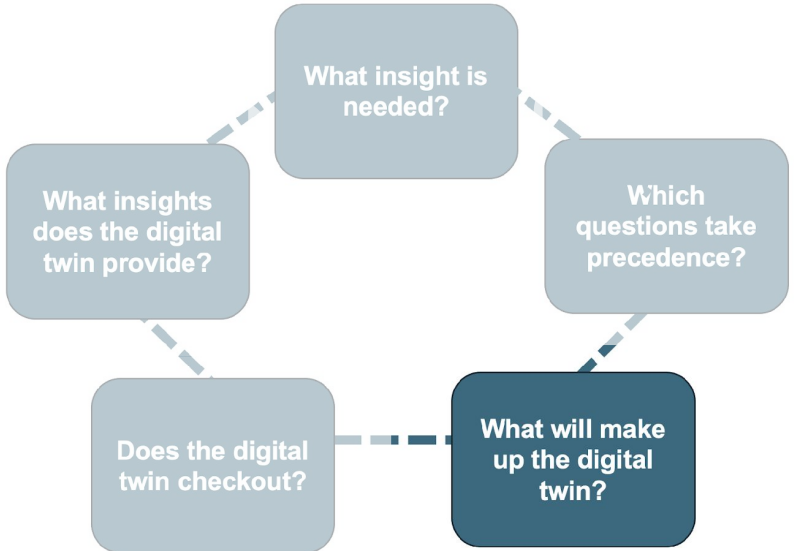
- **What questions are most necessary?**
  - Impact or immediacy
- **What insights appear feasible?**
  - Time to solution, cost, availability of critical information, technical feasibility



- **Summary points**
  - *Medical digital twins will foster new levels of technical transparency*
  - *Information sharing will be essential about prior medical digital twins including technical feasibility, data requirements, model availability, how results were beneficial*

What will make up the digital twin?

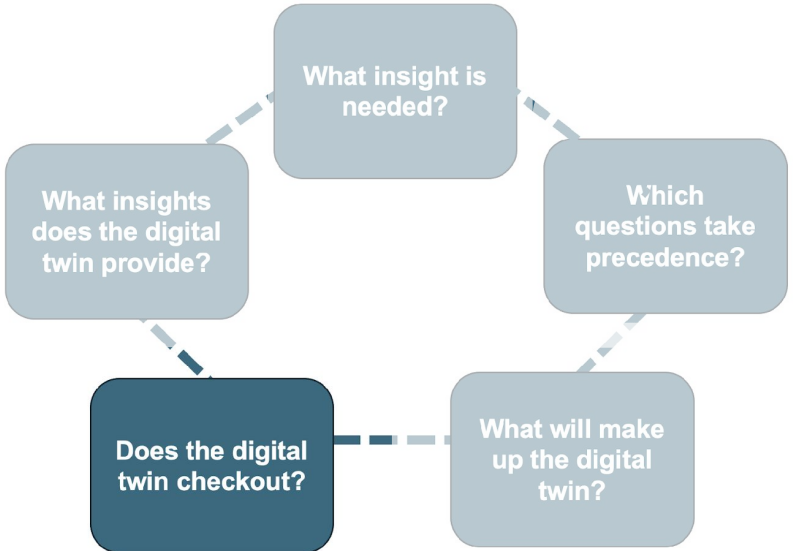
- **What will compose the digital twin?**
  - Which models are available?
  - What data are available for the individual?
- **What assumptions will be used?**
- **What predictive approaches can be used?**
- **How will the models be personalized?**



- **Summary points**
  - *Given the relatively limited information on available models, usable data, successes, and limits, expectations will need to be managed early*
  - *It will be essential to make information available about the elements used to create digital twins*

Does the digital twin checkout ?

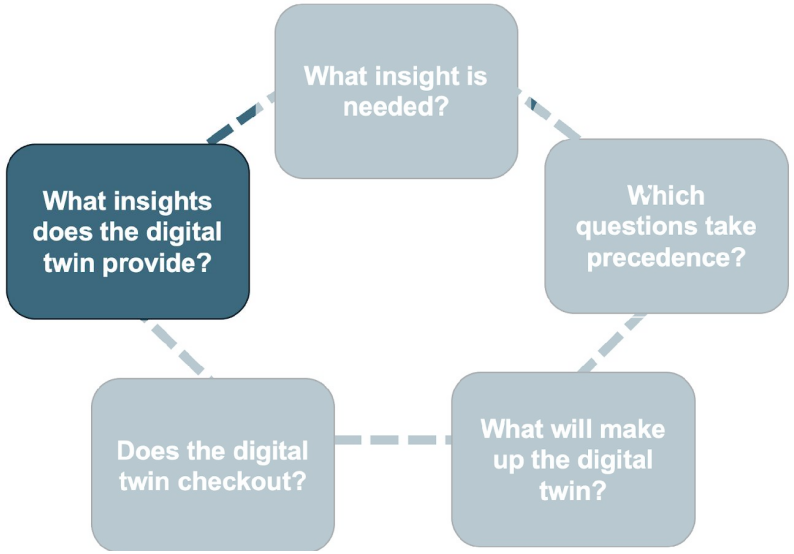
- **Is the digital twin composed as intended?**
  - Are the intended models used?
  - Have they been correctly adapted?
  - Are the data streams working as intended?
- **How well can the results be trusted?**
- **Are the results reasonable, repeatable, or reproducible?**
- **Does the digital twin inform the questions and decisions of interest?**



- **Summary points**
  - *Validation, Verification, and Uncertainty Quantification are essential*
  - *Measures information are needed to qualify the components of digital twins*

How can the medical digital twin be best used?

- **Technical infrastructure**
  - How do I use this digital twin and what insight is it providing?
  - What are the assumptions supporting this digital twin?
  - Is this digital twin still valid?
- **Social infrastructure**
  - Ownership
  - Privacy
  - Liability
  - Unintended and unauthorized use
  - Ethical



- **Summary points**
  - *Education and policies are needed in many areas for medical digital twins*
  - *The need for transparency needs to be balanced with privacy for increasingly precise digital twins*

Virtual Human Models and Digital Twins

Emerging learning health system

- **Technical pathways emerging to support digital twin**
  - FAIR ecosystem (data, models, software)
  - Cloud computing
  - Affordable computing
  - AI, trusted and sustainable AI
  - Data sharing and data security
  - 5G
  - Blockchain
  - Medical IoT
  - Exascale computing

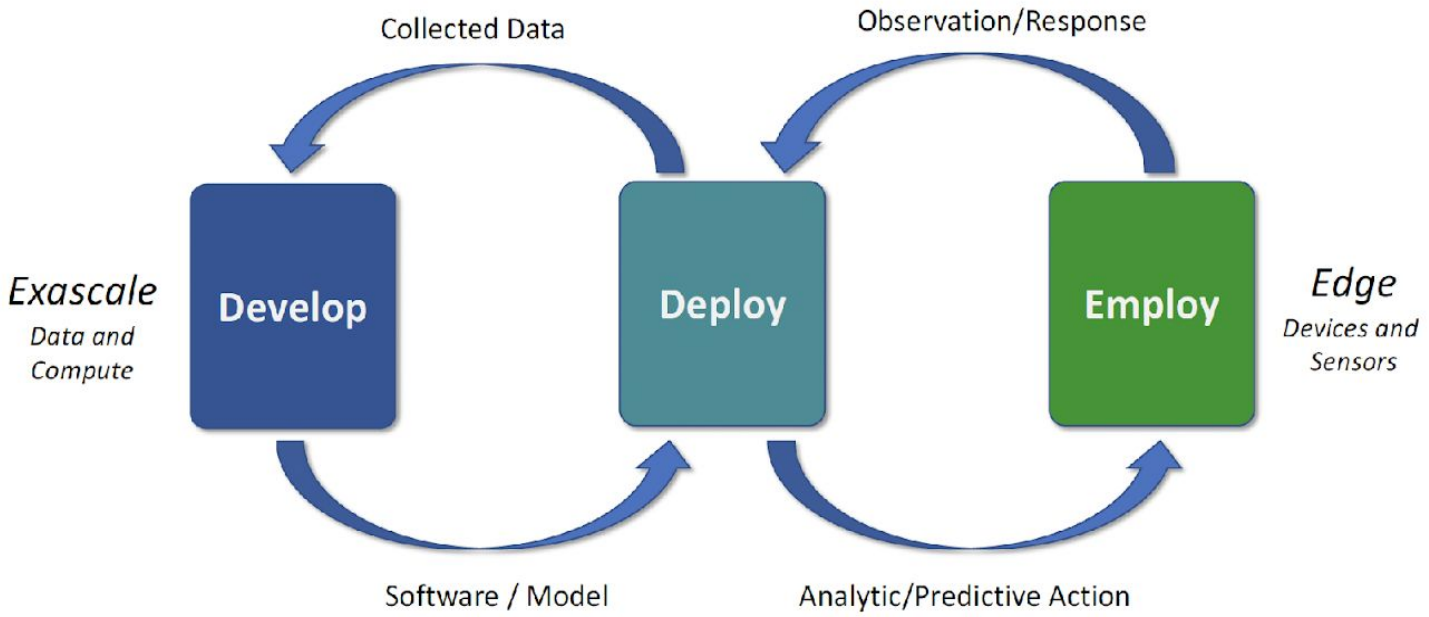


Image From 2019 Panel at SC19 on "Edge to Exascale"

Changing Landscape for Drug Evaluation

- **In December 2022, FDA recently amended 1938 requirement for animal testing of drugs**
- **Previously, typically required testing in rodent and non-rodent animals**
- ***Allows* FDA to approve a new drug without animal testing**
- **Opens avenue to evaluate alternatives including computational modeling, organoids, organ-on-a-chip and other emerging approaches**
- **Future is developing**
  - Non-animal models are in their infancy
  - Non-animal models are limited in their scope
  - Animal models have not been fully indicative (high failure rate of drugs in trials)
- **Discussion is underway about adequacy of alternatives**

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

Digital Twin Vision

- Virtual humans are *digital twins* of the human body that reproduce the way the body works.

Why it is significant?

- Current medicine is not predictive, save in the limited sense that doctors expect "Patient X" should respond like similar patients who have been studied in the past.
- Will be predictive and personalized

BUT

- Requires education and training of medics

Slide courtesy of Peter Coveney, UCL

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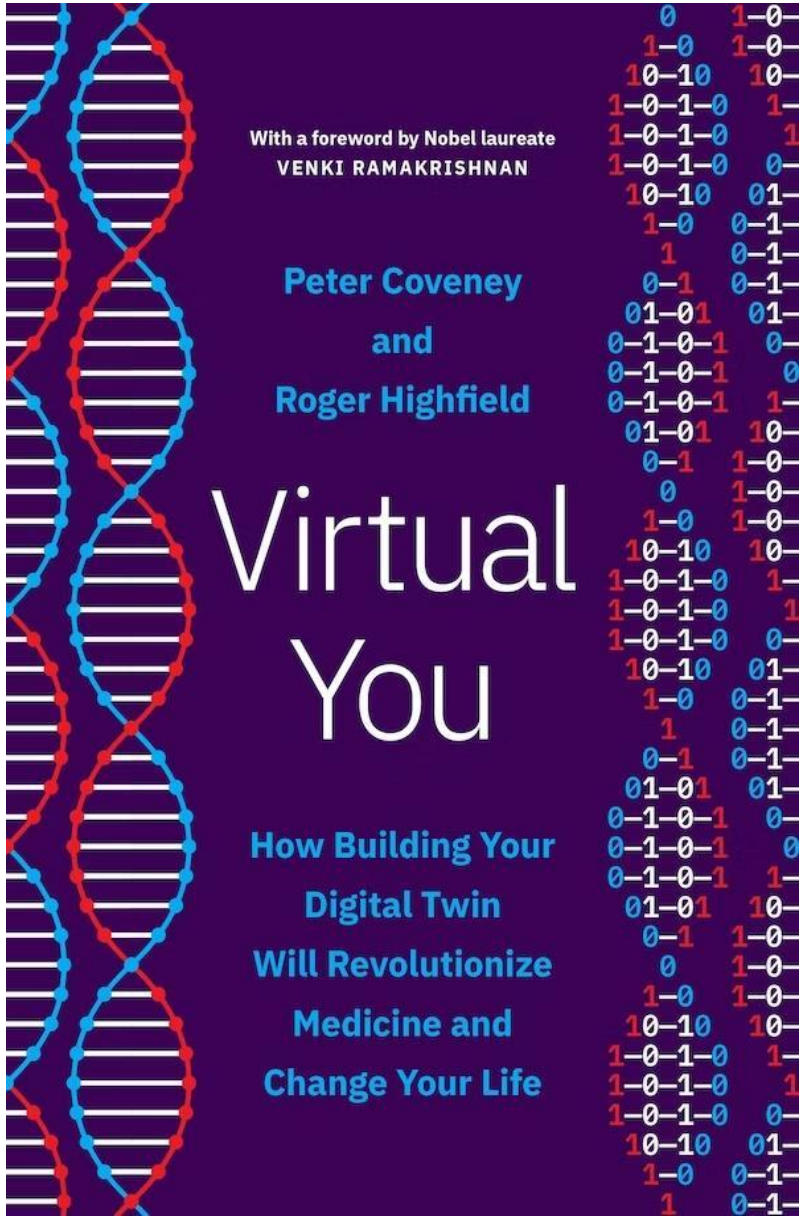
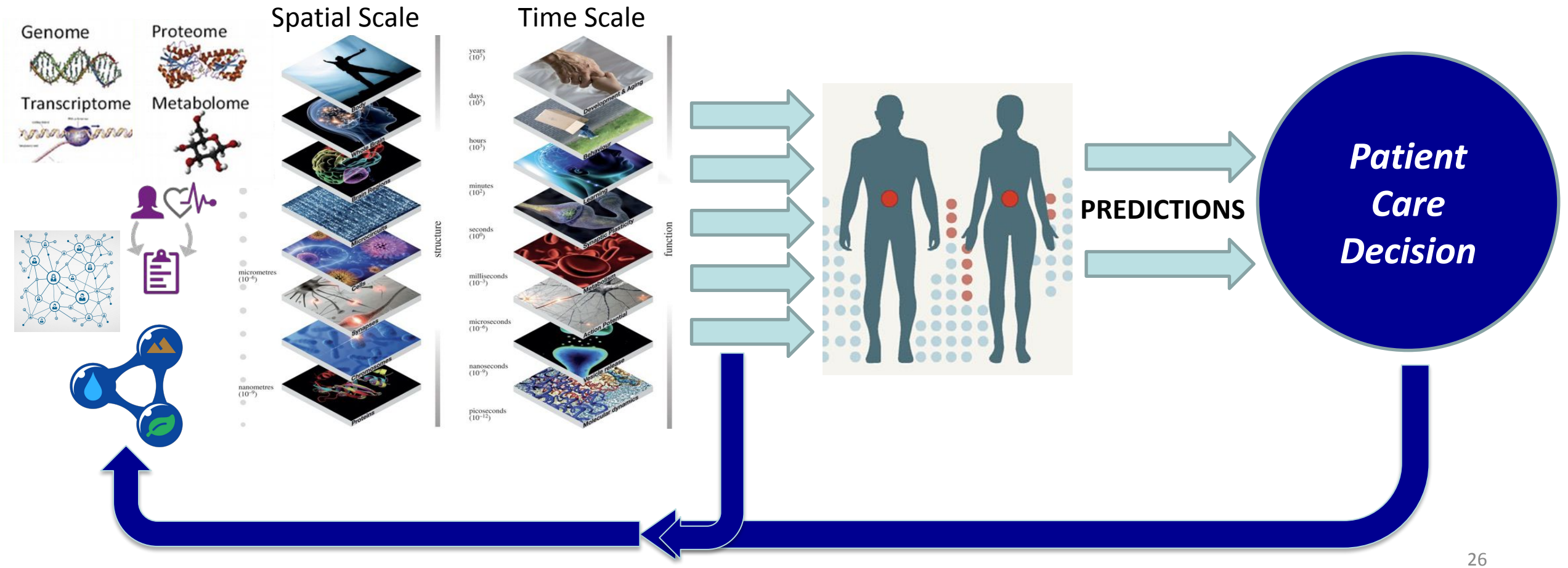


Slide courtesy of Peter Coveney, UCL

The Challenge: Digital Twin Learning System

Frederick National Laboratory for Cancer Research
sponsored by the National Cancer Institute

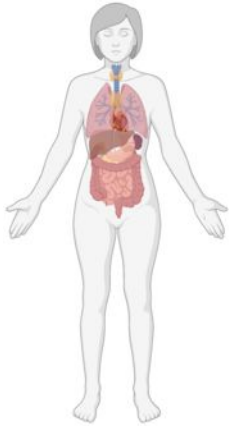
Patient-tailored models incorporating multi-omic, clinical, environmental and social data that can evaluate and predict the most effective prevention and therapeutic plans

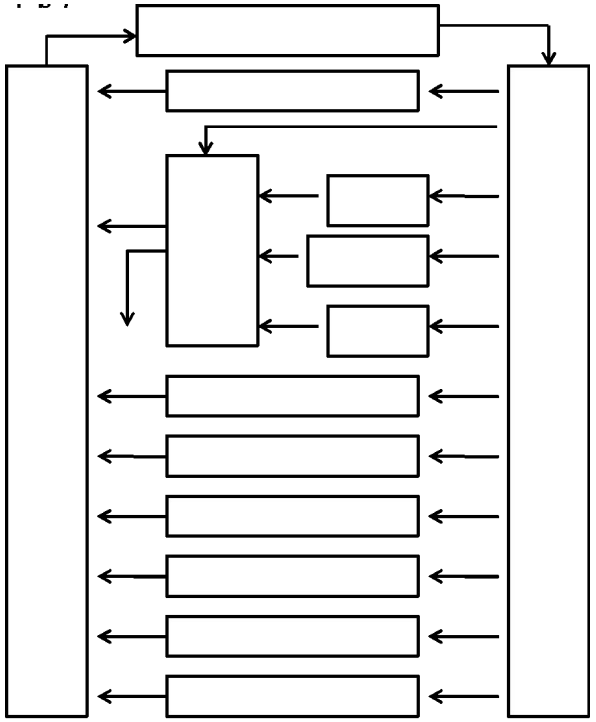


Human systems biology models provide essential insights

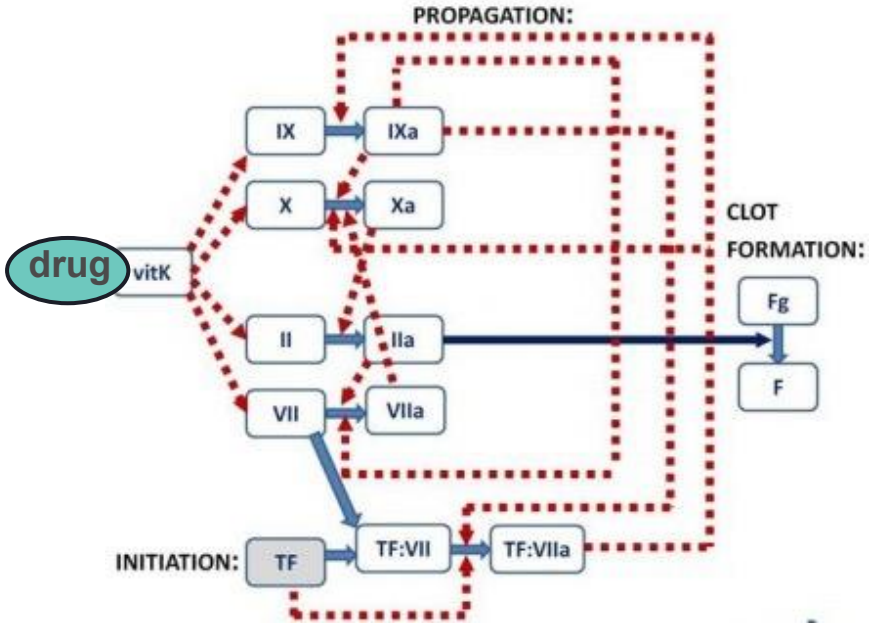
Pharmacokinetics

Absorption
Distribution
Metabolism
Elimination





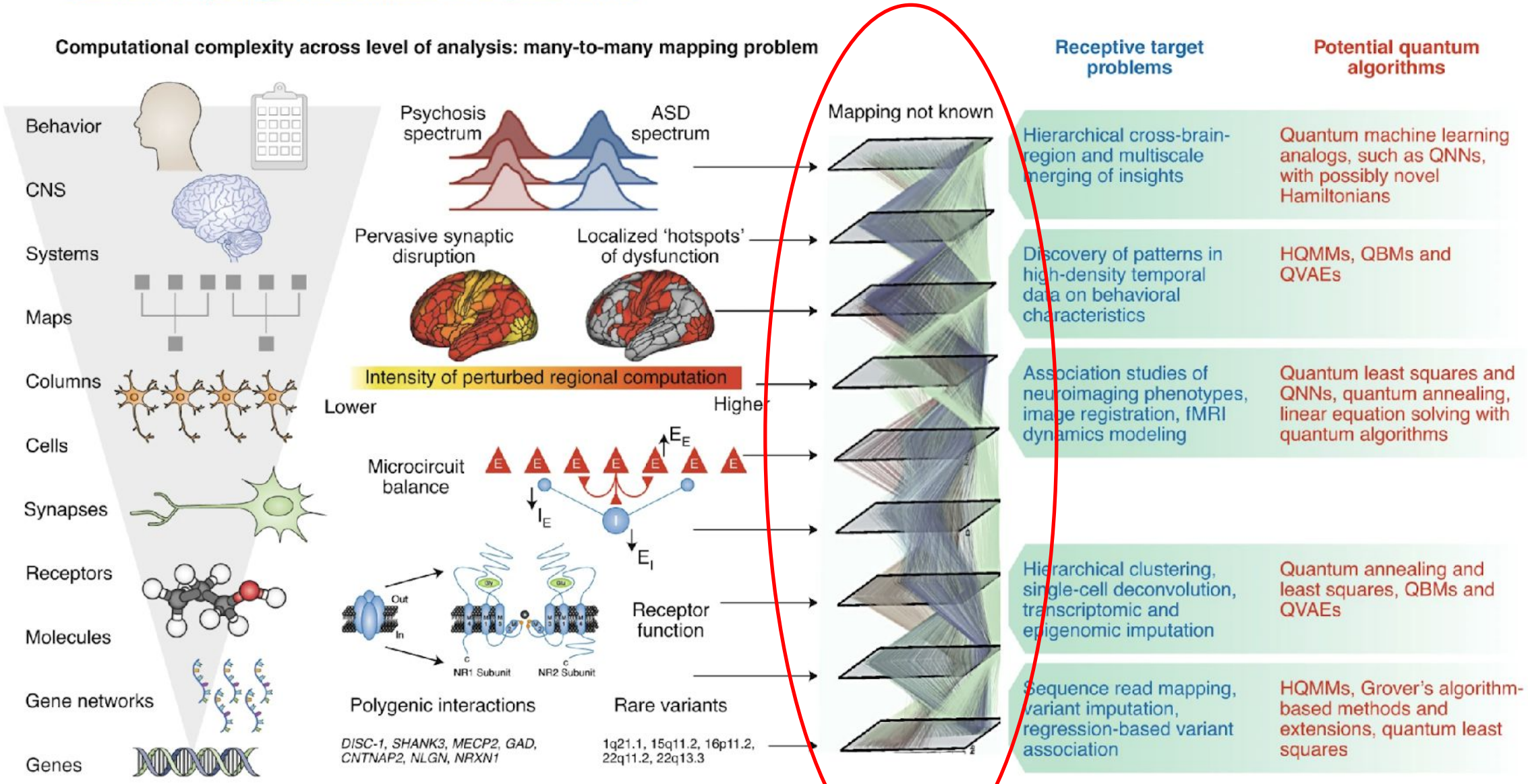
Pharmacodynamics



Digital Twin Informed Systems Biology Models

Slide courtesy of Jim Brase, LLNL

From: Quantum computing at the frontiers of biological sciences



The challenge consists, in part, of the need to interrogate the enormous search space for determining the mapping across levels, which constitutes a many-to-many probabilistic problem. Computational innovation will be a key effort to help close these gaps. Portion of figure adapted with permission from ref. [62], Elsevier. Also shown are some of the ways in which QC can aid in the interrogation of these levels.

2020 Ideas Lab Cancer Patient Digital Twin Teams

GEORGETOWN UNIVERSITY

Simulating One Million Pancreatic Cancer Patient Digital Twins to Plan Precision Medicine Treatment Strategies and Improve Long-term Survival. **PI: Matthew McCoy, PhD**

Project Aim: Simulate one million pancreatic Cancer Patient Digital Twins (CPDT) in a models repository by parameterizing input from real patient trajectories for drug sensitivity and resistance

Stanford University

An Adaptive Digital Twin Approach for Monitoring Treatment Response and Resistance **PI: Olivier Gevaert, Ph.D., Assistant Professor in Medicine (Biomedical Informatics)**

Project Aim: Advance the hypothesis that optimal pathways for a specific cancer patient can be selected by exploring the treatment pathway space through a dynamical, multiscale digital twin derived by harnessing patient's own data and leveraging data from similar patients in the population.

South Carolina

Dynamic Multiscale Digital Twin for a Lung Cancer Patient. **PI: Qi Wang, Professor of Mathematics**

Project Aim: Build the first prototype of an individualized digital twin of non-small cell lung cancer for identifying the optimal treatment pathway and adaptive treatment monitoring, leveraging the population information and new test results.

Prototyping a Self-learning Digital Twin Platform for Personalized Treatment in Melanoma Patients **PI: Paul Macklin, PhD, Associate Professor of Intelligent Systems Engineering**

Project Aim: Rapidly prototype a 3D multiscale model of melanoma metastases that interact with the host immune system with or without treatment (autologous vaccine immunotherapy)—and verify that it recapitulates a broad variety of clinically relevant patient trajectories.

UMass Amherst

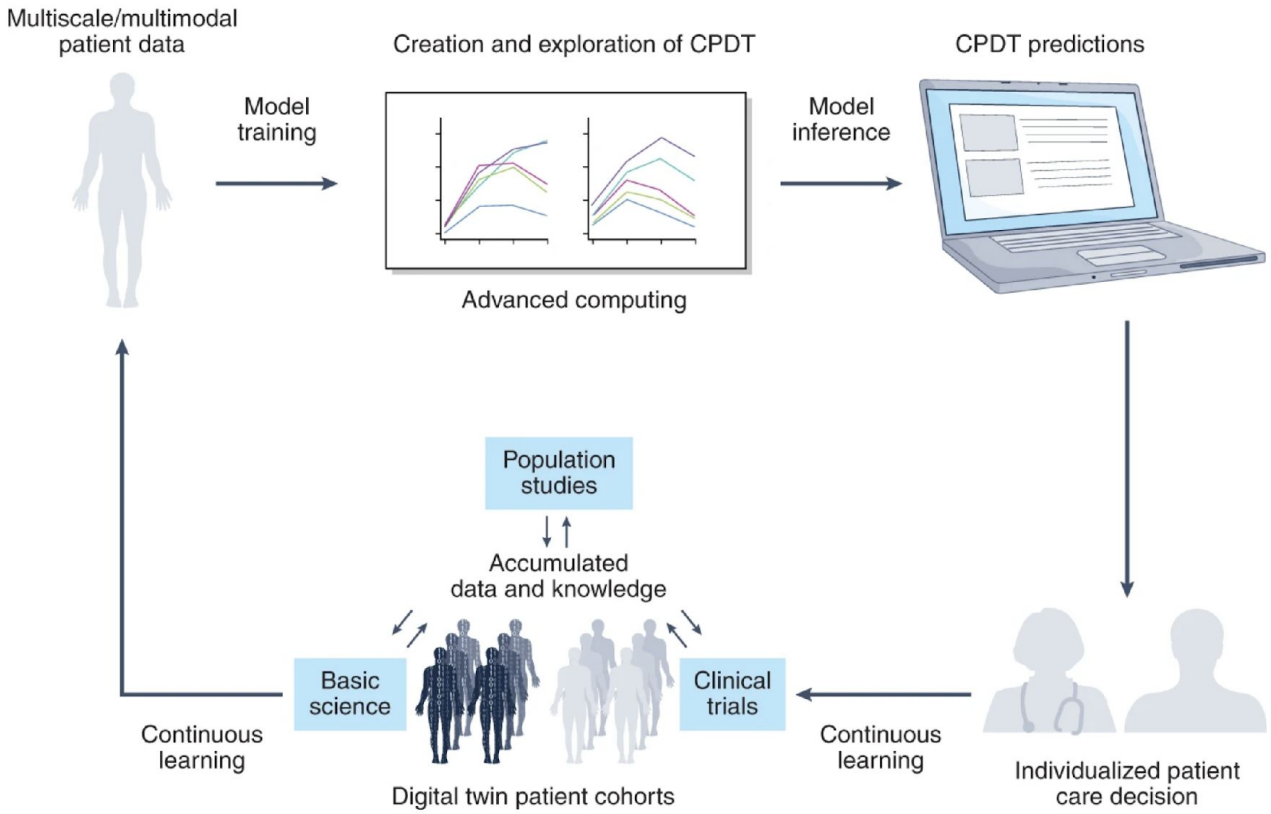
My Virtual Cancer. **PI: Leili Shahriyari, PhD., Assistant Professor, Mathematics and Computer Science**

Project Aim: Combine mechanistic, machine learning, and stochastic modeling approaches to create a DT platform that utilizes biological, biomedical, and EHR data sets. Will focus on one common cancer—breast cancer—and one rare cancer—uveal melanoma— to evaluate the performance of the DT for both common and rare cancers.

ISB · Stanford University · GEORGETOWN UNIVERSITY · The University of Oklahoma · icbi Innovation Center for Biomedical Informatics · Georgetown | Lombardi Comprehensive Cancer Center · University of Minnesota · Sandia National Laboratories · UMass Amherst · University of Virginia · Yale University · OHSU · IBM Research · MAYO CLINIC · UiO: University of Oslo · The Ohio State University · University of Pittsburgh · PennState · UMass | Dartmouth 125 Years · BROAD INSTITUTE · VA | U.S. Department of Veterans Affairs

"Exploring approaches for predictive cancer patient digital twins: Opportunities for collaboration and innovation"
https://www.frontiersin.org/articles/10.3389/fdgth.2022.1007784/full

Digital Twin Paradigm for Cancer Patients



Digital twins for cancer patients based care bring together data, models, computing, and technology together with researchers, patients and physicians to improve the care options for each individual.

Image from Hernandez-Boussard, T., Macklin, P., Greenspan, E.J. *et al.* Digital twins for predictive oncology will be a paradigm shift for precision cancer care. *Nat Med* **27,** 2065–2066 (2021). https://doi.org/10.1038/s41591-021-01558-5

Digital Twin on Frontier

HemeLB meets Frontier

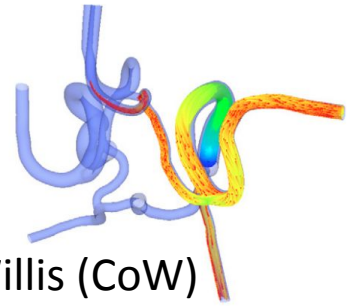
- Lattice Boltzmann solver
- Massively paralleled high-performance code
- Available on both CPU and GPU (CUDA/Hipified)
- Designed for sparse geometry, ideal for hemodynamics simulations

The world's only exascale machine. Access to it by a pathway that has gone via Titan, BlueWaters and Summit.

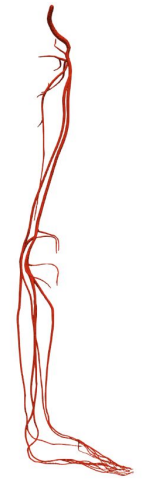
Frontier strong scaling plots

Full-human scale simulation requirements

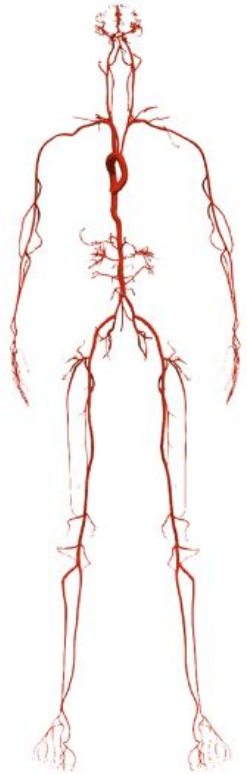
- 140 billion lattice sites (1.4×10^{10})
- Full deployment on Frontier (Exascale computing)
- A few cardio cycles to produce a high-fidelity simulation



Circle of Willis (CoW)

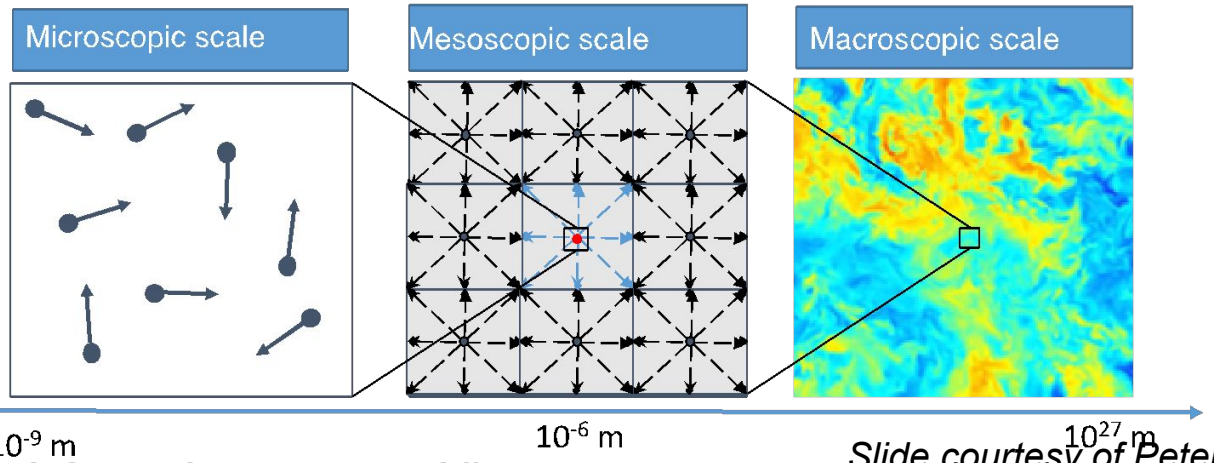


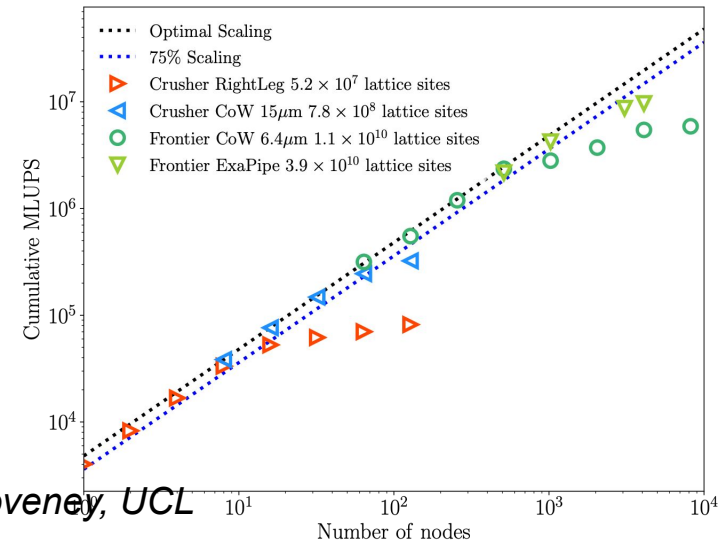
Human Right leg



Full-human scale arterial system

The lattice Boltzmann method





Slide courtesy of Peter Coveney, UCL

© Crown Copyright, Met Office

Recent Biomedical Digital Twins

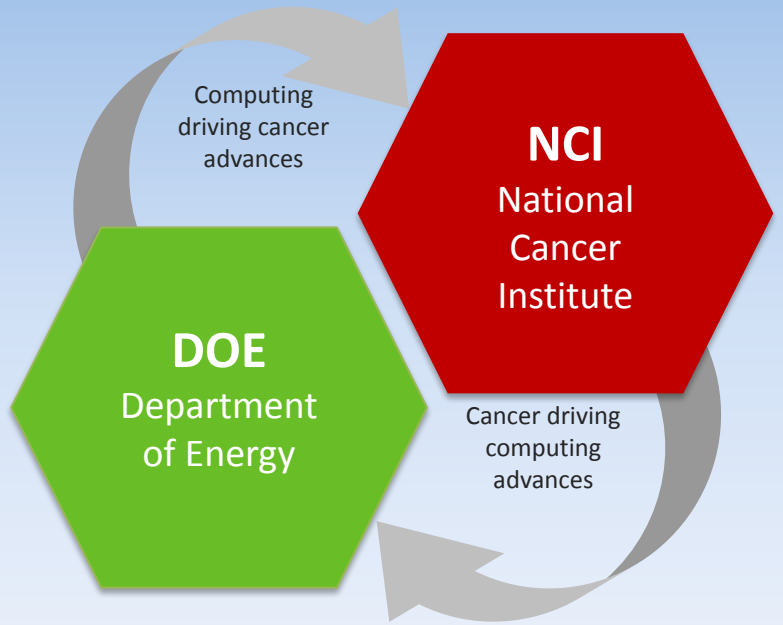
- **Cancer -** Chaudhuri A, Pash G, Hormuth DA 2nd, Lorenzo G, Kapteyn M, Wu C, Lima EABF, Yankeelov TE, Willcox K. Predictive digital twin for optimizing patient-specific radiotherapy regimens under uncertainty in high-grade gliomas. Front Artif Intell. 2023 Oct 11;6:1222612. doi: 10.3389/frai.2023.1222612. PMID: 37886348; PMCID: PMC10598726.

  Wu C, Lorenzo G, Hormuth DA 2nd, Lima EABF, Slavkova KP, DiCarlo JC, Virostko J, Phillips CM, Patt D, Chung C, Yankeelov TE. Integrating mechanism-based modeling with biomedical imaging to build practical digital twins for clinical oncology. Biophys Rev (Melville). 2022 Jun;3(2):021304. doi: 10.1063/5.0086789. Epub 2022 May 17. PMID: 35602761; PMCID: PMC9119003.
- **Cardiovascular -** Coorey, G., Figtree, G.A., Fletcher, D.F. *et al.* The health digital twin to tackle cardiovascular disease—a review of an emerging interdisciplinary field. *npj Digit. Med.* **5**, 126 (2022). https://doi.org/10.1038/s41746-022-00640-7
- **Diabetes -** The Cleveland Clinic. Randomized Controlled Trial of Digital Twin Precision Treatment: A Novel Whole Body Digital Twin Enabled Precision Treatment for Type 2 Diabetes (TPT), https://clinicaltrials.gov/ct2/show/NCT05181449 (2023)
- **Multiple Sclerosis -** Voigt I, Inojosa H, Dillenseger A, Haase R, Akgün K, Ziemssen T. Digital Twins for Multiple Sclerosis. Front Immunol. 2021 May 3;12:669811. doi: 10.3389/fimmu.2021.669811. PMID: 34012452; PMCID: PMC8128142.
- **Nutrition -** Gkouskou K, Vlastos I, Karkalousos P, Chaniotis D, Sanoudou D, Eliopoulos AG. The "Virtual Digital Twins" Concept in Precision Nutrition. Adv Nutr. 2020 Nov 16;11(6):1405-1413. doi: 10.1093/advances/nmaa089. PMID: 32770212; PMCID: PMC7666894.
- **Migraine -** Gazerani P. Intelligent Digital Twins for Personalized Migraine Care. J Pers Med. 2023 Aug 13;13(8):1255. doi: 10.3390/jpm13081255. PMID: 37623505; PMCID: PMC10455577.
- **Precision medicine -** Cellina M, Cè M, Alì M, Irmici G, Ibba S, Caloro E, Fazzini D, Oliva G, Papa S. Digital Twins: The New Frontier for Personalized Medicine? *Applied Sciences*. 2023; 13(13):7940. https://doi.org/10.3390/app1313794

Advancing Capabilities and Building Community

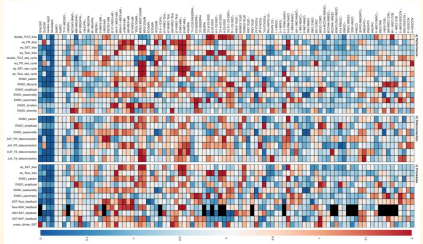
NCI-DOE Collaborations Advance Cancer Research Using Computing

A collaboration between the Department of Energy and the National Cancer Institute



IMPROVE

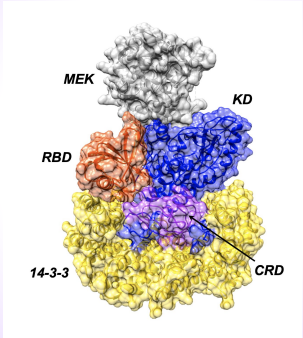
Innovative Methodologies and New Data for Predictive Model Evaluation



Rick Stevens (ANL)
Jeff Hildesheim (NCI)
Ryan Weil (FNLCR)

ADMIRRAL

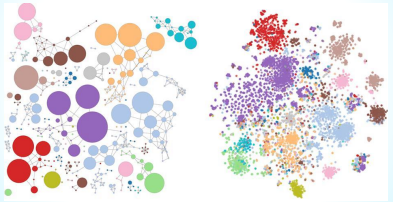
AI-Driven Multiscale Investigation of RAS-RAF Activation Lifecycle



Dwight Nissley (FNLCR)
Fred Streitz (LLNL)

MOSSAIC

Modeling Outcomes using Surveillance data and Scalable AI for Cancer



Betsy Hsu (NCI)
Heidi Hanson (ORNL)

Cancer Patient Digital Twin:
New insights and approaches from molecular to patient scale!

New observables
New data
New approaches

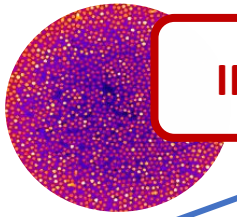
Multiple perspectives
Integrated objectives

MOSSAIC

Prescriptive cancer models

Patient specific disease ensembles

IMPROVE



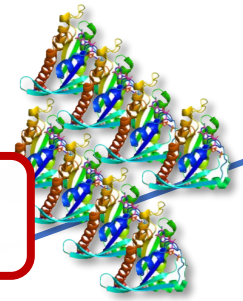
Multiple distinct cancer models

Single cancer ensemble

Multi-scale
Multi-cell models

Reaching the Patient for Impact

ADMIRRAL



Single mechanism
Single ensemble

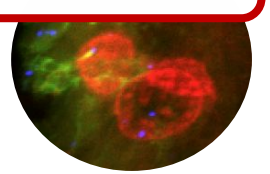
Single mechanism
Single trial

Multi-mechanism
Multi-ensemble

Multi-mechanism
Single ensemble

Multi-scale

ATOM



Multiple starting points team collaborations

New Molecular Entity Discovery

The opportunity for transformation…

Target ID & Selection

Reductionist & functional screening of millions of molecules to inform selection

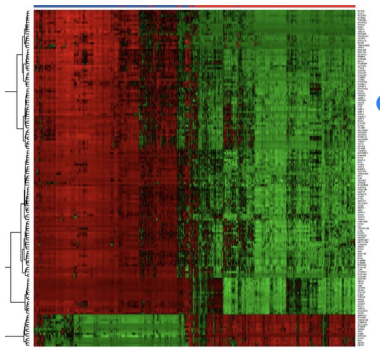
Design, make, & test 1000s of new molecules

Optimize empirically by sequential evaluation

Lengthy *in-vitro* and *in-vivo* experiments

Continuous tradeoffs

~33% of total cost of medicine development



~ 5 years

Lead Discovery 1.5 yrs

Lead Optimization 3 yrs

Preclinical 1.5 yrs

~12% clinical success

~ $40B 2020 NIH Budget

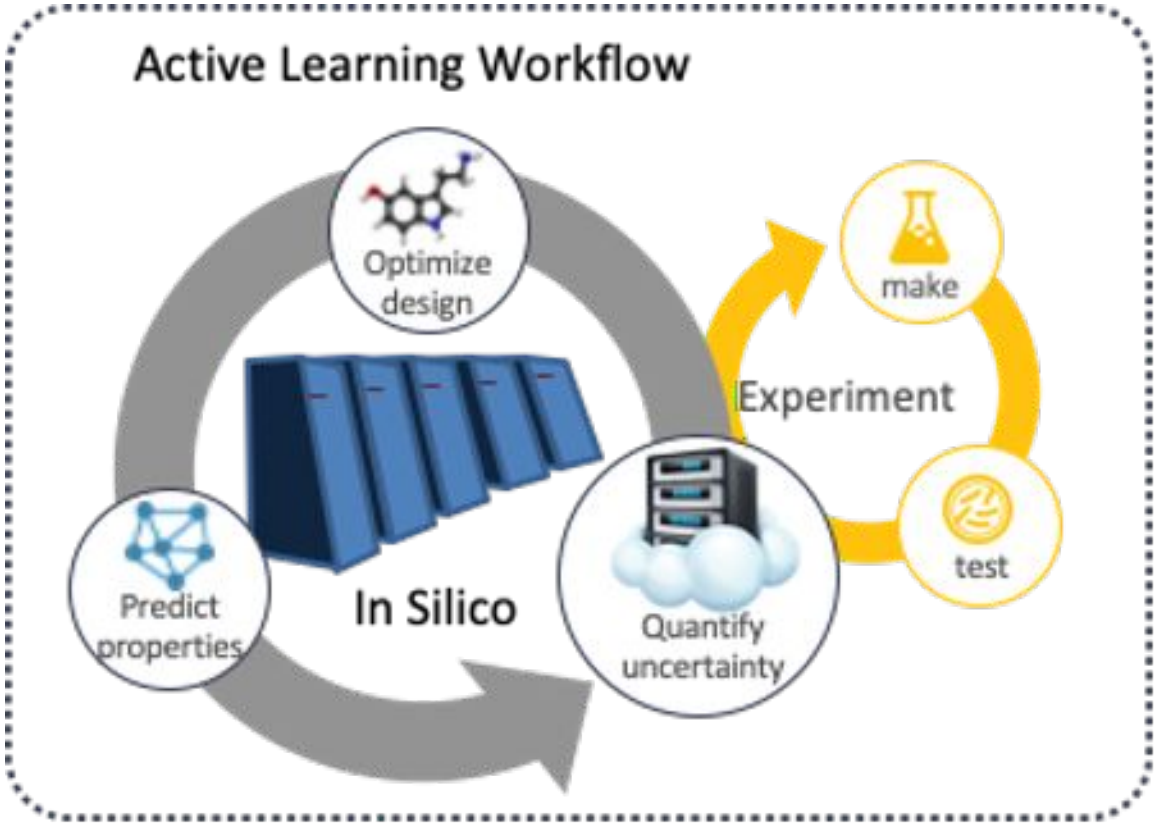
1/3 of ~ $189B 2020 Private sector spend in Pharma R&D

~ $40B 2020 NIH Budget

ATOM

http://www.nature.com/nrd/journal/v9/n3/pdf/nrd3078.pdf
https://www.nih.gov/about-nih/what-we-do/budget
https://www.statista.com/statistics/309466/global-r-and-d-expenditure-for-pharmaceuticals/

ATOM: Computing and experimental technologies enable a new approach

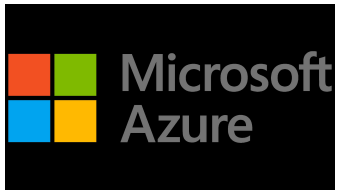


1. **Active learning** –Predictive computational models incorporating AI and high-performance simulation specify exactly which experimental to do
2. **Multiparameter molecular design** simultaneously optimizes efficacy, safety, pharmacokinetics, and manufacturability
3. **Human relevant models** – both computational systems models and experimental human organoids – in the design loops to improve success rates in human testing

Open source on github

Growing Global Utilization

- **Increase Access**
  - Current AMPL Availability
    - FNLCR FRCE computing environment
    - NIH Biowulf
    - DOE ORNL Frontier system
    - DOE LLNL system
    - NSF Darwin (University of Delaware)
    - NCI supported Cancer Genomics Cloud
    - Zuse Institute Berlin (supporting Charite' collaboration)
    - Multiple sites in India
  - Availability in Process
    - FDA – Precision FDA Environment (working through subcontractor)
    - Cloud computing – Microsoft Azure, AWS, Google Cloud
    - Collaborative Drug Discovery (CDD) utilization
  - Future support in computational.cancer.gov portal





Predictive Oncology Model and Data Clearinghouse (MODAC)

Frederick National Laboratory for Cancer Research

- Build confidence and trust in models
  - Data and models together
- Support repeatability, reproducibility and transparency
- Foster adoption of FAIR principles for models
- Encourage portability and use of standards
- Assure stable versions of models and datasets to reference
- Require registration for upload and download
  - Tracking and accountability
- Maintain simplicity, flexibility, and future focus

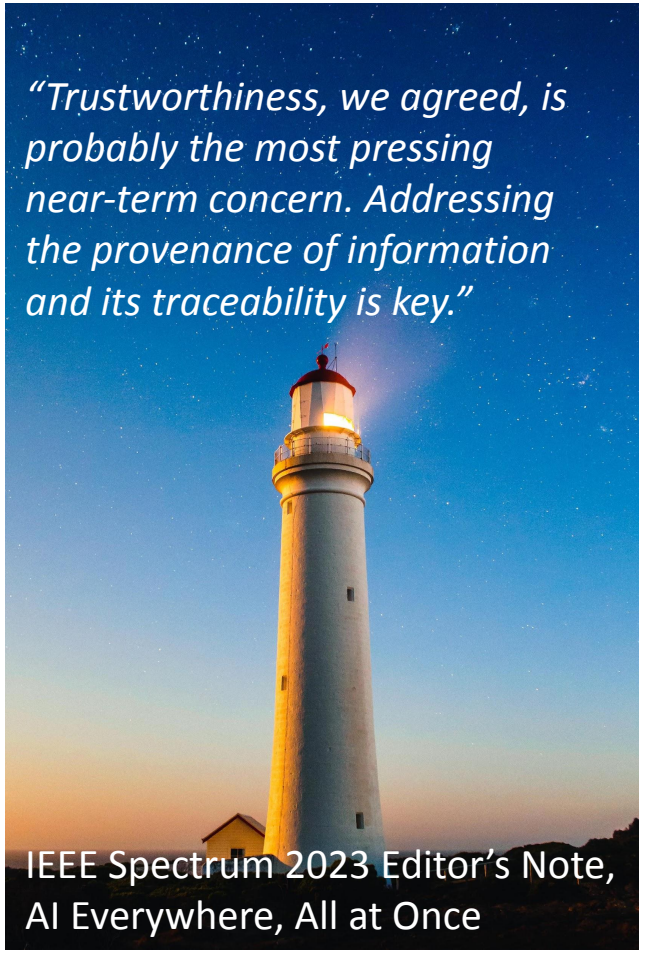
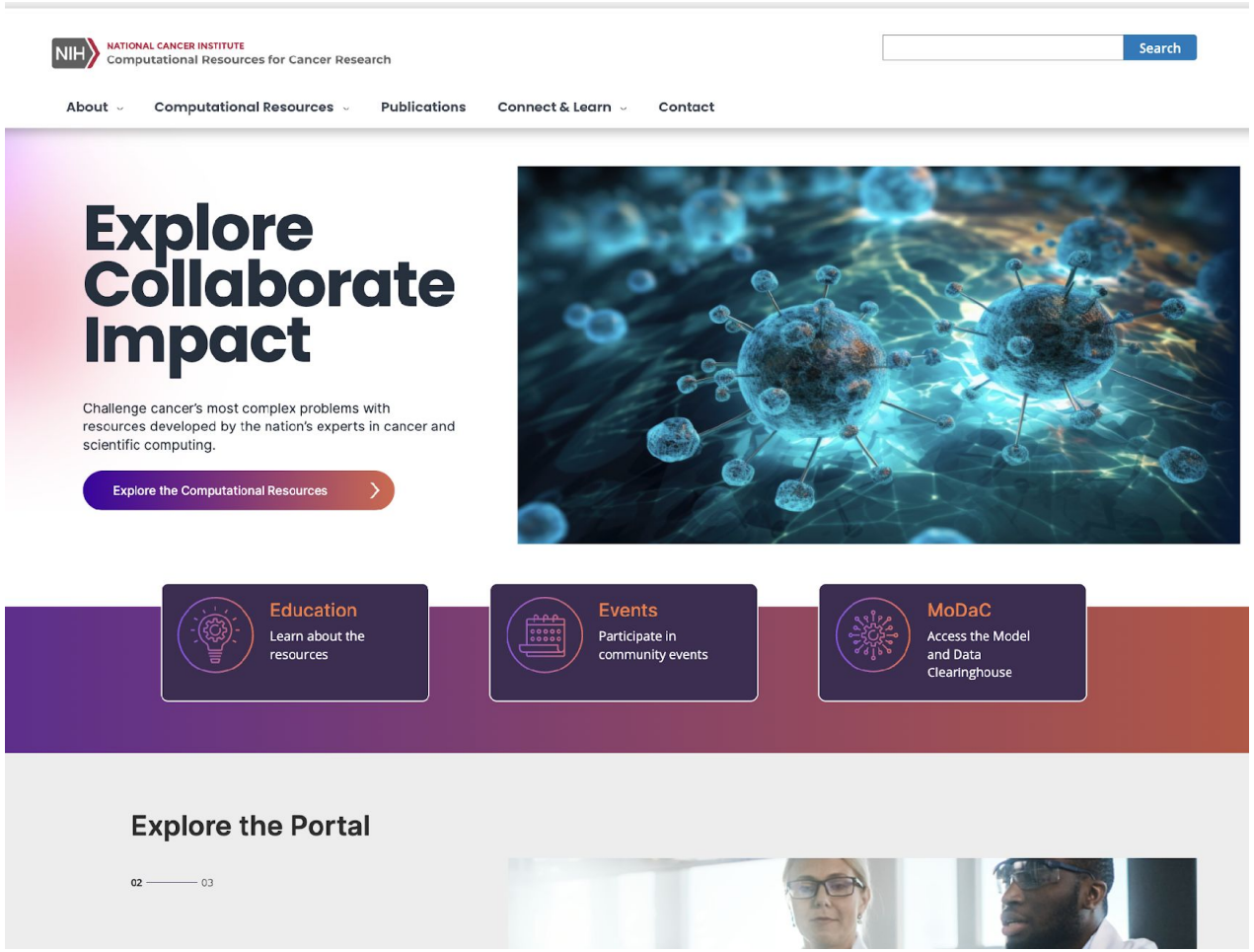


Photo by Joshua Hibbert on Unsplash

modac.cancer.gov

Bringing resources to the community

- **NCI supported computational portal for cancer**
- **Software, Models, Datasets**
  - Referenced and/or downloadable
  - Leverages Predictive Oncology Model and Data Clearinghouse (modac.cancer.gov)
  - Reviewing and characterizing
- **Community Engagement**
  - Broadening user community
  - Use cases
  - Education resources
- **Model runner under development**
- **Visit computational.cancer.gov**



Advancing Medical Digital Twins Globally

Uniting Global Perspectives Around Medical Digital Twins

- Research
- Infrastructure and Industry
- Clinical Translation
- Community Health
- Government
- Global Collaboration

“Individual at the Center”

First Virtual Human Global Summit – October 3-4, 2023

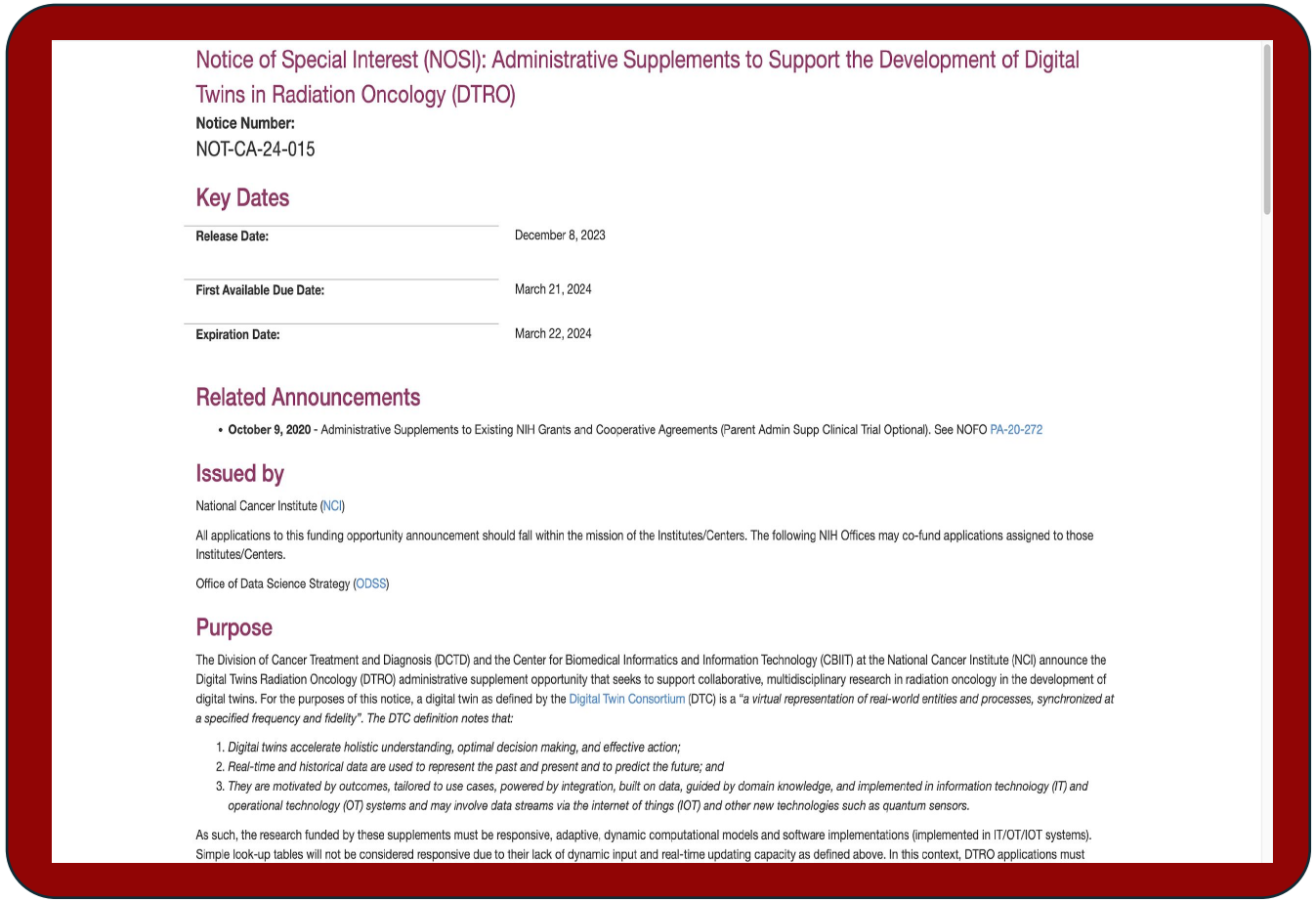
- **Bringing global digital twin communities together from research to patient**
- Over 80 attendees from multiple countries, domains, disciplines, and perspectives
- **Website:** https://www.bnl.gov/virtual-human-global-summit/

Summit report soon to be prereleased on Medrxiv!

First Virtual Human Global Summit – October 3-4, 2023

NCI Support for Medical Digital Twins

- **National Cancer Institute**
- **Administrative supplement**
- **Digital twins advance holistic understanding**
- **Multiscale**
  - Molecular
  - Acellular
  - Cellular
  - Organ
  - Person
  - Society



Notice of Special Interest (NOSI): Administrative Supplements to Support the Development of Digital Twins in Radiation Oncology (DTRO)

Notice Number:
NOT-CA-24-015

Key Dates

Release Date:	December 8, 2023
First Available Due Date:	March 21, 2024
Expiration Date:	March 22, 2024

Related Announcements

- **October 9, 2020** - Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp Clinical Trial Optional). See NOFO PA-20-272

Issued by

National Cancer Institute (NCI)

All applications to this funding opportunity announcement should fall within the mission of the Institutes/Centers. The following NIH Offices may co-fund applications assigned to those Institutes/Centers.

Office of Data Science Strategy (ODSS)

Purpose

The Division of Cancer Treatment and Diagnosis (DCTD) and the Center for Biomedical Informatics and Information Technology (CBIIT) at the National Cancer Institute (NCI) announce the Digital Twins Radiation Oncology (DTRO) administrative supplement opportunity that seeks to support collaborative, multidisciplinary research in radiation oncology in the development of digital twins. For the purposes of this notice, a digital twin as defined by the Digital Twin Consortium (DTC) is a *"a virtual representation of real-world entities and processes, synchronized at a specified frequency and fidelity". The DTC definition notes that:*

1. *Digital twins accelerate holistic understanding, optimal decision making, and effective action;*
2. *Real-time and historical data are used to represent the past and present and to predict the future; and*
3. *They are motivated by outcomes, tailored to use cases, powered by integration, built on data, guided by domain knowledge, and implemented in information technology (IT) and operational technology (OT) systems and may involve data streams via the internet of things (IOT) and other new technologies such as quantum sensors.*

As such, the research funded by these supplements must be responsive, adaptive, dynamic computational models and software implementations (implemented in IT/OT/IOT systems). Simple look-up tables will not be considered responsive due to their lack of dynamic input and real-time updating capacity as defined above. In this context, DTRO applications must

European Support for Medical Digital Twins

European Union
Virtual Human Twin

https://edith-csa.eu

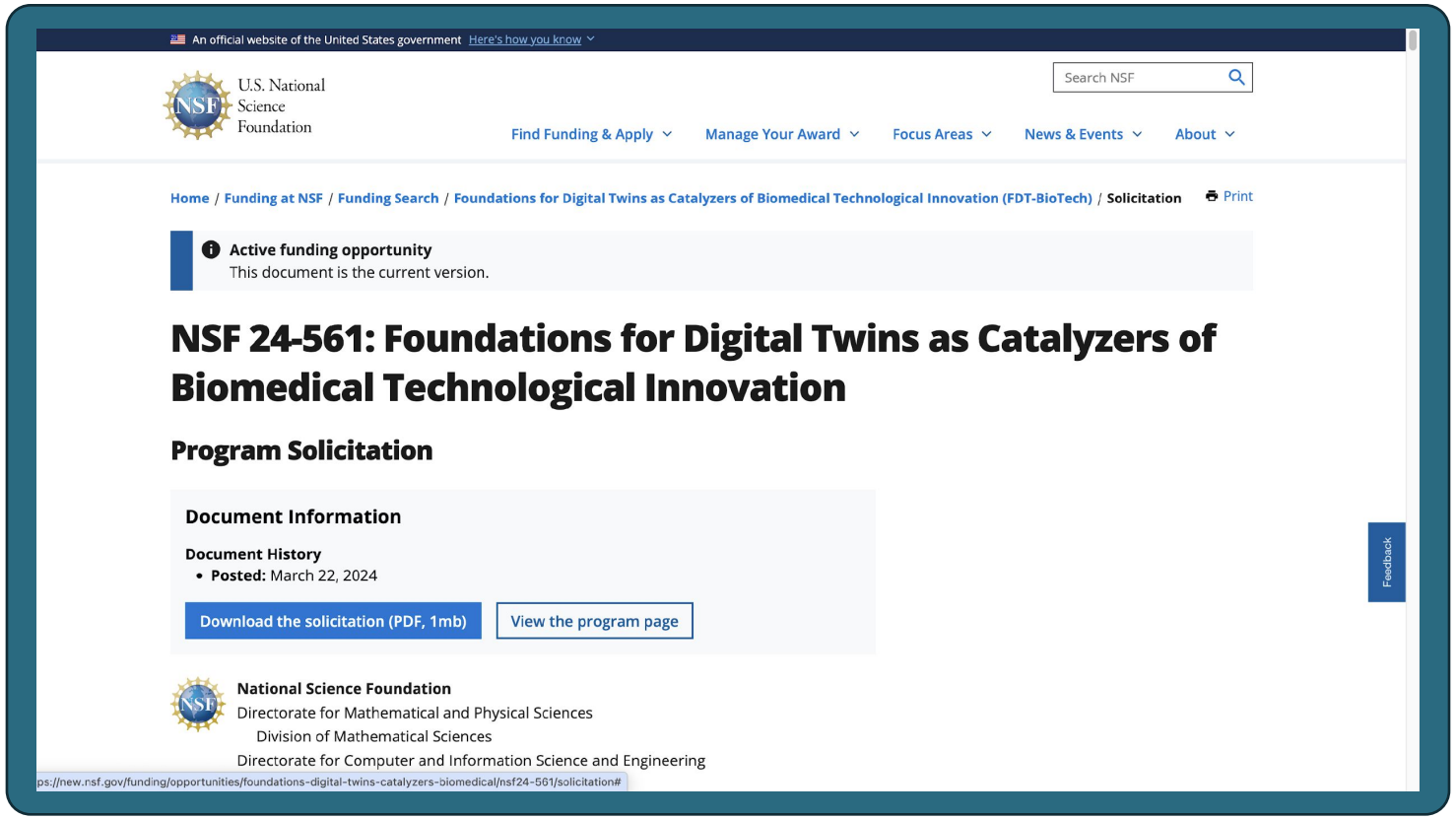
Many collaborators

Roadmap developed –
final meeting last week

Deliverables, brochures,
papers, videos

US Cross Government Medical Digital Twin Efforts

- US Efforts
- Joint solicitation between NSF, NIH and FDA
- Addressing mathematical and engineering foundations for digital twins in biomedical innovation
- Interdisciplinary
- Annual submission



Workshops and Conferences

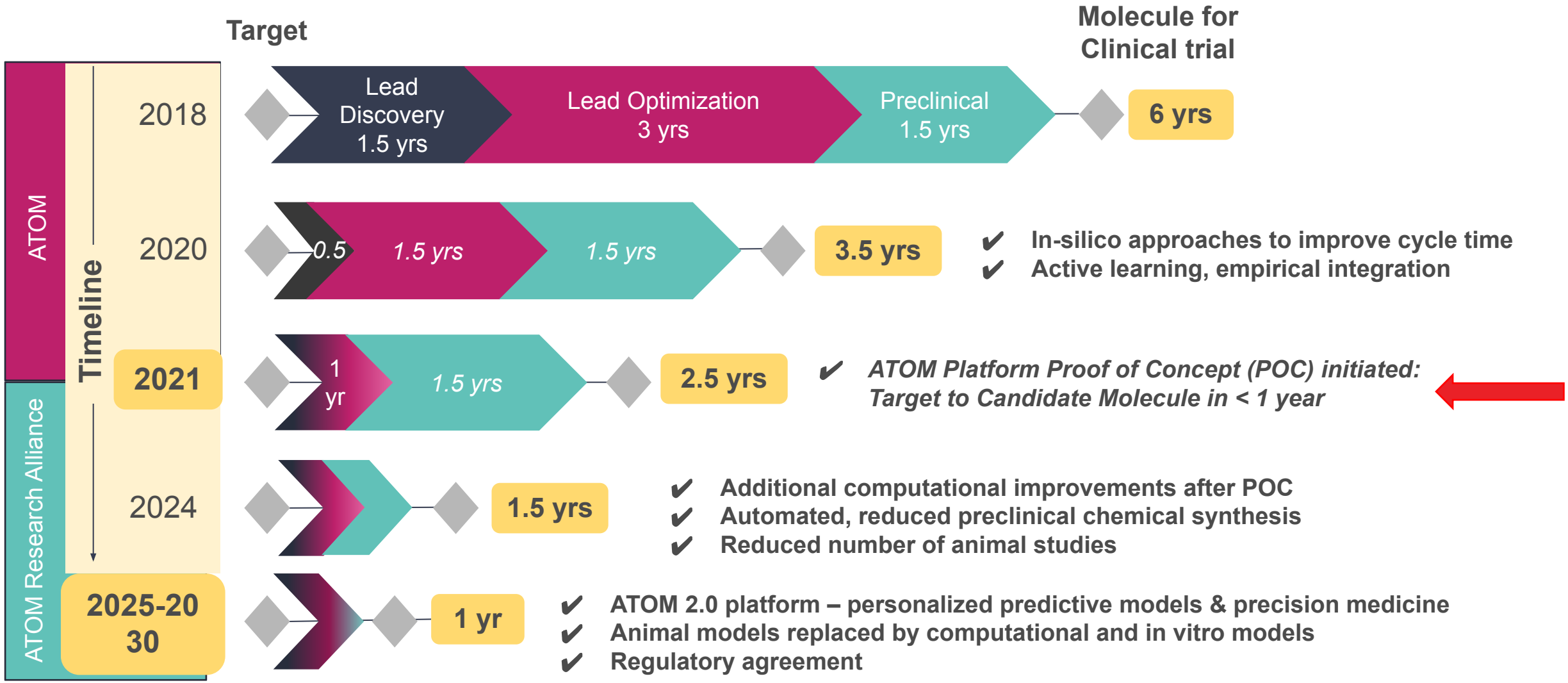
- **Many workshops, meetings and conferences!**
- **NASEM**
  - Public webinars
- **CompBioMed**
- **BioITWorld**
  - Biomedical Digital Twin workshop – Third workshop in 2024
- **Supercomputing**
  - SC24 – Digital Twin Workshop and Computational Approaches for Cancer Workshop
  - Visit sc24.supercomputing.org
- **Meetings**
  - Just search!

Tenth Computational Approaches for Cancer Workshop

Rethinking Drug Discovery

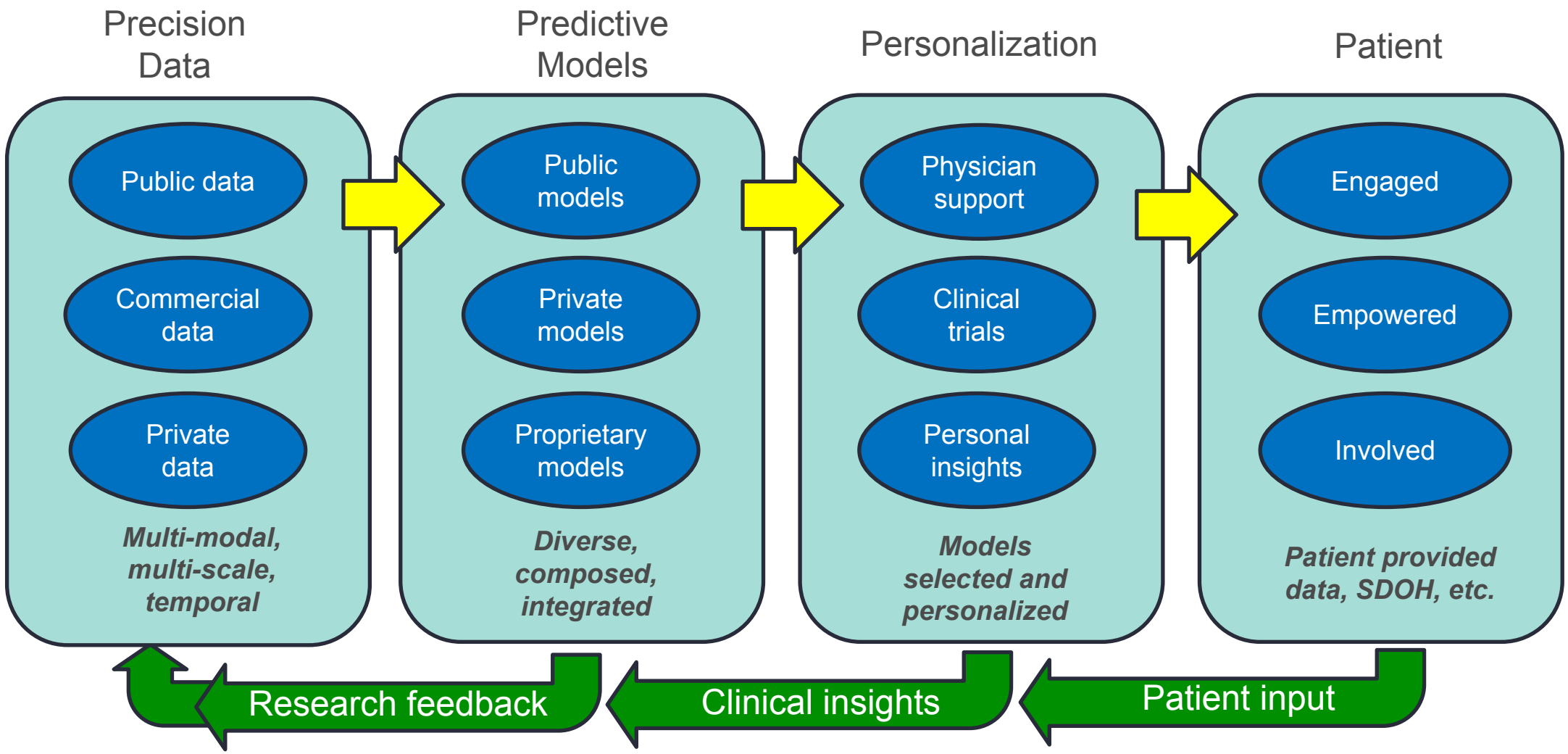
“2017” ATOM target-to-clinical trial roadmap

Active learning approaches to accelerate timeline and reduce experimentation

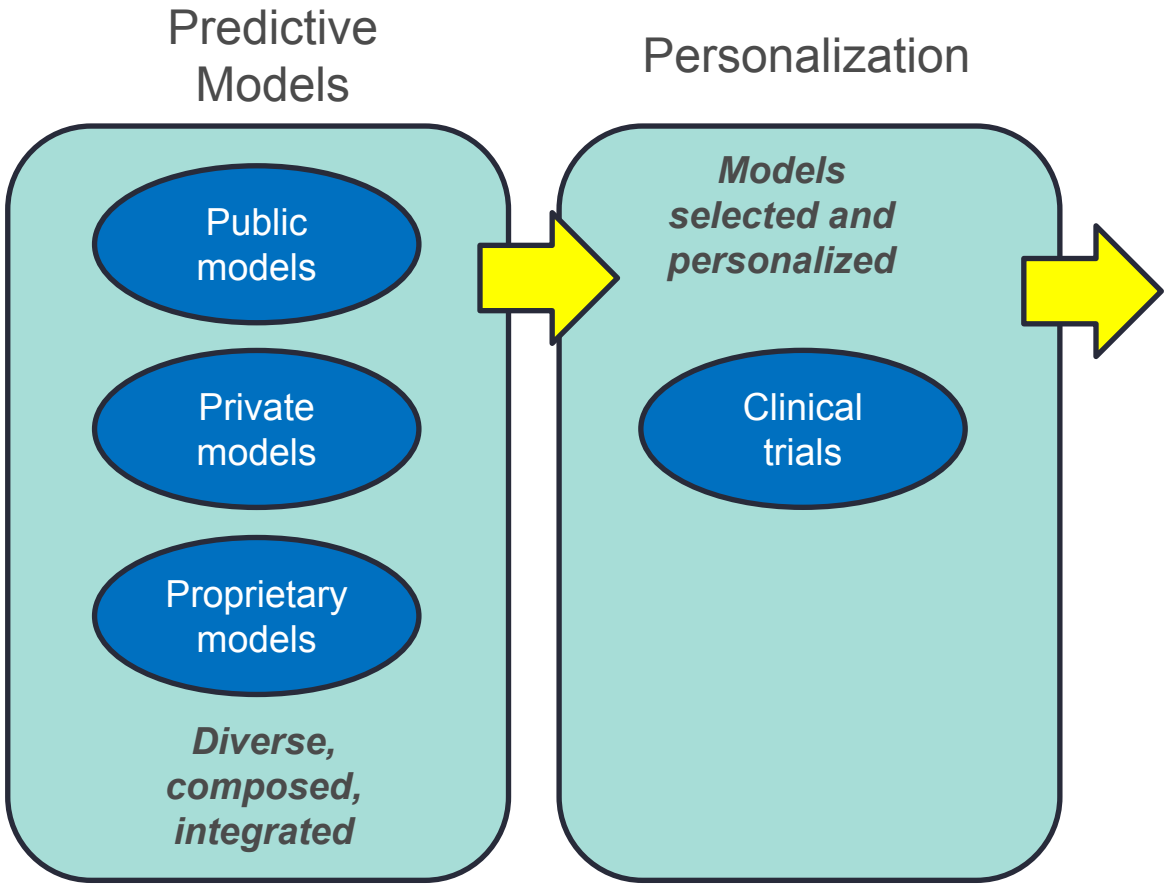


Reaching the Patient to Improve Outcomes

Frederick National Laboratory for Cancer Research

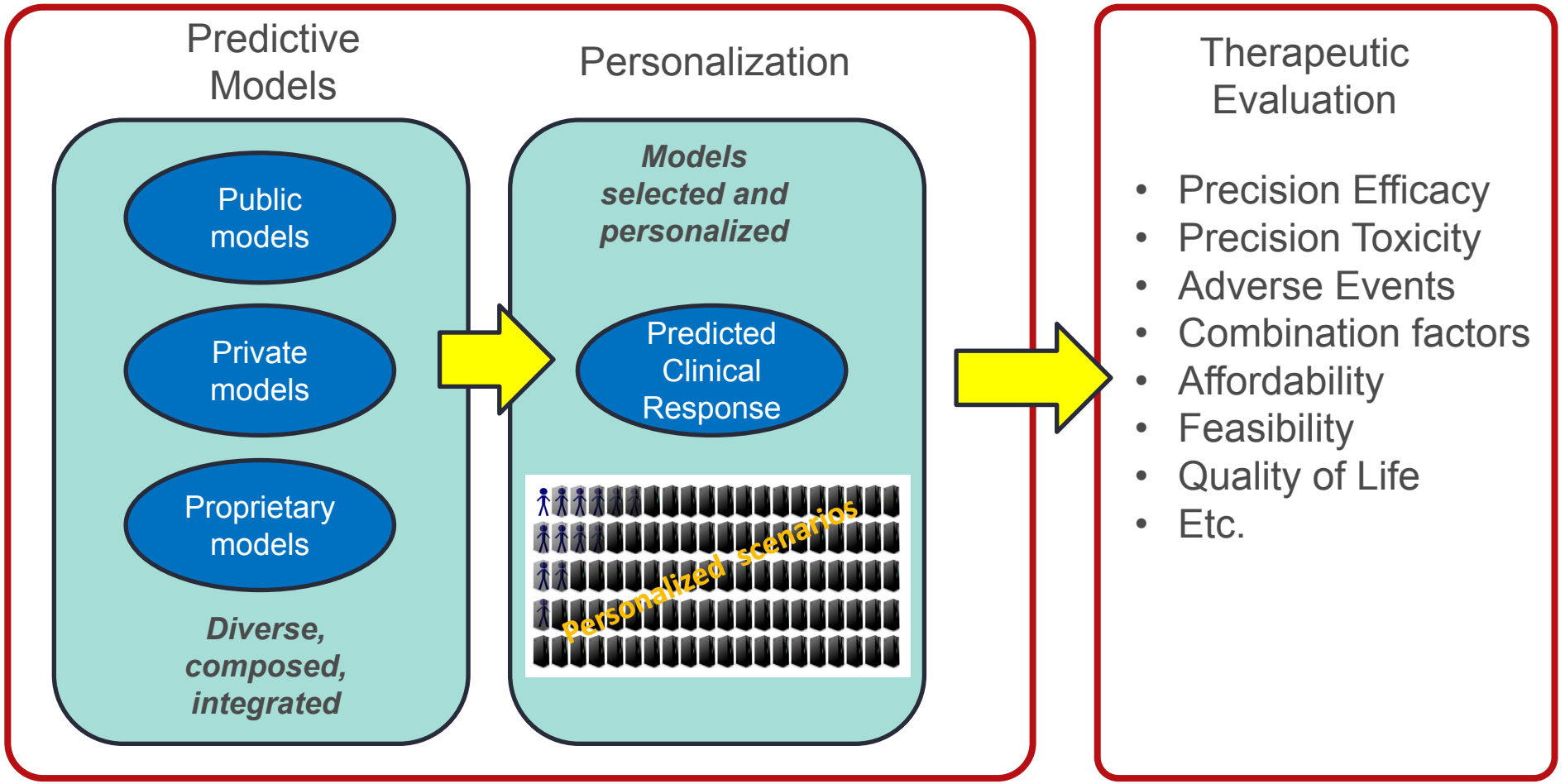


Precision Human Virtual Models



Treatment Optimization with Predictive Clinical Response

Frederick National Laboratory for Cancer Research



Treatment Optimization with Predictive Clinical Response

Frederick National Laboratory for Cancer Research

Generative Approaches
(AI and other methods)

- Small molecules
- Antibodies
- Biologics
- Complexes
- Mixtures
- Formulations
- Dosage
- Sequencing
- Nutritional
- Etc.

Predictive Models

Public models

Private models

Proprietary models

Diverse, composed, integrated

Personalization

Models selected and personalized

Predicted Clinical Response

Therapeutic Evaluation

- Precision Efficacy
- Precision Toxicity
- Adverse Events
- Combination factors
- Affordability
- Feasibility
- Quality of Life
- Etc.

Predicted clinical response feedback

Treatment Optimization with Predictive Clinical Response

Frederick National Laboratory for Cancer Research

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- Feasibility
- Quality of Life
- Etc.

Predicted clinical response feedback

Build the community

Contact Info: Eric.Stahlberg@nih.gov

frederick.cancer.gov

The Frederick National Laboratory for Cancer Research is government owned
and contractor operated on behalf of the National Cancer Institute.