

ARPA-H: The Mission

Advanced Research Projects Agency for Health (ARPA-H)

Tyler Best, Senior Advisor

November 8, 2023

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President Biden's Vision

"ARPA-H will **pursue ideas that break the mold on how we normally support fundamental research and commercial products** in this country."

"Ideas so audacious that people say they just might work only if, only if, we could try. Well, we're about to try in a big way."

– President Biden Remarks, March 18, 2022



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DELIVERING BIPARTISAN PROGRESS

THROUGH PRESIDENT BIDEN'S UNITY AGENDA

- ✓ Made it easier for doctors to prescribe effective treatments for opioid addiction
- ✓ Passed a gun safety law making historic investments in youth mental health
- ✓ Launched ARPA-H to drive breakthroughs in the fight against cancer, Alzheimer's, and diabetes
- ✓ Expanded benefits and services for veterans and their survivors

WH.GOV/SOTU

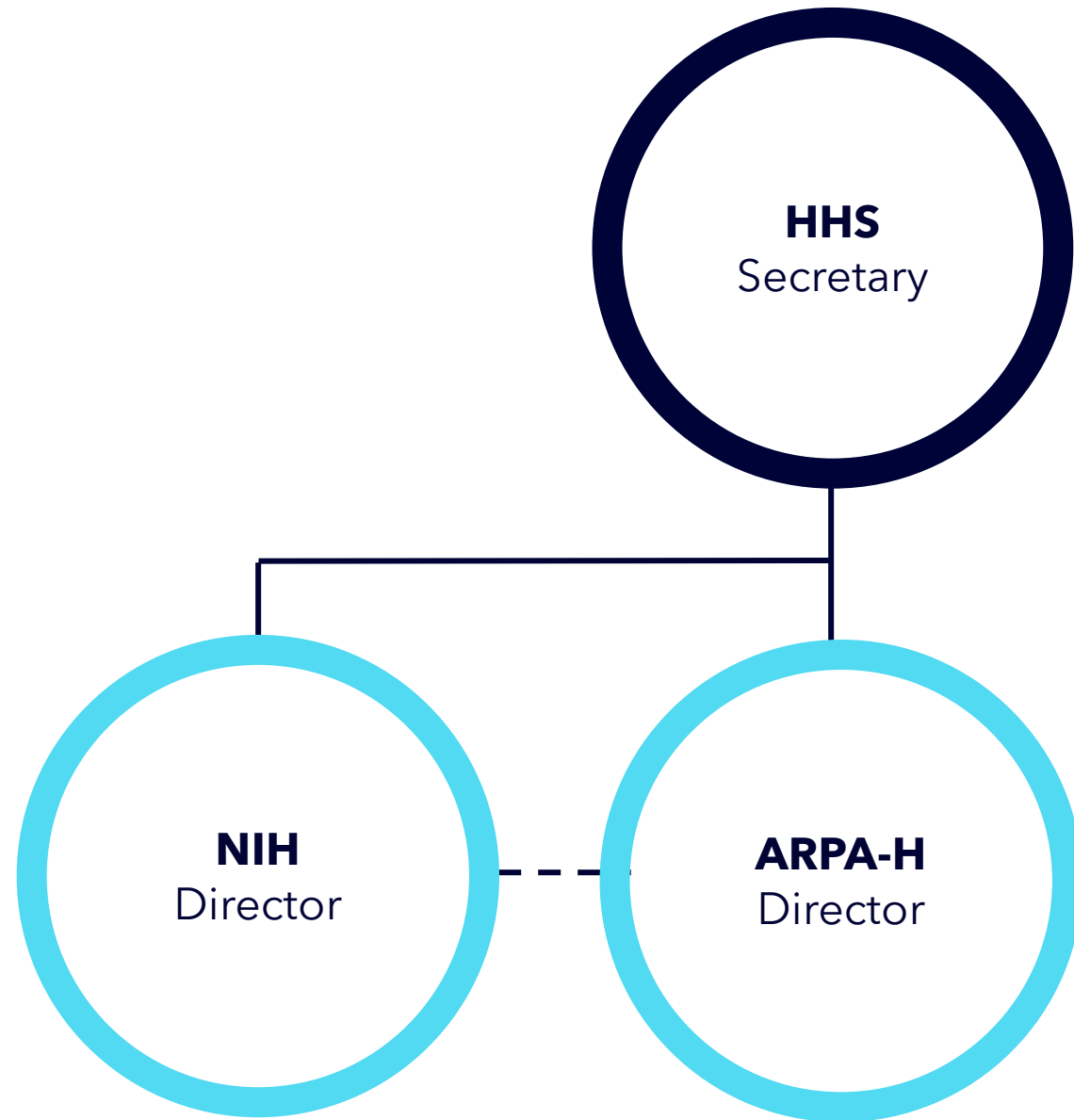
Mission

Accelerate better
health outcomes
for everyone.

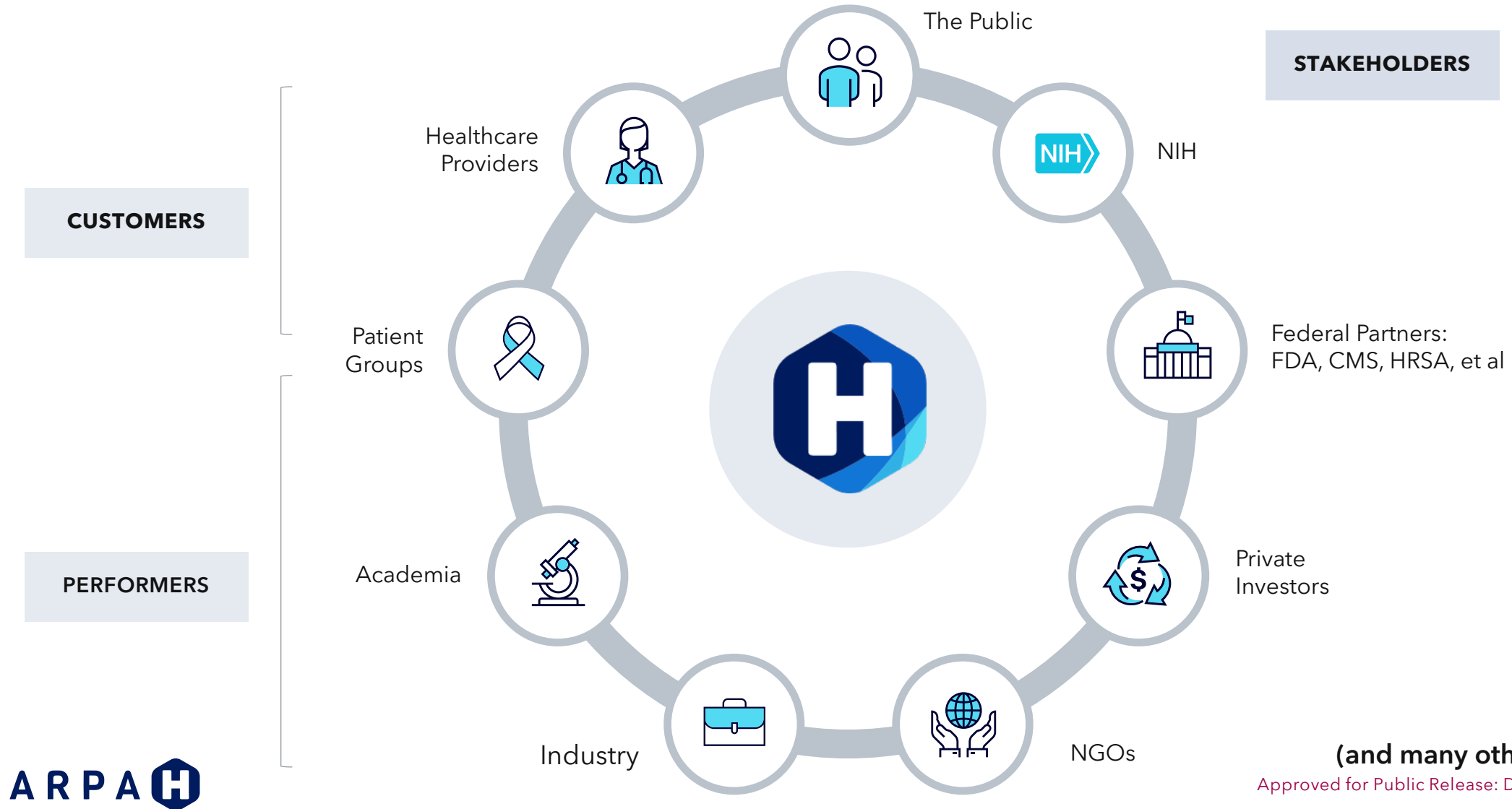


ARPA-H Organization within HHS

- Independent component of HHS within NIH; not an Institute
- ARPA-H Director reports directly to HHS Secretary
- No internal research labs; disease agnostic
- \$2.5B initial appropriation; budget independent from NIH
- Generally funds contracts, not grants
- Ability to directly reimburse other Federal agencies

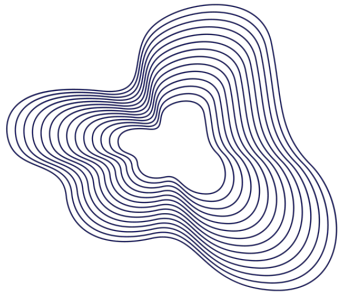


ARPA-H Accelerates the Entire Health Ecosystem



Initial Mission Focus Areas

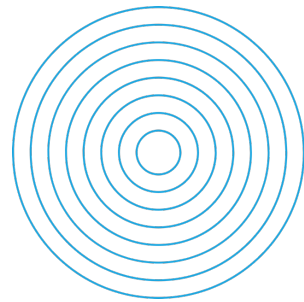
Further ARPA-H investment in these areas will generate **asymmetrical benefits** to the health ecosystem



Health Science Futures

Expanding what's technically possible

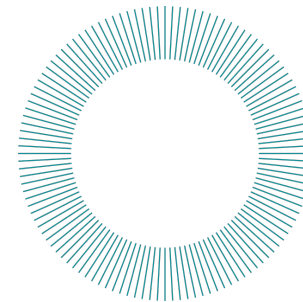
Accelerate advances across research areas and remove limitations that stymie progress towards solutions. These tools and platforms apply to a broad range of diseases.



Scalable Solutions

Reaching everyone quickly

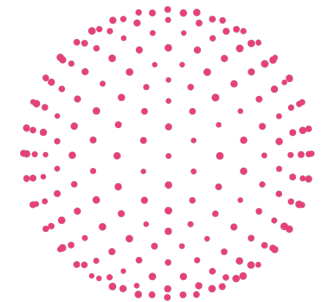
Address health challenges that include geography, distribution, manufacturing, data and information, and economies of scale to create programs that result in impactful, timely, and equitable solutions.



Proactive Health

Keeping people from being patients

Preventative programs will create new capabilities to detect and characterize disease risk and promote treatments and behaviors to anticipate threats to Americans' health, whether those are viral, bacterial, chemical, physical, or psychological.

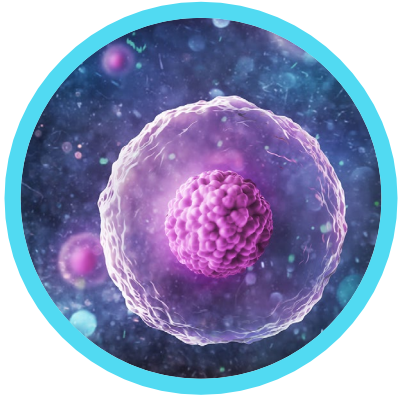


Resilient Systems

Building integrated healthcare systems

Create capabilities, business models, and integrations to weather crises such as pandemics, social disruption, climate change, and economic instability. Systems are sustained between crises—from the molecular to the societal—to achieve better health outcomes.

Organizational Attributes that Support the Mission



Problem-focused Program Managers

Facilitating the Future

PMs are the nucleus of the organization, and their energy and passion drive the mission.

PMs are responsible for the full program lifecycle, from new problem formulation to transition of capability out of ARPA-H

PMs are supported from Day 1 with a business operations team to support their R&D agenda, including a creative contracting team.



Radical Change

Evolutionary proposers need not apply

ARPA-H investments should seek to address seemingly impossible barriers in demonstrating “proof of concept” for solutions to major challenges—not incremental advances.

Projects should be high-risk, high-payoff, with the most forward-looking science and technology.

Seek innovation at “convincing scale”.



Autonomy

PMs are empowered to assume (and mitigate) program risk

PMs practice “full contact” management to maintain vision and deliver results, with metrics/ milestones for program, empowered to stop underperforming projects.

PMs manage multiple programs, including programs they inherit from departing PMs.

Workshops, consultations, seedlings are encouraged, but no advisory committees or study sections.



Term limits

A transactional projects agency

Terms limited to 3 years (renewable once for 6 total years) for PMs, Office Directors, and Deputy Directors, allowing inflow of new ideas.

Limits create urgency and focus on impact and outcomes for R&D, and execution speed for contracts.

Limits remove incentives for empires, organization-building, span of control, bureaucracy, etc.



Program Managers

What are the phenotypes?

Uncommon people with common traits
"Think Like a CEO"

Recognized
Expertise

Serious Drive

Insatiable Curiosity

No Fear of Failure

Interdisciplinary
Track Record

Technical Honesty

Decisive

Customer-Centric



Different Approaches and Career Stage

The Problem Solver

Motivated by personal experience; can't let it go.

The Rookie

Early career. Unbiased, looks at the world with fresh eyes.

The Dreamer

Intensely curious about how the world works, motivated by search for objective facts/truth.

The Status Quo Challenger

Mid-career. Frustrated by the limits of the existing system.

The Sprinter-Tinkerer

Intrinsic desire to build and experiment and quickly iterate to achieve path to market. Cares about application, not theory.

The Sage

Late career. Experience yields deep understanding.



ARPA-(H)eilmeier Questions

Towards a well-defined problem

- 1 What are you trying to do? What health problem are you trying to solve?
- 2 How does this get done at present? Who does it? What are the limitations of present approaches?
- 3 What is new about our approach? Why do we think we can be successful at this time?
- 4 Who cares? If we succeed, what difference will it make? What Health Outcomes are we accelerating?
- 5 What are the risks? That may prevent you from reaching your objectives? Any risks the program itself may present?
- 6 How long will the program take?
- 7 How much will the program cost?
- 8 What are our mid-term and final exams to check for success?
- 9 To ensure equitable access for all people, how will cost, accessibility, and user experience be addressed?
- 10 How might this program be misperceived or misused (and how can we build trust and prevent that from happening)?

ARPA-H Model: Program Formation

Program Manager

Program Manager identifies a difficult health-related challenge that is ripe for solving.

Challenge

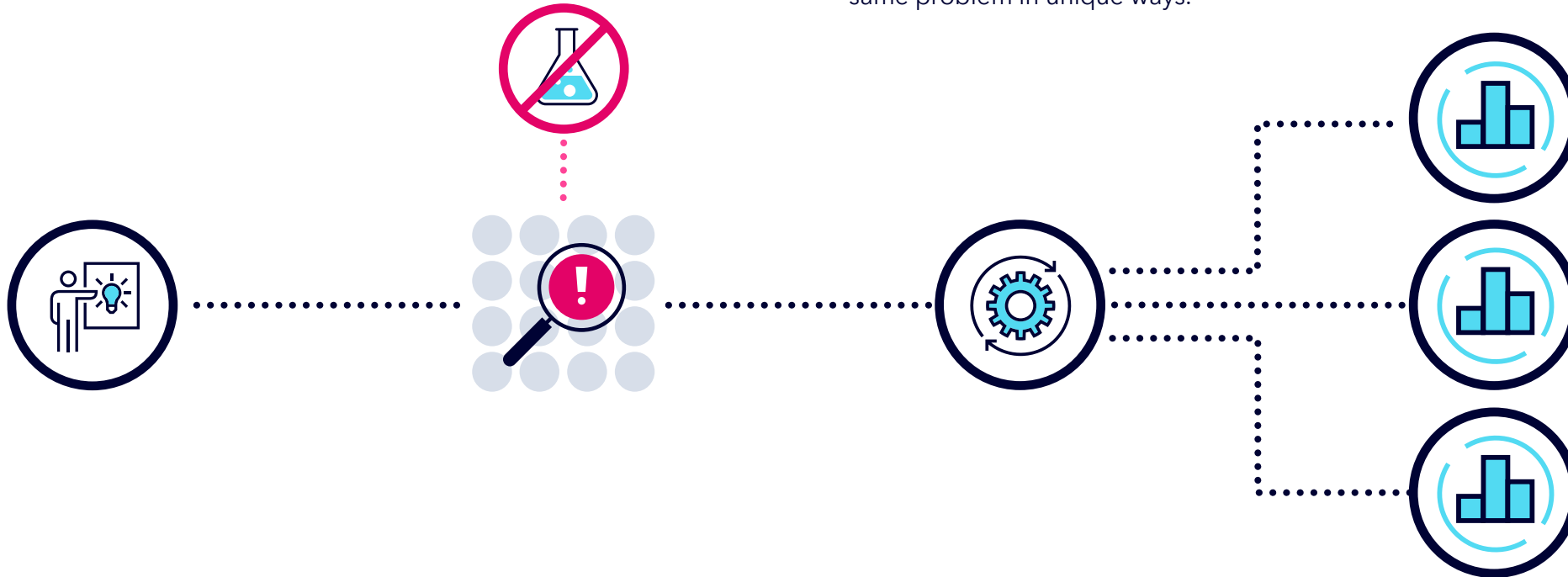
The challenge should NOT be easily solvable through traditional activities.

Program Launch

A Program Manager seeks – and oversees – several groups of performers aiming to solve the same problem in unique ways.

Performers

Performers compete to carry out their potential innovative solutions to the challenge

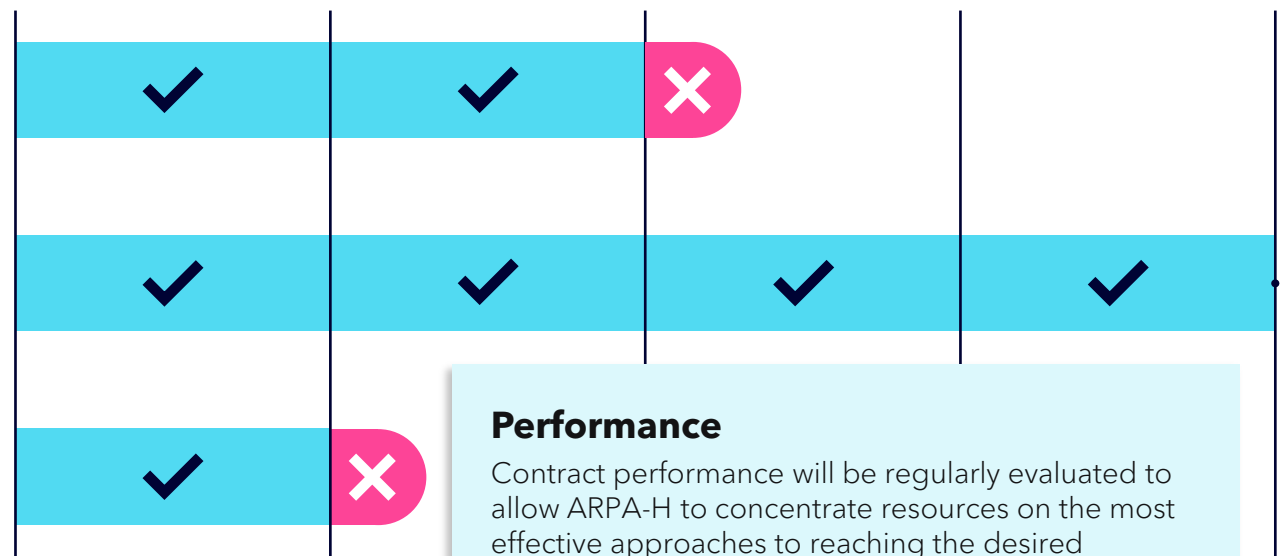


ARPA-H Model: Support and Evaluation



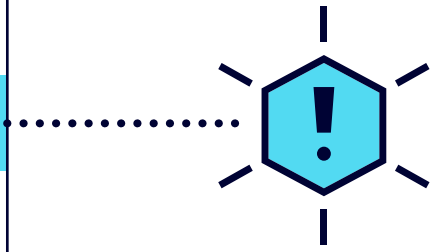
Support

ARPA-H will provide contracts – not grants – for projects with well-defined endpoints. Additional support will be provided by Program Managers, partners, and ARPA-H offices to ensure the best chance of success throughout the process.



Performance

Contract performance will be regularly evaluated to allow ARPA-H to concentrate resources on the most effective approaches to reaching the desired goals. Valuable lessons are learned and shared from each project.



Engage with ARPA-H



Submit your Project Idea

Calling for proposals to outline breakthrough research and technological advancements to improve health outcomes across patient populations, communities, diseases, and health conditions



Become a Program Manager

ARPA-H is seeking to hire Program Managers that will bring well-defined problems to ARPA-H and build the teams to solve them.



Collaborate with Us

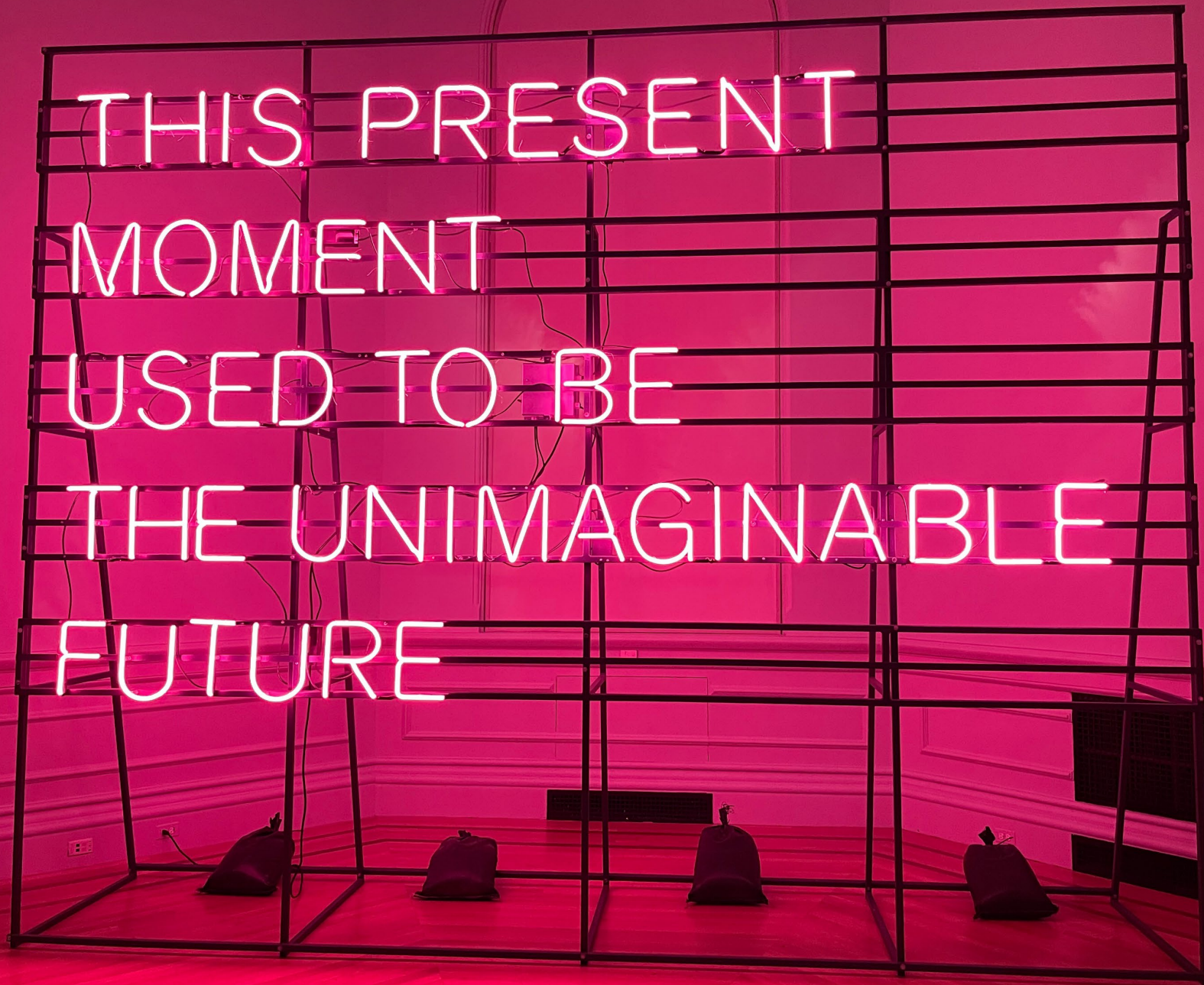
We want to partner with State and Federal governments, community health centers, patients, caregivers, patient advocate groups to ensure we are delivering on our mission

Keep Up to date with the ARPA-H
Vitals Biweekly Newsletter





@ARPA_H



Alicia Eggert
This Present Moment
2019 - 2020
Currently @ The Renwick Gallery
Washington, DC

Project Accelerator Transition Innovation Office (PATIO)

Increase the probability—at each step—that solutions can survive in the wild

Program Lifecycle



Program Design

- Support PMs to find opportunities and gaps
- Market assessment
- Human-centric design



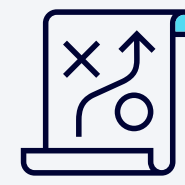
BAA Development

- Who are possible performers? Innovation Hubs?
- VC style due-diligence
- Validate transition potential



Early Program Performance

- De-risk for investors
- Design MVPs to drive adoption
- Demystify regulatory process



Mature Projects

- How to protect IP?
- Help company formation
- Business strategy, legal and marketing services



Transition/Outputs Survive in the Wild

- SBIR/STTR
- Transition partner/ Third-party investment
- Ongoing mentorship
- Access to key customers and investors

Antigens Predicted for Broad Viral Efficacy through Computational Experimentation (APECx)



Dr. Andy Kilianski,
Program Manager



Proposers' Day:

November 17, 2023

Visit the QR link to sign up
and learn more

Vision: Develop the toolkit that makes broadly effective and evolution-resistant vaccines against viral pathogens possible for all.

Approach: Harness cutting-edge computational methods alongside unprecedented scales of biochemical and immunological data.

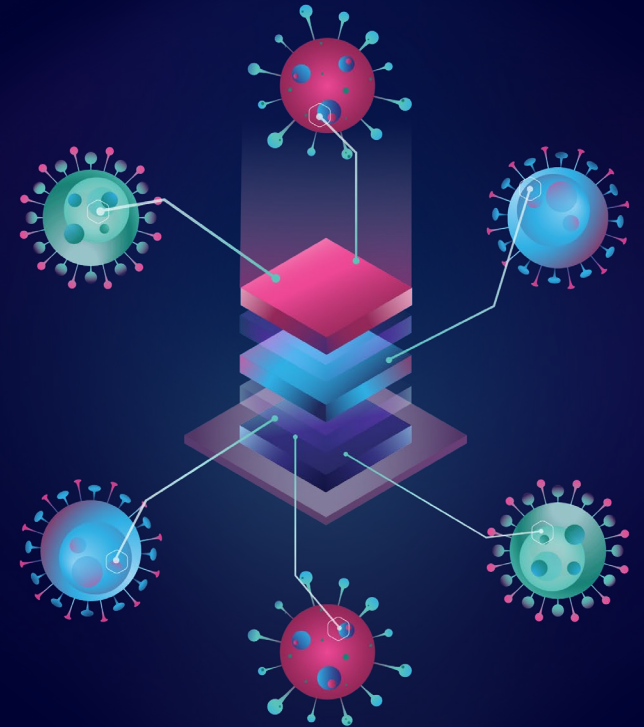
Why ARPA-H? Create a fast-track vaccine development pipeline that'll neutralize whole classes of viruses using groundbreaking tools not yet to be applied in vaccine R&D.

Technology Focus Areas

1. High-throughput biochemical analysis and protein function engineering
2. Antigen design and modeling pipelines for vaccine development
3. Proof-of-concept translational candidate development and clinical trials



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**What if we could eliminate viruses as
current and future health threats?**

Resilient, Extended, and Automated Cellular Therapies (REACT)



**Dr. Paul Sheehan,
Program Manager**

Link to
REACT
webpage



Vision: Develop a platform that enables patients to easily manage chronic diseases: an implanted Living Pharmacy, controlled by the patient, would automatically produce therapies long-term; an implanted Living Sentinel would inform the patient of the state of their disease

Technology focus areas:

- Resilient cellular factories that produce therapy on demand from inside the body
- Bioelectronic devices to control the cellular factories
- Sentinel cells that track hormones or cytokines
- Improved encapsulation to protect the device from the immune system

How to apply:

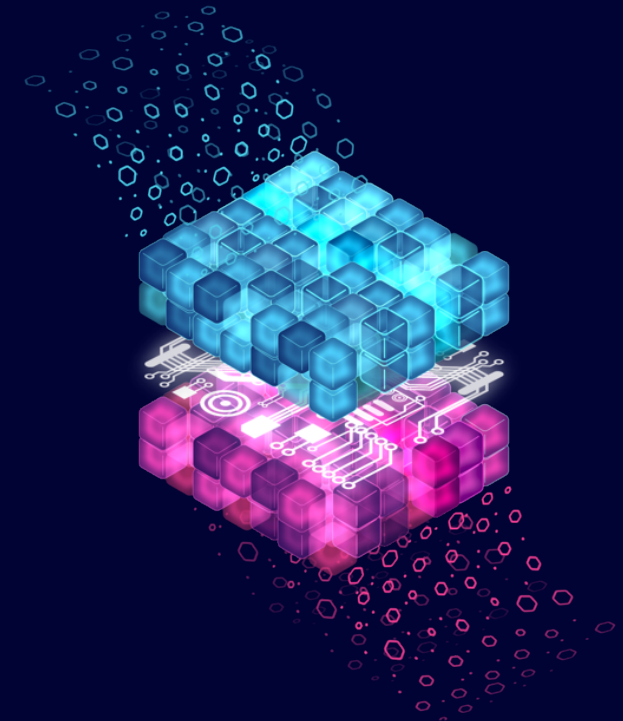
- Stay tuned for the solicitation; submit abstract and, if invited, full proposal
- Visit our program website to register for Proposers' Day and to learn more about REACT

Important dates:

- **November 16, 2023:**
Proposers' Day
- **November 30, 2023:**
Abstracts due



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**What if your body could make its
own medicine?**

ARPA-H Key Features and Authorities

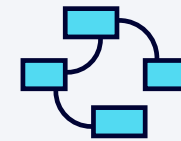
ARPA-H has unique structures and legal authorities that allow it to **function like a business – quickly, nimbly, and decisively.**



Bottom-up decision-making. PMs have autonomy to make decisions quickly.
ARPA-H is a problems focused organization



Accelerated contracting mechanisms that allow ARPA-H to quickly go from approval to contract; generally fund contracts, not grants.

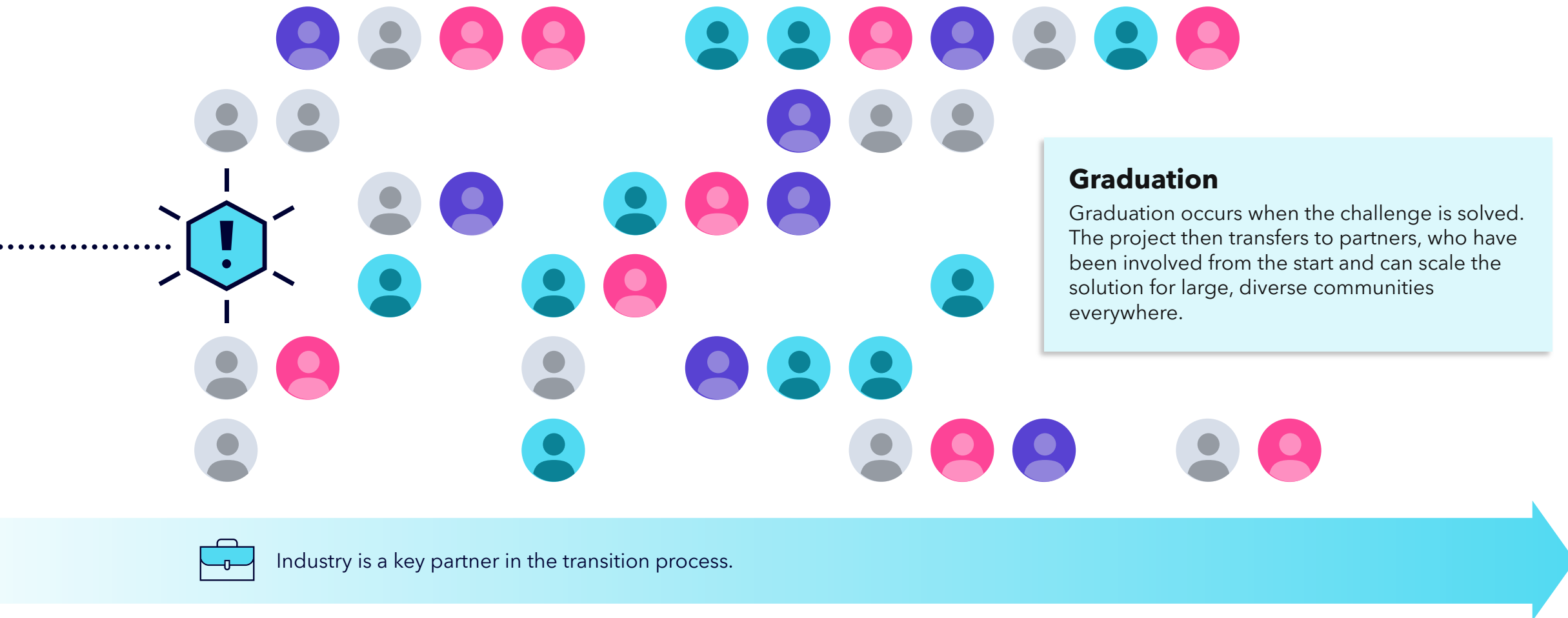


Lean and nimble management structure with autonomy in decision-making.



Flexibility in hiring that allows ARPA-H to compensate top performers at levels competitive with industry.

ARPA-H Model: Transition



New Open BAA Awards



CUREIT

Curing the Uncurable via RNA-Encoded Immunogene Tuning

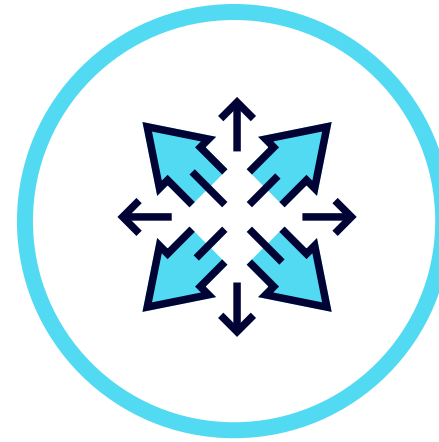
What if incurable, debilitating diseases could be easily treated through mRNA-encoded therapies that tune your immune system?



HEART

Health Enabling Advancements through Regenerative Tissue Printing

What if we could 3D print a human heart in an hour?



CDTR

Stem Cell-Derived Thymus Rejuvenation

What if thymus function and immunity could be restored by a simple injection?

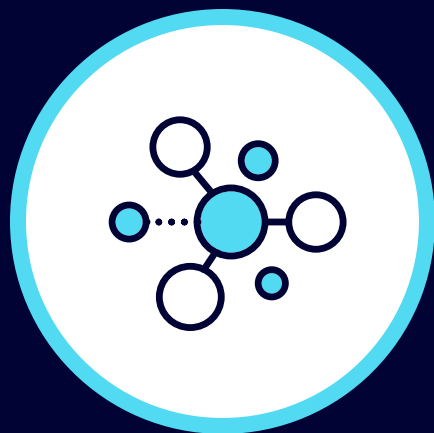


DARTS

Defeating Antibiotic Resistance through Transformative Solutions

What if we could identify antibiotic-resistant bacteria in minutes?

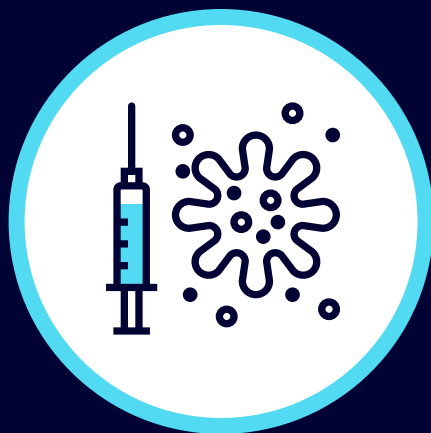
Recent Announcements on ARPA-H Cancer Efforts



THOR

Targeted Hybrid Oncotherapeutic Regulation

What if we could boost therapy response rates to peritoneal or solid tumor malignancies from 10% to 50%?



SPIKEs

Synthetic Programable bacteria for Immune-directed Killing in tumor Environments

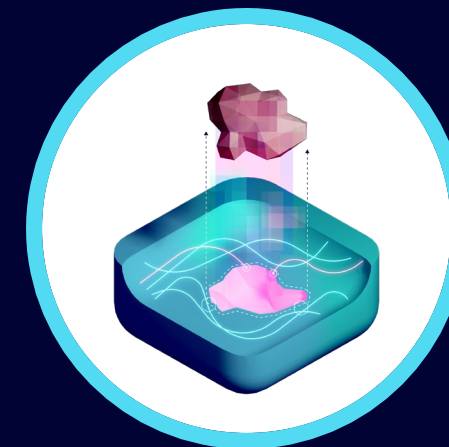
What if programable bacteria could be directed to kill cancer inside the body?



CODA

Cancer and Organ Degradome Atlas

What if a single system could detect a broad range of cancers at the earliest stages of formation?



PSI

Precision Surgical Interventions

What if surgeries fixed problems flawlessly, the first time?

Curing the Uncurable via RNA-Encoded Immunogene Tuning (CUREIT)

Vision: Develop molecular tools capable of reprogramming immune function to address a breadth of currently incurable diseases including cancer, autoimmunity, transplantation rejection, and infection by resolving incomplete or ineffective immune responses to disease.

Technology focus areas

- mRNA-LNP based targeted therapeutics
- Autologous engineered immune cell therapies
- Proofs of concept for cancer, autoimmunity, and infectious disease

Why ARPA-H? Unlike vaccines which *indirectly* stimulate your immune system, this effort *directly* regulates your immune system in a tunable way, dialing the response up or down in a controlled and targeted manner

Performer Team

Prime: Emory University

- PI: Dr. Philip J Santangelo

Subcontractor Teams:

- Yale University
- TransImmune
- University of Georgia



Important Dates

- **Project Approved:** June 6, 2023
- **Selection notification and contract negotiations:** June 8, 2023
- **Awarded:** August 23, 2023

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What if incurable, debilitating diseases could be easily treated through mRNA-encoded therapies that tune your immune system?

DARTS

Defeating Antibiotic Resistance through Transformative Solutions

Project Goal: This effort will build on an ultra-high throughput imaging and culturing system that can track billions of bacteria one-by-one. The platform will be advanced to identify those rare bacteria, the persister bacteria, that lead to antimicrobial resistance (AMR) and so reveal the basis for their recalcitrance. The effort will also identify novel antibiotic peptides, rapidly optimizing them for commercialization. The final goal will be a portable device that identifies an infection's antibiotic susceptibility *before the patient leaves the clinic*, ending the mis-prescription of antibiotics.

Technology focus areas

- Optics and microfluidics
- Rapid antimicrobial susceptibility testing
- Antibiotic discovery optimization

To learn more:

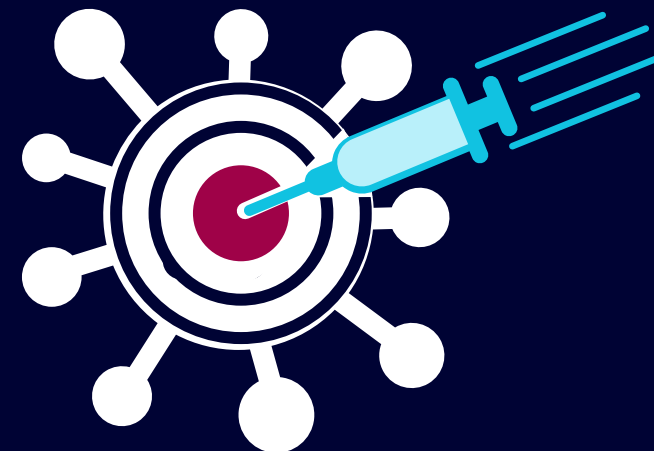
Visit arpa-h.gov for more information about DARTS or email at DARTS@arpa-h.gov

Important dates

The Kickoff date for interested stakeholders is scheduled for **October 17, 2023**



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What if we could identify
antibiotic-resistant bacteria
in minutes?

HEART

Health Enabling Advancements through Regenerative Tissue Printing - 3D printing a human heart

Project Goal: *Additively manufacture a functioning human heart in one hour.*
The effort will integrate automated, organ-scale biomanufacturing, entirely new and rapid 3D collaborative printing robots, and continuous layer-free bioprinters for the rapid-production of complex tissue models, beginning the era of rapid organ biofabrication.

Technology focus areas

- Cell engineering and scalability
- 3D printing technological advances
- Vasculature printing
- Organ maturation strategies

To learn more:

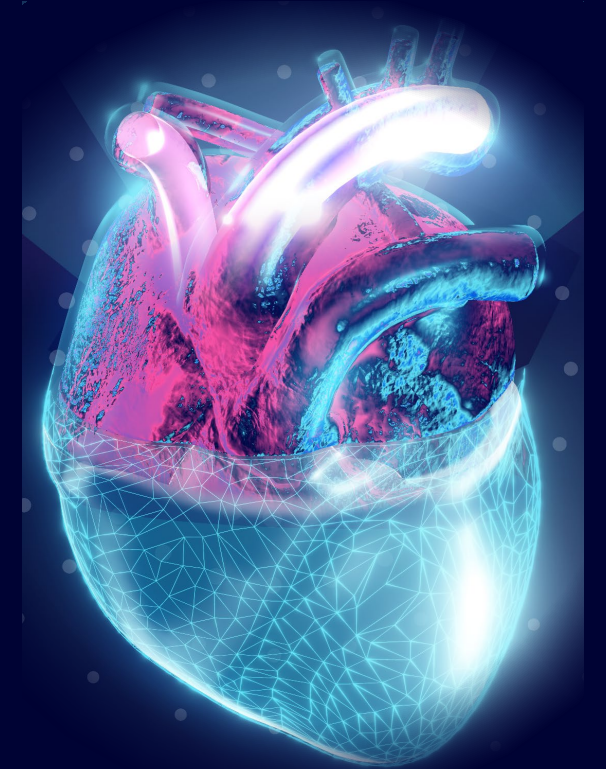
Visit **arpa-h.gov** for more information
about HEART or email at
HEART@arpa-h.gov

Important dates

The Kickoff date for interested
stakeholders is scheduled for
September 26, 2023



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What if we could 3D print
a human heart in an hour?

CDTR

Stem Cell-Derived Thymus Rejuvenation

Project Goal: To treat or cure patients lacking a fully functional thymus from morbidity and mortality and addresses a crucial unmet need to rejuvenate immunity in the aging population by engineered stem-cell treatment.

Technology focus areas

- Develop best in class human induced pluripotent stem thymic epithelial cells (iPS-TECs) using combination of chemical and genetic factors to support T-lymphocytes (white blood cells) development in vitro
- Provide proof of concept for transplantation and long-term engraftment of iPS-TEC in animal models to achieve effective immune function.
- Ultimately deliver a revolutionary, disease-agnostic platform to combat thymus dysfunction by bolstering immune responses against pathogens, cancer, and vaccines.

Performer Team

- Prime: Thymune Therapeutics
- Location: Cambridge, MA
- PI(s): Bing Lim, M.D., PhD. and Stan Wang, MD, PhD

Important Dates

- **Award Date:** September 25, 2023



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What if thymus function and immunity could be restored by a simple injection?

Novel Innovations for Tissue Regeneration in Osteoarthritis (NITRO)

Vision: To eradicate OA through targeted, regenerative therapeutics that will revolutionize the care algorithm, prevent pain, decrease the economic burden, and eliminate the need for repeat joint surgery.

Technology focus areas

- Needle-based and/or non-invasive bone regeneration
- Needle-based and/or non-invasive cartilage regeneration
- Replacement joints built from human cells

Equitable Access

- 1st clinical trials that match the national demographics of the disease
- Equity Officers (EOs) per team TBA.
- >5 demo-specific listening sessions.
- Road Map to Equity (RME), Insurance Action Plan (IAP), and Equity Symposium per team

To learn more:

Visit arpa-h.gov for more information about NITRO or email at NITRO@arpa-h.gov

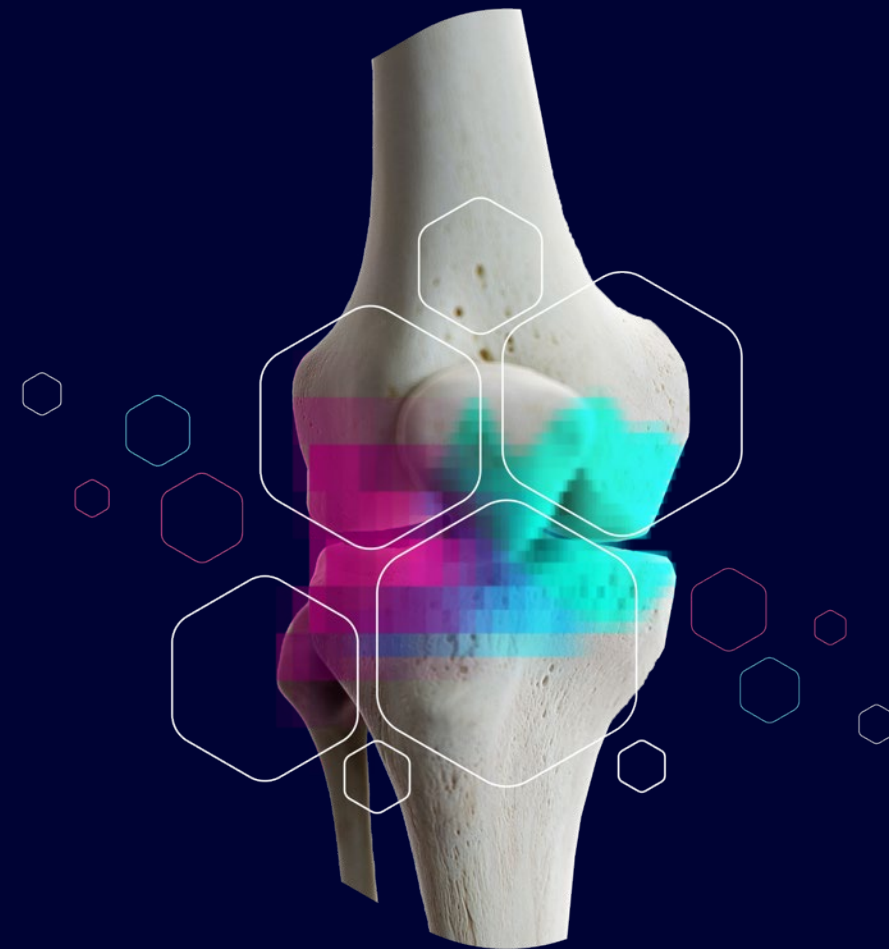


Important dates

SRO is scheduled for
October 19, 2023



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What if we could make our joints
heal themselves?

Precision Surgical Interventions (PSI)

Vision: Develop technology to significantly decrease reoperations in oncological surgery and to ensure critical anatomical structures such as nerves, lymph ducts, and glands are not inadvertently injured during surgery.

Technology focus areas

- Devices, dyes, and algorithms to assess tumor edges during surgery, at the bedside or *in vivo*
- Devices, dyes and algorithms to visualize critical anatomical structures during surgery

How to apply

- View the BAA at <https://sam.gov/opp/5f30e440824a4c1493e0008fa6ab8bd3/view>
- Visit our program website at arpa-h.gov/engage/programs/psi/ to register for Proposers' Day and learn more about PSI

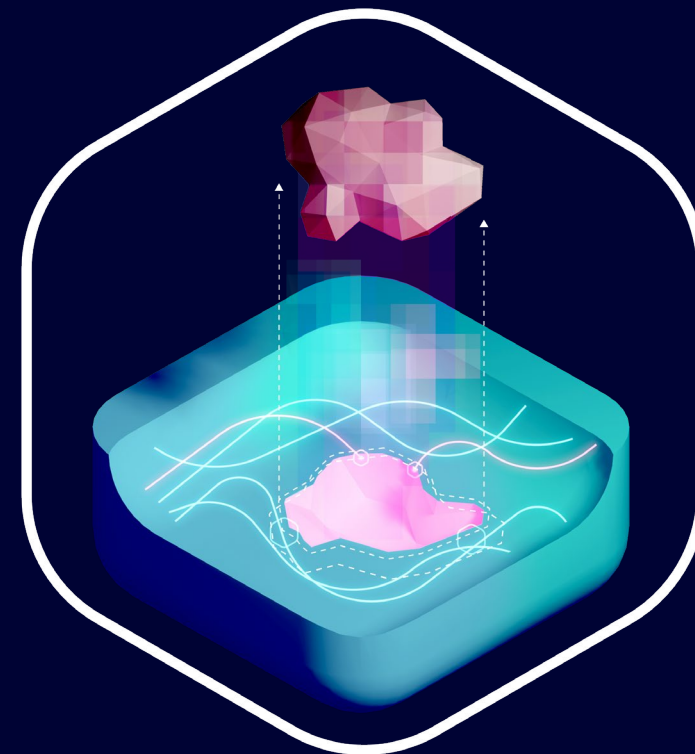
Important Dates

- **August 21, 2023:** BAA Live on SAM.gov
- **September 7, 2023:** Proposers Day event in Chicago
- **September 21, 2023:** Abstracts due

Link to PSI
Special Notice
on SAM.gov



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What if surgeries fixed problems
flawlessly, the first time?

DIGIHEALS (Digital Healthcare Security)

Vision: Advance digital health security, software assurance, and software usability technologies to address weaknesses (e.g., prevent ransomware attacks) in current U.S. healthcare infrastructure to increase system resiliency and improve the quality of care rendered to patients.

Technology focus areas

- Automated vulnerability discovery
- Large-scale testing of device and system interactions
- Secure-by-design implementations of common data formats and protocols

Approach

- Adapt novel research from non-traditional cybersecurity performers to healthcare
- Iterate rapidly to identify promising areas for further investment
- Develop transition strategies to ensure equitable impact

Important Dates

- **Aug 4, 2023** - BAA release
- **Sep 7, 2023** - Proposals due

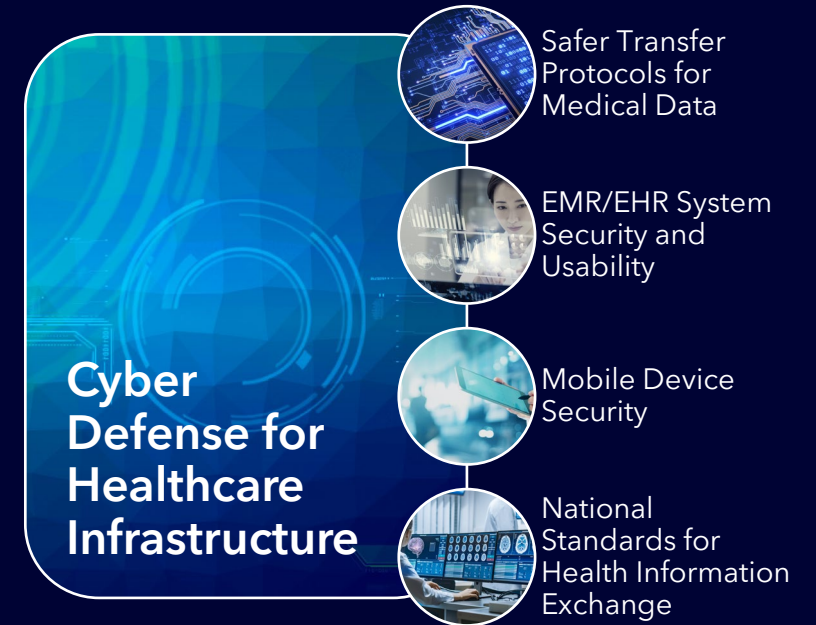
WIRED magazine
article highlighting
DIGIHEALS project



Link to BAA: Scaling
Health Applications
Research for Everyone
(SHARE)



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What if we had resilient healthcare infrastructure with advanced digital security for data, software, and devices?

The Program and Program Manager Flywheel

The ARPA-H portfolio is:

- (1) a reflection of the PMs
- (2) dynamic, and
- (3) will – and should! – change frequently

