Massachusetts Institute of Technology

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Thoughts on ARPA-H

As biomedical, bioengineering, and healthcare researchers at the Massachusetts Institute of Technology, we write to offer our views on the proposal to establish an Advanced Research Projects Agency for Health (ARPA-H). We support the creation of ARPA-H, and we believe that, if properly focused and organized, it would have great potential to advance science and technology, and improve the prevention and treatment of disease. We believe ARPA-H could offer a significant addition to the portfolio of research approaches to biomedical science and engineering, which must of course continue to include robust programs at the National Institutes of Health (NIH) and other federal agencies.

The Gap to be Filled by ARPA-H

NIH's traditional programs have many strengths, but they are not well adapted to tackle problems that require a concentrated effort involving collaborations among many fields of science and technology (and experts outside of biomedicine). Therefore, biomedicine has much it might gain through the addition of the ARPA model – which emphasizes a focus on the solution of specific problems, a team-based approach, linkages between engineering and science, risk-taking, milestones designed to enable projects to fail quickly or advance, and partnerships between academia and industry.

Problems such as figuring out how to predict the onset of certain cancers (such as pancreatic and ovarian cancers, which today are usually discovered when it is too late to treat them effectively) could benefit from fundamental advances that are more likely to occur through an ARPA approach, in part, because of the need to draw on computation, engineering, and other fields in addition to studies of basic disease biology.

An ARPA-H approach could also facilitate the invention of new instruments and materials for medical care; such efforts require close collaboration among physical and life scientists and engineers.

ARPA-H should focus on issues that do not fit the current two mechanisms for medicine and health research: fundamental science (essential research supported by federal agencies such as NIH, before translation to commercial products); and translational (product-focused research to gain access to the commercial sector). ARPA-H should take a portfolio approach to solving health challenges, with an emphasis on fundamental research breakthroughs to solve problems, but including the range of work needed to ensure that research advances are finding their way into medical practice. It should be careful, though, to avoid funding work that can be readily done by the thriving U.S. biotech and pharmaceutical sectors.

Work Across Disciplines Will be a Key to ARPA-H Advances

As noted above, multidisciplinary work at the intersection of the physical and life sciences, and engineering, sometimes called "convergence," holds greater promise for accelerated advancements in health than traditional life sciences alone.

The work of DARPA's Biological Technologies Office (BTO) – created in 2014 – can provide a sense of what an ARPA-H might achieve. The DARPA office, for example, helped fund research on the technology that would lead to mRNA vaccines which have proved so central to the fight against COVID-19. (The DARPA effort built on prior NIH-funded research, and the DARPA funding helped move the mRNA technology into use.) BTO also funded technology research that has accelerated the development of organs on a chip, and neural-controlled prosthetics. But DARPA is defense-focused and cannot alone fill the current gap in biomedical research.

NIH has not fully embraced such interdisciplinary approaches. According to MIT's 2016 report *Convergence: The Future of Health*, in fiscal 2015, less than 3 percent of NIH award funding was allocated to principal investigators in engineering, physical sciences, or math/statistics and computation. Scientists in these disciplines are frequently not familiar with NIH and feel their expertise is not given sufficient weight by NIH's peer-review system.

Biomedical and Health Problems Well Suited for ARPA-H

Building on our general points above, here are some initial thoughts on the kinds of problems (spanning from pre-clinical to post-market) that ARPA-H could take on:

- Advancing precision medicine by integrating state-of-the-art computation sciences such as machine learning, physics-based modeling, and data systems to link real-world clinical and demographic data to genetic and molecular biomarkers. Such work could improve the ability to predict which drugs will be most effective in which subpopulations.
- Analyzing the intersection of medical data, molecular tests, and imaging technologies to predict the onset of disease earlier. Intercepting disease processes before a patient becomes debilitated would advance the treatment of cancers that are currently hard to identify in their early stages such as pancreatic and ovarian cancers.
- Developing surveillance platforms to integrate data that are now held by different private and public organizations on how well drugs and other treatments are working under real-world conditions, improving the use of such treatments by better tailoring them to patients.
- Creating innovations in biomanufacturing technologies to help decrease the costs of biologic drugs.
- Developing broad approaches to propel new breakthroughs in synthetic biology. One promising area is ultra-sensitive biological circuits which have potential applications as environmental sensors or diagnostics that could reveal disease states (like heart attacks) in real time.
- Developing better disease surveillance tools including sensors and data systems to help counter outbreaks of infectious diseases.

Essential ARPA-H Characteristics

Regardless of whether ARPA-H is part of NIH or is established as an independent entity, it must operate differently from the rest of NIH to be successful. Its leadership must have the latitude to set up and operate an entity with its own goals, approaches and procedures. If ARPA-H is established within NIH, it should report to the NIH Director, not to another institute or center. ARPA-H will need new legal authority to bring in program managers, who – like DARPA's – should be hired for limited three- to five-year periods and should come from a range of technical backgrounds with an emphasis on expertise in computing and information sciences, machine learning and AI, physics-based modeling, physics and engineering, in addition to the life sciences. ARPA-H contracts should be larger than typical NIH grants and should go to multi-disciplinary and multi-sectoral teams (rather than funding individual groups).

The ideal ARPA-H director would have personal experience with the ARPA model, with work in a range of scientific fields, and with coordinated efforts across academia, industry, and governmental agencies. The director should be someone willing to forge an independent path. Crucially, the director should have a deep understanding of what can be gained from utilizing knowledge from areas beyond biomedical science to advance health, including understanding the importance of computation and engineering. The culture of a new entity tends to lock-in very quickly and the expertise and abilities of the first director, including working experience with the ARPA model, will play a key role in creating the agency's lasting culture.

Addressing Concerns

One source of DARPA's success that is not easily transferrable to other ARPA agencies is that DARPA often has a direct link to a Defense Department-supported customer base for its ideas, through its procurement activities. While the linkages between the government and the health sector are substantial, they are not as direct as the Pentagon's – NIH is not a procurement agency. ARPA-H should examine models both from DARPA and from ARPA-E in working to move promising new ideas into widespread use. For example, the Tech-to-Market teams that both ARPA-E and now DARPA use could be a constructive approach to help move ARPA-H's advances toward implementation.

At the same time, ARPA-H's approach should include working on important health problems that are not of immediate interest to the private sector. Creating new vaccines, overcoming antibiotic resistance, and addressing the health concerns of relatively small and underserved subpopulations in the U.S. or in poor countries are kinds of work that should engage ARPA-H even though they may not have the immediate private sector appeal of the next "blockbuster" drug. Even in such cases, ARPA-H would need to create linkages to the private sector to create pathways to the marketplace.

ARPA-H should pay attention to many aspects of diversity. Its staff and its awardees should reflect the rich diversity of our population. Among other reasons, this will help ensure that ARPA-H intentionally pays sufficient attention to the health needs of minorities and other marginalized populations.

Also, ARPA-H should work to involve researchers at a wide range of academic institutions. This could also strengthen the link between ARPA-H work and the public health community.

NIH should recognize that ARPA funding models are often not ideal for training graduate students given the speed of progress expected and the uncertainty of consistent funding. To ensure that graduate students who are funded through ARPA-H awards have sufficient, enduring support, NIH may want to consider providing additional funding for their work.

In addition, ARPA-H may want to examine ARPA-E's approach of hiring a group of fellows who are recent PhDs to assist program managers.

We hope that the ARPA-H initiative will be part of a broader effort to enhance U.S. research and education capacity in a way that benefits all Americans and improves health around the world.

We would be happy to elaborate on our views on ARPA-H. We do want to emphasize that we are drawing on our experience, and are not attempting to speak on behalf of others at MIT, or for MIT as an institution.

Signed,

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