Funding the future

The Biden administration has proposed a new agency to drive innovation in health research, including cancer. The focus on cancer and accelerated development is welcome, but for the time being, whether and how these plans will materialize is less clear.

The positive winds of change for science were apparent from the election of Joe Biden to the presidency¹. With the announcement of the president's fiscal year 2022 budget proposal, his vision has begun to take shape, with proposed funding boosts for both foundational research and applied research. At \$51.96 billion, the National Institutes of Health (NIH) are slated for a funding increase of ~21%, which, if approved by Congress, would be cause for celebration, bar one notable twist that has sparked excitement but also questions. \$6.5 billion of the requested NIH budget has been earmarked for the launch, over three years, of the Advanced Research Projects Agency for Health (ARPA-H), a new entity proposed to sit within the NIH with the goal of making breakthroughs in health research “that cannot readily be accomplished through traditional research or commercial activity”². Highlighting cancer, Alzheimer's disease and diabetes as starting points, the ARPA-H proposal has gathered early congressional support. The focus on cancer research is certainly a welcome follow-up to the President's promise earlier this year to “end cancer as we know it” once the COVID-19 pandemic is addressed, but how will this new agency help achieve this?

Modeled after the Defense Advanced Research Projects Agency (DARPA), which was created by the Eisenhower administration to support technological innovation for national security, ARPA-H would aspire to emulate DARPA's successes, which include contributions to the development of the internet and global positioning systems, by supporting high-risk, high-rewards application-focused research. According to [the Biden administration's plans](#), ARPA-H would be a separate entity within the NIH, run by a limited-term director overseeing a flat structure of project managers who would be tasked with selecting which projects to fund within their portfolios and facilitating progress by brokering partnerships between government, academic, industry and non-profit stakeholders. Projects would be time-constrained and goal-oriented and, following the DARPA model, funding decisions would be disengaged from the traditional peer-review system, with project

managers having not only broad autonomy to select projects but presumably also the latitude to terminate those deemed to be unsuccessful.

The Biden administration and NIH leadership issued strong support for ARPA-H's being part of the NIH by explaining that the new agency's mission sits squarely within that of the NIH itself and that both organizations would benefit by close synergy—ARPA-H by hitting the ground running as part of the existing NIH infrastructure, and the NIH by housing an entity that would facilitate rapid translation of bold, riskier research³. [Criticism that this decision would make ARPA-H subject to the NIH's existing culture and practices](#) was rebutted by stressing the new agency's independence and operation under different, nimbler practices, rather than as a 28th NIH institute. Precisely what these new practices would be, beyond the DARPA blueprint, remains to be seen. Nevertheless, the scientific successes in response to COVID-19 have demonstrated that when urgent need demands it, government mechanisms can speed up, establish broad collaborations and provide rapid, clinically translated results. ARPA-H is proposed to operate on a similar basis of accelerated use-driven research. An agency that would incorporate the lessons learned over the past 18 months to cut through unnecessary red tape and speed up translation to benefit patients with cancer in an equitable manner would be a welcome addition to existing federal programs, including the National Cancer Institute (NCI). A key difference that could reduce the length of the ARPA-H award process substantially compared with existing NIH practices is of course the absence of peer review and, by extension, of the delays and sluggish bureaucracy that often come with federal funding. In contrast, the ARPA-H model would endow project managers with considerable power in terms of funding decisions, meaning that the success of the operation would very much depend on the skills and vision of the people chosen for these crucial positions. At this time, information is scant on the decision-making processes based on which the ARPA-H director and project managers would operate and how the DARPA model

would be adapted to suit the realities of biomedical research.

In a co-authored article, Eric Lander, Director of the Office of Science and Technology Policy and science advisor to the president, and Francis Collins, the NIH director, stressed that “ARPA-H should expect that a sizable fraction of its efforts will fail,” to avoid building yet another risk-averse organization³. It is refreshing to have this truism about the nature of biomedical research voiced so plainly by science leaders in government. It will be interesting to see how this will be reconciled within a federal agency tasked to promote application-focused, results-oriented research. The sizable congressionally approved funds needed to support, evaluate and, ultimately, terminate a majority of unsuccessful projects will have to be justified to the taxpaying public and counterbalanced with substantial successes. Again, a lot will depend on the people and mechanisms put in place to select competitive projects that combine high-risk innovation with the feasibility of shorter-term completion. This is no mean feat, and some argue it is one that is better tackled by the pharmaceutical and biotechnology industries, as is already the case for many of the topics listed as potential ARPA-H-driven work³.

On that front, critics question what the ARPA-H concept offers that is not already encompassed by existing initiatives, including within the NIH itself. For instance, the National Center for Advancing Translational Sciences is the NIH institute that was formed in 2011 to accelerate the translation of scientific discoveries through innovative technology and wide collaborations. Despite efforts to differentiate ARPA-H from this and other NIH-run programs³, the degree to which purviews may overlap remains unclear. Partially overlapping goals between government agencies would be less of an issue if funds were abundant. However, given the traditionally low funding rates within the NIH system, questions abound about how ARPA-H's addition will affect them, especially at a time when solid financial support is essential for the post-pandemic recovery of the research enterprise. For cancer researchers, the

potential influence of ARPA-H's creation on the NCI's goal of increasing research project grant paylines by one percentile every year, to reach the 15th percentile by 2025, is a pressing question. Added to that is how the new agency will interact with the NCI—the scope for developing synergies between the two is broad and exciting, but hard to define without a clearer idea of ARPA-H's structure.

Initiatives to revamp funding mechanisms and accelerate scientific discovery are necessary. Support for the president's expressed desire to end cancer as we know it is unquestionable. However, it is important to define what shape these efforts will take. The drive for application-focused translational work raises concerns about a stymying effect on foundational cancer

research. It is important to fund science that will advance our understanding of cancer biology, diagnosis and treatment and will have a meaningful impact on the lives of patients. However, setting aside the rollout of new, life-saving diagnostics and treatments, impact in science is hard to measure in the shorter term. To imply that research that does not yield results that are immediately translatable to the clinic is not valuable would be a mistake. Biomedical breakthroughs most often rely on a body of discoveries that builds up over time. The work that formed the basis of targeted therapies, immunotherapies and the vaccine against human papillomavirus are but a few such examples. Balancing blue-skies discovery research with high-risk, high-benefit translational work will be

essential to laying the foundation for future breakthroughs. A healthy collaborative relationship between traditional agencies such as the NCI and new entities such as ARPA-H will be key to achieving that balance.

For now, whether and in what form the president's fiscal year 2022 science budget and ARPA-H proposal will materialize awaits the final say of the US Congress. □

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