Enthusiasm, Questions about ARPA-H

Proposed biomedical research agency could accelerate progress in cancer, other diseases

The Biden administration recently proposed creating the Advanced Research Projects Agency for Health (ARPA-H), a biomedical research agency intended to accelerate research for widespread diseases such as diabetes, Alzheimer disease, and cancer. Although many cancer researchers express enthusiasm for ARPA-H, they wonder how it will function and mesh with existing institutes and agencies.

“It’s a strong concept,” says Leonidas Platanias, MD, PhD, of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University in Chicago, IL. “There is an absolute need to find a way to push biomedical breakthroughs to the clinic. Now, the devil is in the details.”

A NEW RESEARCH MODEL

The new entity would be modeled after the Defense Advanced Research Projects Agency (DARPA), “which follows a flexible and nimble strategy, undeterred by the possibility of failure, and has driven breakthrough advances,” write NIH Director Francis Collins, MD, PhD, and colleagues (Science 2021;373:165–7). Like DARPA, ARPA-H would fund bigger, higher-risk research projects—relying on program managers to “make connections across organizations, help clear roadblocks … and monitor projects closely,” among other responsibilities. For example, ARPA-H might fund research on mRNA vaccines for cancer or new manufacturing processes for T-cell therapies. As proposed, the agency would fall under the NIH, but Congress will have the final say on how it is structured. A bill passed by the U.S. House of Representatives would provide $3 billion to establish ARPA-H as part of a $6.5 billion funding increase for the NIH for fiscal year 2022, if enacted.

For some, ARPA-H would be a welcome change from the traditional funding mechanisms. “The NCI and the NIH are wonderful, but they’re more on the discovery-science side. They’re funding individuals or small groups,” says Elizabeth Jaffee, MD, of Johns Hopkins University in Baltimore, MD. They “never have the kind of funding you need, nor do they have the mechanisms to administer big funding quickly. It’s like a big ship that takes a while to turn.” As proposed, ARPA-H would operate differently, and putting it under the NIH could foster collaboration between institutes, she says.

David Agus, MD, of the Ellison Institute for Translative Medicine of the University of Southern California in Los Angeles, says that the NIH and the NCI haven’t sufficiently prioritized innovation. He hopes that ARPA-H will function more like a business than a government agency. “We don’t need more singles; we need people to hit home runs,” Agus says, possibly leading to more failures, but also more significant breakthroughs.

Researchers are often hindered by the persistent pressure of publishing and securing grants, says Chi Van Dang, MD, PhD, of the Ludwig Institute for Cancer Research in New York, NY. “There’s this treadmill that we go on that limits the ability to take [scientific] risks, because you risk your career,” he says. By relieving that pressure, researchers could dream bigger. Dang thinks the agency could be modeled after programs that involve large teams of scientists, like Cancer Grand Challenges or Stand Up To Cancer. “The concept is extremely exciting. I just hope that the execution is going to be equally exciting.”

QUESTIONS ABOUT PRIORITIES, FUNDING

Setting appropriate expectations will be key, Dang adds. DARPA focuses on engineering and physical sciences, whereas ARPA-H will be rooted in biological sciences, which tend to be more complex and unpredictable, he notes. Thus, biological questions can’t be answered by simply giving researchers large amounts of money; ARPA-H would need to foster new research approaches that can break down complex science into basic principles.

As for ARPA-H’s priorities, “we’re hypothesizing what they are based on what we know the Cancer Moonshot looked like and what DARPA looks like,” along with other models that brought government, industry, and academia together, Jaffee says. “It would be nice to know what worked, what didn’t work, [and] how we could do it better.”

Platanias hopes that cancer will be a priority for the agency. “I think cancer is probably the biggest biomedical problem currently, and I just want to make sure the emphasis will be there,” he says. He would like to see ARPA-H more closely aligned with the NCI and perhaps focused entirely on cancer. However, Jaffee and Agus agree that a multidisciplinary approach could be beneficial because advances in one disease may apply to others.

Perhaps the most significant question about ARPA-H is what it could mean for NIH and NCI funding. In recent years, the payline for R01 grants at the NCI has hovered around 10%. “We’re going to lose the best people,” including young investigators and underrepresented minorities, Jaffee cautions. Funding the new entity shouldn’t “decrease funding to any of the NIH institutes.”

Ross Levine, MD, of Memorial Sloan Kettering Cancer Center in New York, NY, calls the proposed $3.5 billion increase for the NIH base budget “relatively modest” given the allocation for ARPA-H. “I feel like there’s a pressing need for a substantive increase in funding at the NCI itself, and right now that’s missing.”

He thinks that further increasing funding for the NIH and the NCI would go a long way in speeding up research. “The nature of the review process, and the paylines being where they are, are part of why it takes so long for people to get funding for their research,” he says. “If we had a higher payline and more grants were funded on the first round, we would accelerate that.”

Although he is excited about the general increase in biomedical research funding, Levine wants more details about ARPA-H: “How is something like ARPA-H going to accelerate research in a way that we don’t with the conventional funding structure? And how is it going to allow people to ask important albeit risky questions?” he asks. “I have questions at this stage and not answers.”–Catherine Caruso