

The scientific enterprise must change: A conversation on systemic flaws in biomedical research

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Credit: Steve Lipofsky

That funding for basic science research in the U.S. is bordering on crisis is hardly news to any researcher submitting grant applications today. While the future of funding is unclear, there is no compelling reason to believe it will ever return to the explosive growth witnessed in recent decades. As such, many believe that the scientific enterprise—the very culture in academia of how we train scientists and run laboratories—is unsustainable.

Marc Kirschner, head of the HMS Department of Systems Biology and the John Franklin Enders University Professor of Systems Biology, has been thinking a lot about this.

Recently, Kirschner teamed up with Bruce Alberts, professor emeritus at UCSF and former editor of the journal *Science*; Shirley Tilghman, former president of Princeton University; and Harold Varmus, director of the National Cancer Institute, former director of the National Institutes of Health and a Nobel laureate, to author an article on how the scientific community might consider addressing the situation.

Published in *PNAS*, [the article's](#) authors intended not to issue a prescription with clear-cut mandates, but rather to begin a national conversation on a topic that should be of vital interest to the scientific community as well as the general public.

Harvard Medicine News took a moment to sit down with Kirschner and discuss the current state of science and what might be done to ensure its future.

HM News: What is the current problem with the scientific enterprise?

Kirschner: The system is under considerable stress. There's not enough money to do what people want and need to do. There are not enough jobs. And because the whole profession is based on trainees doing most of the work, and with many of them aspiring to jobs as principal investigators themselves, we see an exponential kind of problem, especially in light of the money actually decreasing from NIH, an estimated decline of about 25 percent over the last several years.

HM News: After how many years of notably increasing?

Kirschner: After many years of the budget doubling. That caused institutions to build more space, to hire more faculty. But, at the same time, they tended

more and more to put faculty on soft money positions that depended on grants.

And science is more expensive. Science is going very, very well in many ways. But that has created a situation where there's a tremendous amount of stress in the system. And the stress itself is operating not to support the best science, but actually to discourage some of the best science.

One feature is that the scientific effort is not achieving what it could achieve, but also that the kind of things that are being supported, the kind of hyper-competition, is producing a situation where the science is getting less creative and more risk averse.

HM News: That sounds counterintuitive, namely, that more competition would result in poorer quality science?

Kirschner: Competition itself at some level is a good thing. But when people's livelihood depends on getting the grant, it undermines a lot of the cooperative nature of science, the open and sharing nature of science.

It has never been the case that the most creative and original projects get the most uniform approval. But grants have become so hyper-competitive, you end up with things being proposed that seem safe, that everybody can agree are reasonable. People in the past were willing to take chances, pursue something that no one before them had been able to make work, but now such risky propositions hardly ever get funded.

The less risky an idea is, the more likely it is to get approved. But it's the risky ideas that really advance science.

HM News: What is the root cause of the crisis? Does it all boil down to diminished funding?

Kirschner: There are other factors. It's harder to operate an effort like science at a larger and larger scale. And so the effect of diminished funding at a large scale is actually worse than it is at a small scale. Because at a small scale, things are more informal. You can move money around. You can

help each other out. But at the real large scale, we've gotten much more rigid.

But I do feel that we need a steady state or a plan where the number of people in the system will meet the amount of resources that are going into the system. Some of our proposals are really aimed to create more jobs in science—not necessarily more labs, but more jobs.

HM News: Is industry a viable option for people who have trained in academia?

Kirschner: That was the other option. But that isn't growing very much at all. We now have a long queue [of applicants] waiting on these post-doctoral positions, who won't be paid great salaries, and whose likelihood of getting the position that they expected is diminishing.

HM News: Much of the debate seems to focus on funding agencies. But what about institutions themselves? What sort of things should research institutions look at?

Kirschner: One issue is that there is more money being put on grants for salaries than there used to be. Of course it makes the livelihood of everyone dependent. If they don't get a grant, they don't have a job. They don't have an income. And that's putting a lot of stress on science, which is not a positive force. It's just a desperate force.

Now I'm not saying you shouldn't put any salaries on grants. But I think you have to revisit and look at this closely.

HM News: You and your coauthors also recommend not simply increasing funding, but changing it. Can you elaborate?

Kirschner: Currently, government agencies provide short-term, project-oriented funding, and that creates a lot of inefficiencies and unnecessary stress. An investigator's overall track record should be part of the equation as well when his or her grant proposal is reviewed. Put another way, funding agencies should invest in careers as well as specific projects.

Also, we're using these crazy metrics like how many papers you published, or what journal were they published in, instead of more qualitative metrics. This has created an unholy effort for people to get papers into certain journals, making them arbiters of science. It creates a frenzy. This doesn't make sense, yet it's hard to not play that game.

Again, it's important to keep in mind that the most creative and innovative things usually don't have a consensus when they start. It's usually a few people, or one person, having an idea. We need funding mechanisms especially for young people who are starting out that recognizes their creativity, innovation, risk-taking and new ideas.

HM News: What are the consequences of this?

Kirschner: By hampering basic science you inhibit translational science. I am just not convinced that the barrier to new developments in science is at the translational level; it's really at the more fundamental level. That can be proven in retrospect. It's hard to prove something in prospect. But you can go back and look at the history of biomedical research and see that so many discoveries that have revolutionized science and medicine did not begin with some translational roadmap. In fact, if you look at an area like cardiology, only a small percentage of the developments were self-consciously translational at their inception. The great majority of breakthroughs came from basic science.

There are people who say that, you know, we've done a lot of fundamental [science](#), and now we should just apply it. And that's a great aspiration. If that were true, then I'd say we should just shut down all of the fundamental labs and just apply what we know. But I don't think anyone believes that we know enough to do that.

We're surrounded by so many opportunities to apply what we do. But by requiring researchers to anticipate the application at the start, that's putting an additional squeeze on the smaller scientific laboratories, the fundamental scientific laboratories.

HM News: You and your coauthors have made a

number of provocative suggestions. Does one strike you as particularly the most challenging?

Kirschner: I just think the problems we pointed out are quite real. And I think they can be confirmed very easily by going around and talking to people in the [scientific community](#). The remedies are not likely to be easy, and we have to make sure we don't damage the system while trying to correct it. We never felt this to be a prescription. Our intention is to start a public discussion.

This is something that needs to be discussed at every level: institutions, government and Congress, scientists, we all have to mull these things over. And some things we may find are somewhat distasteful. But we have to do them in order to achieve some other end.

Science is a continuum from one generation to the next. And our society will be ill served if we don't attract the best people into this field, if we don't give the right people the opportunity to do something novel and interesting that we never thought of doing.

Provided by Harvard Medical School

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