Conversation with Howard Hughes Medical Institute on June 3, 2013

Participants

- Robert Tjian, *President, HHMI*
- Cheryl Moore, *Executive Vice President and Chief Operating Officer, HHMI*
- Cari Tuna, *Co-Founder, Good Ventures*
- Holden Karnofsky, *Co-Founder and Co-Executive Director, GiveWell*
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Note: This set of notes was compiled by GiveWell and gives an overview of the major points made by Robert Tjian and Cheryl Moore in the conversation.

Summary

The Howard Hughes Medical Institute (HHMI) is a nonprofit medical research organization. GiveWell and Good Ventures spoke with HHMI as part of its initial exploration of the funder landscape in biomedical research.

Landscape of biomedical research funders

In the field of biomedical research, the NIH and other federal organizations spend about $35 billion per year. The Howard Hughes Medical Institute (HHMI), on the other hand, spends about $1 billion per year. HHMI is part of a coalition of private funders of biomedical research, which includes the Gordon and Betty Moore Foundation, the Alfred P. Sloan Foundation, the W.M Keck Foundation, the Simons Foundation, the Kavli Foundation and the Research Corporation for Science Advancement. These 7 foundations are the largest private funders of basic research in the U.S., totaling about $1.5 billion per year. The funders in this coalition agree that the country's science funding is moving in the wrong direction - that federal funding, for the most part, is not doing enough to support innovative science.

One of the major issues in biomedical research is that biology is not understood well enough to get to the root of problems, whether in health, agriculture, geology, etc. There's a lot of pressure to push science in applied or clinical directions before it's ready, which can result in money being poorly spent. The NIH has shifted more and more money into clinical research. One of the reasons for this is that patient advocacy groups, which are cause-specific, have a lot of influence on Capitol Hill. Some foundations have shifted their focus and funding the other way – towards fundamental research.

There certainly is a bottleneck in bringing drugs from "bench to bedside." Part of the bottleneck is that it takes the FDA a long time to make decisions because the fundamental science isn't well-understood enough. As long as the basic research is lacking, there will be low returns to translational science to bring drugs from the lab

to production. Better progress on basic, fundamental science would lead to stronger understanding and higher success rates at later stages.

One of the reasons for the lack of basic research is that the funding mechanisms keep shifting further from this type of science. Venture capitalists focus on very late-stage, relatively low-risk-seeming ideas. This discourages innovation and risk in favor of recycling old ideas that have already been developed, and makes it hard for young scientists to obtain funding. From the 1980s-2000s, VCs were funding biotech companies to the point where pharmaceutical companies could buy them up; now, pharma companies are having a hard time with how to best build their pipelines. Universities are beginning to fund earlier-stage research, and there are other possible models, but it's not clear what the best solution is.

HHMI's view is that the later stages of research are important, but a scientist has to be able to understand the basic techniques before he or she can create a therapeutic treatment or diagnostic tool. The basic research is often years away from its clinical application, but can be extremely valuable. One example is treatment for chronic myelogenous leukemia (CML), which used to be a death sentence. Two scientists started with basic research at UCLA; no company wanted to invest in what they were doing; they started their own company and pushed it for about 18 years, took it through every phase: basic research, preclinical, clinical, all the way to post-patient analysis which is taking place now. In general, HHMI-supported scientists have strong track records of working on late-stage research and seeing their research reach the bedside. Having strong fundamental understanding of the science is very useful in getting through later stages successfully.

It's important for money to be available for early career researchers. HHMI already puts a lot of its funding into postdocs and graduate students, but even as junior faculty, it's hard to get funding from the NIH. HHMI plans to put more money into early career scientists. Supporting early career scientists is a possible opportunity for a new funder.

Promoting basic research

The coalition of the 7 private funders is the first time that the major science research philanthropies have worked together. They are considering ways to be more vocal in advocating for basic research, though they do not lobby. Lobbying is a potential opportunity for a new entrant into this space.

HHMI does not rely on donor funding and generally does not accept donations; its budget comes from its endowment.

HHMI has recently begun discussing potential collaborations with the Bill and Melinda Gates Foundation, which is beginning to put more money into basic research. Tuberculosis is an example of a large global health issue that has received

a lot of foundation funding aimed at treatment, but is still difficult even to diagnose because the basic biology of it is not well-understood.

HHMI's approach

Even the highest-level officials and advisors within HHMI are expected to spend time in the lab. In order to advise other scientists, they need to be current on the science. In many other institutions, advisory roles are purely administrative (e.g., editors of journals and program officers at the NIH).

All of HHMI's reviewers are full time academics who receive 3-5 year retainers from HHMI. Most academic scientists work about 60-80 hours/week, so they are able to handle their academic work and HHMI work.

Finding good advisors is a huge part of the job of the President of HHMI. Networking is key for this. HHMI doesn't just look for expertise, but for generalists with a sharp but broad view of biomedical research. Finding generalists is harder than finding experts in particular fields. One of the things HHMI looks for is generalists who can recognize outstanding, high-potential science that is outside their field of specialization.

It is an open question how you retain creativity after you've built the institution. Once you set up an organization that has a physical structure and permanent staff, it's hard to change things. No one at HHMI has tenure, that's one way of keeping things flexible.

There are some groups that HHMI provides with funding because they have great models. HHMI also just put $25 million into UTeach, which develops subject area teachers by encouraging them to study their subjects as undergraduates. HHMI does deep due diligence before funding another institution's project, and checks it out again every 4-5 years, but defers to UTeach's selection process.

HHMI Investigators

HHMI provides relatively long-term funding for outstanding researchers through the Investigators program. Applications for funding ask for a brief description of what the researcher is planning to do, but the emphasis is really on track record – what the researcher has already done. There is a check-in every 5 years for HHMI investigators. At that point, investigators need to present what they have accomplished, but if they have veered from their original plan for good reason, the research will still be supported. HHMI bets on people. The NIH, on the other hand, asks for specific aims in research proposals, and holds researchers to them. HHMI's view is that if researchers are locked into following set plans, they can't go where the science leads them, and that isn't ideal for maximizing innovation. The NIH has a program modeled on this approach (the Pioneer’s award), but this program is very small compared to the bulk of NIH funding.

HHMI does not tell its investigators what to work on. They do what they are best at and what they are passionate about.

HHMI's Janelia Farm campus

HHMI felt its Investigators program had reached optimal size and that newly available funds should be spent differently. It created the Janelia Farm campus, a research center. The criteria for choosing the location for HHMI's Janelia Farm research campus was that it should be close to a major international airport, relatively close to HHMI's headquarters, and have enough land to accommodate the facilities. Based on these criteria, Ashburn, Virginia was chosen. There are pros and cons to its being fairly isolated.

For the Janelia Farm research campus, HHMI chose a focus area based on what 21st century biologists ought to be working on – a less mature area where there were major discoveries to be made. HHMI held workshops with experts in different scientific areas (developmental biology, neurobiology, small molecule screening, bioinformatics, and molecular imaging), asking the experts to identify what should be worked on in each area. Based on these workshops, HHMI chose neuro circuitry and molecular imaging as core areas of research at Janelia Farm. Technology development is not only useful for neurobiology, but for all of biomedical research; the need for better tools came up in many expert workshops. There is currently a major gap in technology development, because universities have the talent but not the resources to support it – it is difficult to get tenure or funding for this kind of research; companies won't invest in technology development either. One success story in technology development from Janelia Farm is that a group of researchers has developed and manufactured a new class of microscopes.

At most research institutes, once you're an independent scientist, you have to spend much of your time writing grants. At Janelia Farm, this is a non-issue, because all funding is internal. This allows scientists to work on projects that are broader, different, and on a longer time horizon. Janelia Farm also changes the culture of research teams. No lab is larger than 7 people, and all senior scientists are active in the research, they do not spend their time grant writing or teaching. People are incentivized to work in teams, and to move away from having one senior author on papers. The environment at Janelia Farm was designed to facilitate inter-disciplinary work. HHMI hired scientists from many different disciplines.