

A conversation with Carolyn Bruzdinski on June 19, 2013

Participants

- Carolyn Bruzdinski – Chief Mission Delivery Officer for the California Division of the American Cancer Society
- Holden Karnofsky – Co-Founder and Co-Executive Director, GiveWell
- Dario Amodei - Postdoctoral Research Fellow, Stanford School of Medicine
- Sean Conley – Research Analyst, GiveWell

Note: This set of notes was compiled by GiveWell and gives an overview of the major points made by Dr. Bruzdinski.

Summary

GiveWell spoke with Dr. Bruzdinski about how the American Cancer Society funds biomedical research. Dr. Bruzdinski discussed ACS's grant mechanisms, its peer review process, and the qualities that ACS looks for in applications for funding. She also described some differences between the ACS's model and that of other organizations such as the NIH.

Dr. Bruzdinski's background and role

Dr. Bruzdinski joined the organization as a scientific program director and directed two of the extramural grant peer review committees. She has had a strong knowledge of how the extramural program has worked. Dr. Bruzdinski left the Extramural Grants Department in 2006 to serve as the Chief Mission Delivery Officer for the California Division of the American Cancer Society.

The Grants

ACS primarily uses two major funding mechanisms for extramural grants. The first is a 3-year post-doctoral fellowship, with an amount of money comparable to the similar NIH fellowship, which is about \$150,000. About 80 of these are given out per year.

The second is a research scholar grant, with a value of about \$720,000. This is focused on Principal Investigators (PIs) who have their own lab. This grant is distinctive in that it is focused on funding scientists that are early in their career, and recipients tend to be in the first 6 years of their academic appointment. Often they are newly hired professors or assistant professors. Such scientists may often struggle to find funding from other sources since they have to compete with more senior people at some funding sources, including the NIH.

In addition, ACS supports a limited number of research professors (about 20 in basic research and 15 in clinical research). This is for people mid-career who have made a seminal contribution to the study of cancer, tend to be well-known, and are often former recipients of ACS grants earlier in their career. They have to write a proposal for their research project when applying, but they can use the money for cancer research as they see fit, and since they tend to mentor other scientists it has benefits for a number of people. The grant both recognizes their accomplishments and supports their future potential. ACS also benefits through the work they do to promote the organization. These scientists can get funded

for up to two terms of five years, after which they maintain a relationship with ACS. The amount of money is \$400,000 for each term of the grant.

The ACS has a robust portfolio that also includes grant mechanisms such as Mentored Research Scholar grants, Institutional Research Grants and the Health Professional Training Grants program.

The Philosophy

ACS provides substantial support to early-career scientists, who often have difficulty getting funding from other sources (as noted above). Evaluating people early in their careers can be difficult and risky. ACS has funded many Nobel Laureates well before they won the Nobel Prize.

The ACS finds some of the benefits of funding such young scientists to include the fact that they're likely to think outside the box and that they maintain relationships with ACS over the rest of their careers. Young recipients of mentored grants often receive further grants from the ACS down the line and many grantees regularly serve on the ACS grant-reviewing committees later in their careers.

The ACS grants programs are mostly investigator initiated, so they don't direct researchers' work. The funding process starts with information posted on their website (www.cancer.org) on which broad areas in the field of cancer they are looking to fund, and scientists and health care professionals are able to learn about deadlines and what the committees are looking for, and can call the scientific program director to learn more about the grant process. ACS also promotes the programs at scientific meetings.

Although the process is normally investigator initiated, the ACS occasionally uses an RFA, calling out for applications in a specific area. They might do this if funds are available for some specific purpose. They also have the capacity to organize different mechanisms should a donor desire. Donor-driven funding mechanisms should involve enough funding to support multiple applications, since any given funding mechanism will result in many submissions and one has to consider the value of scientists' time applying. For smaller donations, it normally makes sense to put that money through one of the existing grant programs.

Roughly \$100million is granted annually via ACS's extramural grant making. Over ten percent of that goes to the postdoctoral positions (roughly 80 people at a cost of \$150,000 each); the vast majority of that spending goes to principal investigators.

ACS seeks to fund the best science related to cancer, and it is for this reason that it does not direct researchers on what to work on. Instead, it normally describes a broad area of the cancer problem that it is interested in and funds the strongest applications.

Because insights regarding one type of cancer can often be relevant to other types, it makes sense to fund the highest quality research rather than set a specific budget for a variety of different types of cancer. By setting aside some fixed amount for something specific, like breast cancer, one runs the risk of getting a set of low quality applications and may end up funding people before they're ready.

ACS depends on the peer reviewers to use their up to date knowledge to help decide which applications have the best chance to achieve the most to help advance our knowledge against cancer.

The Process

Applications are peer reviewed by a committee. There are a number of different committees for the various areas ACS is interested in funding, including epidemiology and health policy. About half of the committees have a basic cancer research approach, but the approximately other half focus on translational and applied cancer research.

Committees tend to be staffed by well-established scientists in the field. These members have four year terms (the Chair and Vice-Chair have slightly longer terms), and whenever openings come up they are filled by the scientific program director recommending a candidate, who is then discussed by a panel of volunteers from the medical and scientific community. An invitation to be a peer reviewer is then extended, which is normally accepted. Finding good reviewers is difficult; ACS has a great deal of experience doing so and still finds it challenging.

There are also “stakeholders” on committees (about 10% of committee members are stakeholders, and committees are normally 15-20 people). These are people from the community who have an interest in cancer research and might have done volunteer work in the past, but they don’t have scientific expertise. They give the layperson’s perspective on the applications and are witnesses to the quality of the process. Although some scientists were initially skeptical of having non-scientists as part of the review process, they now generally appreciate it.

The process is started when scientists write and submit a grant application, which the scientific program director then assigns to a committee based on its abstract. Then, two scientific reviewers and one stakeholder reviewer are assigned to each proposal (the scientific reviewers do thorough reviews of the application; the stakeholder reads a parts of the application understandable to laypeople), the proposals are sent to the entire committee to read, and the committee meets in person in Atlanta. The two reviewers share their thoughts and critiques of their proposal with the group (the primary reviewer gives some background on the topic and a critique, and the secondary reviewer just gives a critique), the committee has a discussion, and then everyone on the committee assigns a score to the application from 1.0 (best) to 5.0 (worst), with increments of 0.1. An average is taken and the proposals are ranked.

At this point, the ranked list is taken back to the committee, to confirm with the reviewers that the rankings make sense, and also to ask what the minimum score should be for funding. This step in the process differs from what is sometimes found at other funding sources, where reviewers submit their scores and do not have a chance for further involvement in the process. The ACS process gives the committee the opportunity to more accurately convey their ranking of applications to the next level of the ACS peer review process. The list of approved applications is then sent to the Council for Extramural Grants, which is composed of respected experts who have substantial experience reviewing grants. Because ACS doesn’t have the resources to fund all the proposals that the committee approves, the Council has to select which to fund. They recommend a funding line and fund everyone with scores better than that line, and designate the rest as “pay-if”, meaning that they would fund the applications if they had the money. “Pay-if” proposals are kept in a portfolio in case other donors are interested in funding them. These can be particularly useful if donors want to fund a specific type of research – ACS can show them a file full of applications in that field that have already been approved by the peer review process. Of course, the Council’s job is a frustrating one in that they have to separate proposals which are sometimes just separated by hundredths of a point, and out of such an exemplary group of applications which have already passed the peer review process it is very difficult to know which ones will lead to great breakthroughs. The funding line is normally no higher than 1.5, and there’s no set

percentage for a committee to fund in any given round – if there aren't enough good applications they don't award funding to inferior projects.

After the decisions are made, award letters and denials are sent out. The ACS is known for presenting their critiques in a particularly nurturing/constructive way, and this is related to its focus on supporting early-career scientists.

ACS applicants can resubmit a proposal up to twice more, incorporating feedback.

ACS won't fund any cancer research that hasn't gone through a peer review process. It also won't fund donor-specified people. Sometimes donors wish for their money to go to somewhere specific, but if they want to send it through the ACS they are required to use the standard process with no guarantee it will go to the person they want. A straightforward solution is to offer the donor the chance to support a project that has already been approved by the peer review process.

The ACS is currently discussing this process. It has been happy with it but is considering other methods, such as whether they should use more RFAs. However, alternatives such as speaking to the applicants in person seem to have their own downsides, such as personality becoming a big factor in the process.

Evaluation criteria

ACS has general guidelines for how to score the applications. For postdoc applications, the reviewers look at the project, the individual's history, and the individual's mentor. Because they are training grants, it is important that the person have a great training experience and so the mentor matters, as well as the institution as the context in which they'll work. The specifics of the project matter comparatively less, receiving only about 1/3 of the weighting in the evaluation, while the individual and mentor combined roughly make up the other 2/3.

For the principal investigator grants as well as the research professorships, it's shifted the other way, and is much more about the project. PI grants put a fairly heavy weight on preliminary data – not the amount of data you'd expect a seasoned investigator to have, but they do need to present the data to support their hypotheses.

Relevance to cancer is another criteria discussed by the committee. In basic research, the questions being discussed are ones that have been identified in the community as likely mechanisms of cancer, and if things have only tenuous connections to cancer applications, they won't be funded. Stakeholders occasionally ask if things are relevant, and the scientists in the committee can defend the relevance if appropriate. However, even well-written, interesting applications get dropped if the link to cancer is tenuous.

The research is hypothesis driven – the evaluators are looking for clear hypotheses to fund. The focus is on how the work would answer some question. ACS is normally not looking to fund broad scientific technologies, but might get involved in such technologies' applications for cancer. Research that is primarily about introducing a new measurement tool (such as a fluorescent cell sorter), and used cancer cells as a model to prove the viability of the tool, would, in Dr. Bruzdinski's opinion, be unlikely to be funded by ACS. This sort of work is generally difficult to get funded.

There are specific rules about conflict of interest, and anyone who has a relationship (through institution, collaboration, etc.) with anyone involved in the application leaves the room, doesn't

participate in the discussion, and doesn't score the grant: ACS wants to eliminate bias as well as any possible perception of conflict of interest. The reviewers take the conflict of interest policy seriously, and there's a double check because the other reviewers in the room tend to know each other's professional relationships.

Other people for GiveWell to talk to

- Other scientific research organizations:
 - NIH
 - Stand Up to Cancer (explores a large team approach to funding)
 - Leukemia and Lymphoma
- Dr. Elizabeth Ward, National Vice President for Intramural Research, ACS
 - Could talk about the ACS' epidemiological program
- David Ringer, Vice President of Extramural Research
 - He could talk about a variety of subjects, including how the ACS decides about the relevance of research to cancer, the percentages of postdoc applications that get funded, and the ACS's current thoughts on alternative processes for making grants