

Forum: The Bill & Melinda Gates Foundation's Grand Challenges Exploration Program

Sponsored by the AIDS Research Institute (ARI) in collaboration with UCSF's Corporate and Foundation Relations

Thursday, September 17, 2009
Genentech Hall, Auditorium
8:00-10:00 am

The goal of the forum was to support all faculty members or scientists from diverse backgrounds working to improve global health with an interest in exploring challenging research ideas.

The program included a panel of speakers and Q & A moderated by John Greenspan, BDS, PhD, director of the AIDS Research Institute. Andrew Serazin, DPhil, program officer from the Gates Foundation's Grand Challenges Exploration program joined via video teleconference to provide context for the Grand Challenges initiative and to answer questions from participants.

Researchers who have received previous Gates Foundation Grand Challenges Exploration grant awards participated on a panel to describe their projects and share information and lessons learned through the process.

Welcome: John Greenspan, BDS, PhD, Director, AIDS Research Institute

Welcome, overview of Gates program (see below, general info about Grand Challenges).

Introduction of the Grand Challenges Exploration Grant Program, Andrew Serazin, DPhil, Program Officer, Global Health Discovery, Bill and Melinda Gates Foundation

Andrew Serazin

The program is an open and competitive window to get the world's best ideas on a continuous basis. The Gates Foundation's mission is to reduce inequity, especially where market forces haven't done so. This program is a continuous channel for investigators to "finally prove that speculative concept you've been arguing over, but no one else will fund – for you to put some experimental data against that concept."

The invitation to apply is made to universities, hospitals, physicians working at point of care, small nonprofits, etc. world-wide.

How They Review Ideas

Applications are not reviewed by committee. Their philosophy on how innovation happens and how ideas get diffused is that it takes a "champion" to push them through a champion-based review system. Your idea is reviewed by 4-5 individuals. *It only takes one reviewer who sees it's worth supporting, and on the basis of that selection your idea will be funded.* This overcomes what frequently happens in review, which can be a popularity contest where some of the best ideas may not stand up to criticism.

The application process is unusual. The application is two pages, with no preliminary data, submitted online. They review apps somewhat rapidly (4 months to decision). Anybody can apply. They mean that. Applications are reviewed without knowledge of investigator's previous track record. Reviewers don't know who you are. The proportion of young scientists has gone

up increasingly with each applicant pool. If you are a post-doc or grad student, your success rate is higher than a tenured professor's.

To date they have received almost 10,000 applications from 100+ countries, about 3,000 per round. They fund 80-100 per round. Of the successful applicants, 50% have submitted before. This shows a refinement of ideas. If at first you don't succeed...

Serazin's vision: identify over 5 years a few transformational solutions that really make a difference for health in the developing world. They seek health *solutions*. Projects must be oriented in practicable way toward solving health problems. They should be thoughts that challenge conventional assumptions...

There are four topics this round; two are repeats.

- Create New Technologies for Contraception – to meet unmet demand worldwide. Current technologies do not address needs adequately.
- Create New Ways to Induce and Measure Mucosal Immunity (repeat)
- Create Low-Cost Diagnostics for Priority Global Health Conditions (repeat)
- Create New Ways to Protect Against Infectious Disease – this topic is the most wide-open and free-flowing. Their philosophy is that they realize vaccines are the most of effective tools in history. They have an interest in things that produce that effect but don't work like vaccines do.

Q & A with Gates Foundation Program Officer

Q. What happens after the \$100k is spent, next step?

A. First \$100k is for the first critical experiment (no stipulation on project timeline, but often a year or 18 months to some outcome). Once investigator achieves positive results with first experiment, they have the opportunity to apply for another grant of up to \$1m. Beyond that, it's hard to say. Government funds. Gates funds. Industry partnership. No specifics are in place.

Q (Doug Nixon): Within Gates, do you have a program that links exploration grants to your other grants? Are grants channeled to bigger programs?

A: They are looking at how to connect the grantees to other programs. For instance, Nixon's project had visibility within gates staff there. As part of phase 2 process, Nixon's grant will be reviewed as part of HIV portfolio. Also, they consider having a "fair" for explorations grantees to meet Gates staff and other partners. Finally, they are looking at making a planning or business development service available for Exploration grantees.

Q: With each round, how do you determine what will be the topics?

A: They have mechanisms to ask public what are most important topics. They ask applicants what they would like to see. The philosophy of topic construction: keep in mind medical need or specific outcome. For example, mucosal immunity is a specific biological outcome they would like to see. They don't specify pathways to that outcome. They paint a broad frame, then rule out processes that are already in use.

Q: Is Bill Gates a reviewer?

A: Bill Gates has been a reviewer. Also, one of early HIV topics was initiated by Bill.

Q: What % of phase 1 grants will go into phase 2?

A: The bar is pretty high. They anticipate substantial attrition from phase 1 to phase 2. Possibly they will fund 15-20% of phase 1 grantees in phase 2. They have also gotten substantial interest from governments—both in US and other countries (Canada)—in partnering around phase 2 type funding.

Q: How many reviewers read phase 1?

A: Fourfold coverage is the standard. Depends on specific application and on the number of applications they receive. Of note: A significant # of applications get selected by multiple reviewers.

Q: How directly translational do you want the ideas to be? Immediately, in a few years, down the road?

A: There is no one answer to that question. They leave it open for reviewers to select the most promising ideas. It could be basic mechanistic study that opens the way to a whole new field, to a new class of compounds, vaccines, etc. Many grants do that kind of basic study. But those studies must be oriented in some way toward a health solution. It doesn't have to be in clinical trials in the next 5 years, but it must have relevance for a potential health impact in the developing world. The range of topics has gone from novel interior design for house dwellings, all the way to basic research.

Q: The application is 2 pages. How important is it to address how this will result in a health solution in the application form.

A: This is the first thing in the application that you should talk about: state your vision for how this is something that matters and is potentially transformational. It doesn't have to be footnoted, long, annotated, but has to be compelling statement of your vision. What is innovative, unconventional; how will it make current products obsolete, how refute dogma?

Q: How many of your applications are likely to be re-worked version of stimulus requests, and do you expect a large pool?

A: If we got 30,000, it would be difficult to work through them, but we will review all.

Q: If you get a fantastic crop, will you put more money in the pot?

A: We're flexible. We like to see great ideas.

Panel Presentations

Joe DeRisi, PhD, Department of Biochemistry and Biophysics/HHMI

Received a grant in round 1, was a reviewer in round 2. He took the opportunity to roll out an idea he wouldn't dare talk about with colleagues. With Jane Kohler. The idea was to use arthrotropic bacteria (sp?) to fight malaria. Bartinella (sp?) kills malaria. But it's hard to work

with, manipulate genetics. The wacky part is that no one likes the idea of injecting people with bacteria. Gates let him examine it.

On reviewing: Grantsmanship matters. A 2-page stream of consciousness application will not work. State succinctly and clearly what is innovative, how this is different, how a game changer, what's your deliverable. If he can't ascertain that in 5 minutes and get that this is a cool idea, he's past it. Summarize your idea in 2 sentences at beginning. If it can't be summarized there's going to be trouble.

Note: don't spend your application reciting how great your lab is. It wastes space, compromises anonymity.

Dennis Hartigan-O'Connor, MD, PhD, AIDS Biology Program of the AIDS Research Institute and Division of Experimental Medicine

He submitted in round 1, received an award. Submitted in round 2, did not get an award. The absence of focus on who applicant is, what your CV is, is great to a young PI. There is no space to put your name. The application process is disconnected from web sign-in. Applications are evaluated *on merit!* Advice: write what you want to write, about the idea. The worst part of process = no feedback.

Bryan Greenhouse, MD, AIDS Biology Program of the AIDS Research Institute and Division of Experimental Medicine

He won a grant for a malaria project – elimination sites, to go from a few thousand cases to 0. Questions: Are cases being imported, what are transmission networks, how to reduce transmission to 0? It was great to have anonymity. You can be disqualified for including any info that identifies you.

Put in bold face in two sentences up front what you will do. He applied in round 2, was unsuccessful, reapplied round, 3 was successful. He didn't change the idea. The changes were in how he sold it. He got feedback from colleagues. Made the idea sound bigger, addressed what could come of this. Looked at round 2 grantees: "Some of what got funded sounded like science fiction." So he bumped up the language – made it seem potentially more innovative.

Mike McCune, MD, PhD, AIDS Biology Program of the AIDS Research Institute and Division of Experimental Medicine

He received a grant in round 2; was a reviewer for the program twice.

Reviewers get 2 big books of as many as 400 applications You get 1 champion card and five recommend cards. So you assign your #1 card to one of those 100-400 applications.

Advice: The title has to grab you, otherwise he will pass to next one. You have to address why this would not funded by anyone else including your mother. This is an opportunity to float ideas "you wouldn't discuss in polite company" Ideas are bold but can be outlandish. Say why it's innovative. Why dramatic. Why a big idea. DeRisi adds: "Say WHY it isn't fundable by others, not just THAT it isn't fundable by others."

Make it perfect so that the reader will continue to read. Otherwise they won't trust you can execute. Easily seen. Enough words, not too many. Deliverable at end of year should be included. You want to get to the "lottery" stage when the reviewer is choosing among his/her top 15-20 applications.

Mention milestones in your application – make it sound like it's something you can *do*. However, don't mention *obvious* milestones, rather what would success look like.

Douglas Nixon, MD, PhD, AIDS Biology Program of the AIDS Research Institute and Division of Experimental Medicine

Works in HIV. Got funding in round 1. His idea: make HIV vaccine without using any HIV antigens in vaccine. They had a small amount of preliminary data to go to phase I grant. He presented his data at conference, where he met a colleague who has done experiments and has some supporting data. Nixon's phase 2 application will be in concert with this colleague.

He submitted unsuccessful applications for rounds 2 & 3; will apply for round 4. Keep applying!

Erik Lium, PhD, Director, Industry Contracts Division and Interim Director, Contracts & Grants

Follow UCSF OSR procedures.

OSR would need to complete agreement with Gates by April 2010. You should aggressively pursue human subjects protocol to meet deadline.

Terms and conditions are a challenge that will be worked through – broad copyright, broad indemnification, governing law = state of Washington.

It is important to consider your intellectual property as you complete application as well as report. If you will disclose something you think will be an invention, work through office of contracts to protect your intellectual property.

Q & A For Panel

Q: How much time did you spend reviewing?

A:

DeRisi started with 10 mins per using stopwatch. As it went on, he spent 5 mins. Finally 2 mins. If he couldn't get it in 2 minutes, it was discarded. Then he went back over the ones that were not discarded.

McCune: The first time he spent 10-15 mins per, got tired, would flag those that were of interest, rip out those that weren't.

The second time, he limited himself to a couple of minutes per. He flagged 50 that he went over. Finally he felt comfortable with 6. He struggled with #1 flag. The last 10-20 were difficult to decide. This was "the lottery" – that's where you want to be.

Q: Are there any applications accepted outside topics? My ideas may not be in the topics.

A: The reviewers saw no off-topic stuff. (Although they had off-kilter stuff.) There must have been an initial review by Gates staff to screen for topic appropriateness.

Q: How do you as a reviewer champion a grant?

A: You assign your #1 card. The card has place where you can briefly write your impression. They don't ask for much info. It only takes one reviewer's champion card to win a grant.

Closing: Greenspan

Show of hands of people in the room who plan to apply for a phase 1 grant.
Some 15-20 hands were raised.

Grand Challenges Exploration Program Background Information

The Grand Challenges Exploration grant program fosters innovation in global health research. The Bill & Melinda Gates Foundation has committed \$100 million to encourage scientists worldwide to expand the pipeline of ideas to fight our greatest health challenges.

The grant program is open to anyone from any discipline, from student to tenured professor, and from any organization - colleges and universities, government laboratories, research institutions, non-profit organizations and for-profit companies. The initiative uses an agile, accelerated grant-making process with short, two-page applications and no preliminary data required. Applications are submitted online, and winning grants are chosen approximately four months from the submission deadline.

Initial grants of \$100,000 are awarded two times a year. Successful projects have the opportunity to receive a follow-on grant of \$1 million or more. Three rounds are complete. Round four is open now, and more rounds are likely.

Andrew Serazin, DPhil

Program Officer, Global Health Discovery
Global Health Program
Bill & Melinda Gates Foundation

Andrew Serazin serves as a program officer on the Global Health Discovery team at the Bill & Melinda Gates Foundation. Andrew received his doctorate degree for his work on genomic aspects of antigenic variation in *P. falciparum* in 2006 from the University of Oxford, where he was a Rhodes Scholar at Balliol College. He has gained valuable experience in Africa as a visiting researcher at the Kenya Medical Research Institute in Kilifi, Kenya; the University of Witwatersrand in Johannesburg, South Africa; and the Centre National de Recherche et de Formation sur le Paludisme (CNRFP) in Ougadougou, Burkina Faso.

Outside the research environment, Andrew has also explored the linkages between medical science and public policy as a delegate to the UN World Summit on Sustainable Development in 2002 and served as an intern at the National Institute for Health Care Management. His work on both parasite and vector biology has been presented at many international meetings and in peer-reviewed journals, including a first-author publication in *Science* magazine. Immediately preceding his employment at the Foundation, Andrew held the position of Lecturer in Biology of Disease for the Zoology Department at University of Oxford.