

**SEATTLE POST-INTELLIGENCER**

[http://seattlepi.nwsource.com/national/278187\\_aidsvaccine20.html](http://seattlepi.nwsource.com/national/278187_aidsvaccine20.html)

**\$287 million to break AIDS vaccine logjam**

**Gates grants will take science off 'usual' path**

*Thursday, July 20, 2006*

**By TOM PAULSON**  
P-I REPORTER

Science "as usual" has become something of an obstacle in the search for an AIDS vaccine, so the Bill & Melinda Gates Foundation is awarding \$287 million over five years to 16 research teams -- four of them in Seattle -- that have agreed to collectively veer off the beaten path.

"These grants bring together some of the best minds from around the world, more than 165 investigators from 19 countries," Dr. Nick Hellmann, interim director for the HIV/AIDS program at the Gates Foundation, said Wednesday.

HIV GRANT RECIPIENTS  
- [List of organizations to pursue HIV vaccine](#)

It is the largest single donation for an AIDS project by the Gateses and comes shortly after Melinda Gates, at last month's event announcing Warren Buffett's donation of his own billions to the Seattle philanthropy, said that her "fondest dream" is for the Gates Foundation to help find an effective HIV vaccine.

Many of the Gates grant recipients are some of the most established names in the HIV vaccine research establishment -- and, as such, responsible for business as usual. But it is what they are planning to do now and how they plan to do it that is intended to blast through a scientific logjam that nearly everyone agreed has been hampering progress.

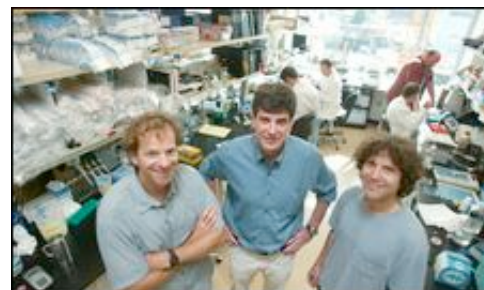
To begin with, the participating researchers all have to collaborate fully -- sharing raw data and even experimental materials -- rather than continue to compete as independent labs.

"Scientists, like artists, prefer to go their own way and do their own thing," said Dr. David Ho, one of the world's top AIDS researchers and director of the Aaron Diamond AIDS Research Center in New York City.

Ho, a maverick researcher who championed the anti-HIV medications known as protease inhibitors credited with preventing the deaths of millions of people with AIDS, will receive a \$24.7 million Gates grant to investigate the critical but incompletely understood role of fundamental immune system cells known as dendritic cells.

"This is the kind of high-risk research that others, like NIH (National Institutes of Health), won't fund," Ho said.

Other examples of high-wire AIDS vaccine science getting Gates support: British researchers will receive \$25.3 million to study some unique antibodies made by llamas; Swiss scientists will get \$15.3 million to test an altered poxvirus as an AIDS vaccine; and a Seattle



 Paul Joseph Brown / P-I

Dr. Leo Stamatatos, center, in his lab at Seattle Biomedical Research, is an HIV grant recipient. With him are UW researchers Bill Schief, left, and David Baker, right, who will be working with him.

team will get \$19.4 million to create computer-designed synthetic proteins that will be tailored to thwart HIV's deadly ability to evade immune system detection.

"I'm kind of new to this whole vaccine thing," acknowledged a wild-haired David Baker, a University of Washington biochemist who rapidly has gained international renown for his innovative work in computerized protein analysis.

"Using computers, one can design proteins to elicit reactive antibodies," said Dr. Leo Stamatatos, an HIV/AIDS expert at Seattle Biomedical Research Institute and lead investigator on the Gates grant. Stamatatos recruited Baker and his UW colleagues to assist with the ambitious project because of their expertise at handling gargantuan analytical tasks.

Baker is the creator of a "distributed computing" network known as Rosetta@home (modeled after the extraterrestrial-seeking SETI@home), which recruits volunteers around the world willing to allow their home computers to be harnessed occasionally for crunching massive amounts of data needed to analyze and predict protein shapes and behavior.

"One of the single biggest limiting factors (in the field of protein analysis) has been the lack of adequate computing power," Baker said.

Similarly, Stamatatos said, one of the biggest problems preventing researchers from identifying the proteins that might provoke an antibody response to HIV has been this inability to rapidly examine and test many different kinds of proteins.

"With this grant, we're going to be able to test more than 200," he said. Baker's program also will allow them to create "from scratch" novel proteins that, based on their sequence and structure, might be expected to prompt an immune response, Stamatatos said.

There are two basic arms to the immune system. One is the antibody, or humoral, response; the other is known as the cellular response. Because of HIV's ability to rapidly change its genetics and disguise its foreign nature from the immune system, nobody in the past two decades of AIDS vaccine research has been able to figure out how to provoke a meaningful antibody response to the virus.

This failure led nearly all scientists to play it safe and focus only on trying to create AIDS vaccines that can elicit a cellular response, Stamatatos said, even though everyone agrees an antibody response is likely going to be needed as well.

As one expert suggested: It's been a bit like the joke about the drunk who looks for his lost keys under the streetlight, rather than back in the dark alley where he dropped them, because the light is better. The \$287 million in Gates grants aims to encourage AIDS vaccine researchers to go back into the dark alleys and even into some new dark corners.

"This is going to push the science according to a more industrial model," said Dr. Seth Berkley, president of the International AIDS Vaccine Initiative, which will receive a \$23.7 million Gates grant to explore new approaches to vaccine delivery.

It's a lot of new money, Berkley said, but still not nearly what is needed to get ahead of the global epidemic.

Of the 16 Gates grants, five go to research teams like the one led by Stamatatos searching for neutralizing antibodies while six go to scientific consortia focused on novel attempts at making progress with an AIDS vaccine that stimulates a cellular response.

"It's clear we need both," said the Gates Foundation's Hellmann.

Dr. Jose Esparza, an AIDS expert at the Gates Foundation, said a major goal is to accelerate progress by requiring an unprecedented level of collaboration and laboratory standardization.

"We're really trying to push the envelope on that," said Esparza. Today's lack of collaboration and standardization between labs evolved passively because of how science has been funded, he said, so the Gates Foundation is putting money into actively redirecting this trend back in the direction of bringing everyone closer together.

"The HIV vaccine field has lacked a shared, focused strategy," agreed Dr. Julie McElrath, a top HIV vaccine scientist at the Fred Hutchinson Cancer Research Center and UW who is principal investigator for a \$30.1 million Gates grant exploring the molecular basis of "adjuvants" -- substances added to vaccines that stimulate immunity.

"There's no question these grants will transform how HIV vaccine research is going to be conducted," McElrath said.

Two of her colleagues at the Hutch, Drs. Phil Greenberg and Steve Self, will be in charge of much of that transformation. Greenberg received \$10 million to standardize how experimental vaccines are evaluated in mice. Self got \$9.9 million to establish the project's centralized data repository in Seattle.

One of the big unanswered questions in this project is how industry will react to the Gates Foundation's demand that all data and products be shared immediately -- and that the vaccine be guaranteed accessible to the world's poorest people.

All of the Gates grant recipients had to submit their own "global access strategy" for addressing these concerns, Hellmann said.

But he acknowledged that it's still not clear how this will always play out once a promising experimental AIDS vaccine gets to the stage where industry needs to take up the baton of testing, large-scale manufacturing and distribution.

Ho also expressed concern that the Gates Foundation could, if it's not careful, end up exacerbating the problem these grants are meant to solve.

"You never want to do science by committee or consensus," he said, because this tends to stifle innovation.

Yet the goal of the Gates grants to unify the field of HIV vaccine research, prompt more collaboration among scientists and standardize the methods could devolve into a narrow, consensus-driven game plan.

"There is always a risk of group think," Ho said.

---

*P-I reporter Tom Paulson can be reached at 206-448-8318 or [tompaulson@seattlepi.com](mailto:tompaulson@seattlepi.com).*

© 1998-2006 *Seattle Post-Intelligencer*