

Tackling disease head-on

New US institutes are springing up as the search for a vaccine to combat AIDS intensifies

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Emergency aid

A new initiative promises to deliver vaccines to the frequently overlooked developing world

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Vaccine centres unite specialists in the battle against infectious diseases

The race to produce an AIDS vaccine is just part of the story at some major new research centres working to develop vaccines, says Diane Gershon.

In May 1997, US President Bill Clinton challenged the scientific community to develop an AIDS vaccine within a decade. This intensified effort included the creation of the Dale and Betty Bumpers Vaccine Research Center at the National Institutes of Health in Bethesda, Maryland.

The new building for the centre is now all but complete and will be officially opened in spring 2001. The five-storey glass building, costing between \$35 million and \$40 million, has around 5,100 square metres of space, four research floors, a Biosafety Level-3 (BL-3) containment facility, conference rooms, a vivarium and a cybercafé. It is open and airy, with lots of common areas to facilitate interaction between staff, who — although drawn from an array of disciplines — are directed towards a common purpose.

“We really want to capture under one roof the different aspects of vaccine science. Our investigators start as basic as X-ray crystallographers, and go as applied as AIDS vaccine clinical trials specialists, and everything in between,” says the centre’s director Gary Nabel, whose own earlier research interests were in HIV gene therapy and DNA-based therapeutic vaccines for cancer.

Although the primary goal is to develop an AIDS vaccine, he says, “we do have a broader mission, which is to advance vaccines for all diseases”. Nabel, for example, continues to work on developing a vaccine against the Ebola virus. As he points out, what is learnt with other diseases could help the research into AIDS, and vice versa. The challenge in the early years, he says, will be in striking the right balance.

Jointly funded by the NIH’s National Institute of Allergy and Infectious Diseases and the National Cancer Institute, the centre had a bud-



Work in progress: two new vaccine development institutes are hunting the elusive AIDS vaccine — the Vaccine and Gene Therapy Institute at Oregon Health Sciences University (top) and the National Institutes of Health Vaccine Research Center (left).

get of \$26 million for fiscal year 2000, although “that number needs to rise as we fill the centre”, Nabel says. It will focus on the preclinical and early clinical stages of development and will work closely with the newly created HIV Vaccine Trials Network, which will conduct all phases of clinical trials and replaces the AIDS Vaccine Evaluation Group (AVEG) and the HIV Network for Prevention Trials.

Newly appointed clinical director Barney Graham will be the centre’s main link to the vaccine trials network, having had more than 10 years of experience with the AVEG. “We will conduct early-stage trials on the NIH campus, mainly so we can learn more scientifically about the immune responses in people, but there will be a passing of the baton

from us to them as we identify our more promising candidates,” says Nabel.

The centre will also do research with non-human primates to glean “meaningful information about protection, about the character of the immune responses, and any possible correlates in between,” says Nabel. What is learned in humans and primates will then be used to choose vaccine candidates for more advanced clinical testing. The earliest candidates will probably be DNA vaccines, says Nabel.

Mario Roederer, director of the centre’s flow cytometry laboratory — and, like almost all the core staff, recruited from outside the NIH — says the new post “gives me the opportunity to bring my technology to a much larger group of scientists, and to apply



Gary Nabel is focusing research on AIDS.

NIH

OHSU

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▶ this technology to clinical settings, specifically clinical trials and vaccine trials”.

Even when all the key individuals are in place next spring, there will be spare capacity to allow for future growth and visiting scholars. Although there are no plans at this point to hire any more tenure-track researchers, there will still be a need to recruit staff scientists, postdocs and graduate students.

When asked whether he feels the clock ticking, Nabel says he sees the ten-year time frame more as a point by which the scientific community should be able to say whether a vaccine is a viable approach to containing AIDS. “My guess is that there will be some kind of a vaccine within that time-frame but I don’t know whether it’s going to be the optimal vaccine, because the [clinical] trials take so long.”

Vaccines beside gene therapy

Oregon Health Sciences University (OHSU) — noting that the tools and resources needed for vaccine development have much in common with those of gene therapy — has established a new institute that will span both areas, in a cooperative venture with the Oregon Regional Primate Center.

Although the university had staff with expertise in vaccine development and gene therapy, “the idea was to create a critical mass that would be located in one place”, says Jay Nelson, director of the new Vaccine and Gene Therapy Institute, who has been recruiting heavily over the past year.

In February, the institute will move to a new \$35-million building on OHSU’s new campus in Hillsboro. This will provide 1,800 square metres of laboratory space, 900 square metres of animal facilities, plus four BL-3 and eight BL-2 containment facilities. The institute is next-door to both the primate centre and the Oregon Graduate Institute, which is merging with OHSU. Its strengths in computational science and chemistry complement the functional-genomics aspects of the new institute.

The first phase of recruitment for the new institute has been in vaccine research, with eight of nine core faculty slots already filled, and recruitment continuing at the graduate, postdoctoral and research associate level.

The first new recruit was Louis Picker, director of the institute’s vaccine programme. Picker, who studies T-cell biology in human and non-human primates, will be working on prophylactic and therapeutic vaccines against HIV, its primate equivalent (SIV) and cytomegalovirus. Klaus Früh, director of the institute’s functional-genomics centre, will use approaches such as DNA microarrays, proteomics and laser-capture microscopy, to look at how viruses infect cells.

The next phase of expansion for the institute will be to build up a programme for gene therapy alongside the vaccine programme. ■

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JORGEN SCHITTE/STILL

Developing countries and poorest people targeted by UN centre

Almost a third of all deaths worldwide are caused by infectious diseases, with developing countries being the hardest hit. Although vaccines can be effective against such diseases, vaccine development is a lengthy and costly business. To obtain a return on their investment, companies often sell vaccines at prices that are beyond the reach of developing nations. Moreover, the dire economic situation of many of these countries gives companies little incentive to develop vaccines specifically for the developing world.

In October 1997, the United Nations Development Programme, recognizing the need for more research in this area, launched the International Vaccine Institute (IVI) to speed up the introduction of vaccines to developing countries. The Pacific Rim was targeted as a potential location for the new independent, non-profit institute because it had countries with the necessary scientific infrastructure but was also close to poorer countries, says John Clemens, who became IVI director in July 1999. The South Korean government made a successful bid to host the new institute, which is located in temporary accommodation at Seoul National University.

The IVI is holding off on most of its laboratory activities until construction of a new research facility and vaccine pilot-plant is complete in 2002. Consequently, much of the institute’s effort has so far centred on clinical and field activities in the applied vaccine sciences. The initial focus has been on tackling Asian public-health problems, such as enteric diseases such as enterotoxigenic *Escherichia coli*, shigellosis, typhoid fever and cholera; respiratory infections such as *Haemophilus influenzae* type B and pneumococcal disease; and vector-borne diseases such as Japanese encephalitis. But Clemens, who has worked on vaccines for developing countries for 20

years, hopes soon to turn attention to sub-Saharan Africa with the IVI’s Diseases of the Most Impoverished project. This will target cholera, dysentery and typhoid fever with support from a five-year \$40-million grant from the Bill and Melinda Gates Foundation.

IVI staff are currently conducting some basic research into *Shigella* vaccines — “a very appropriate niche for an institute like ours”, says Clemens. *Shigella* attracts very little industrial interest, he says, although it causes more than one million deaths each year in developing countries. The IVI has no plans to develop vaccines commercially, but will strengthen ties with industry and other public-sector organizations to push promising candidates through to clinical practice.

At present the institute has fewer than 40 staff, but eventually Clemens expects to have 200, a quarter of whom will be scientists. He hopes soon to recruit a deputy director of the institute for the laboratory science programme. Most of the scientists recruited to date are biostatisticians, clinical epidemiologists and data managers. As the new laboratory space nears completion, the IVI will also begin recruiting staff with expertise in vaccine production, process research, molecular genetics (particularly microbial genetics), human immunology and microbiology.

Scientific appointments are for fixed terms — something that Clemens says is typical of international research institutes. Clemens himself is on a five-year contract, on leave from the US National Institutes of Health. Jobs in international institutes tend to attract people who “see the uniqueness of the professional opportunity for productivity”, says Clemens. “Most people who come to work at an international institute would not do so with the idea that this would be their life-long career,” he says. **D.G.**