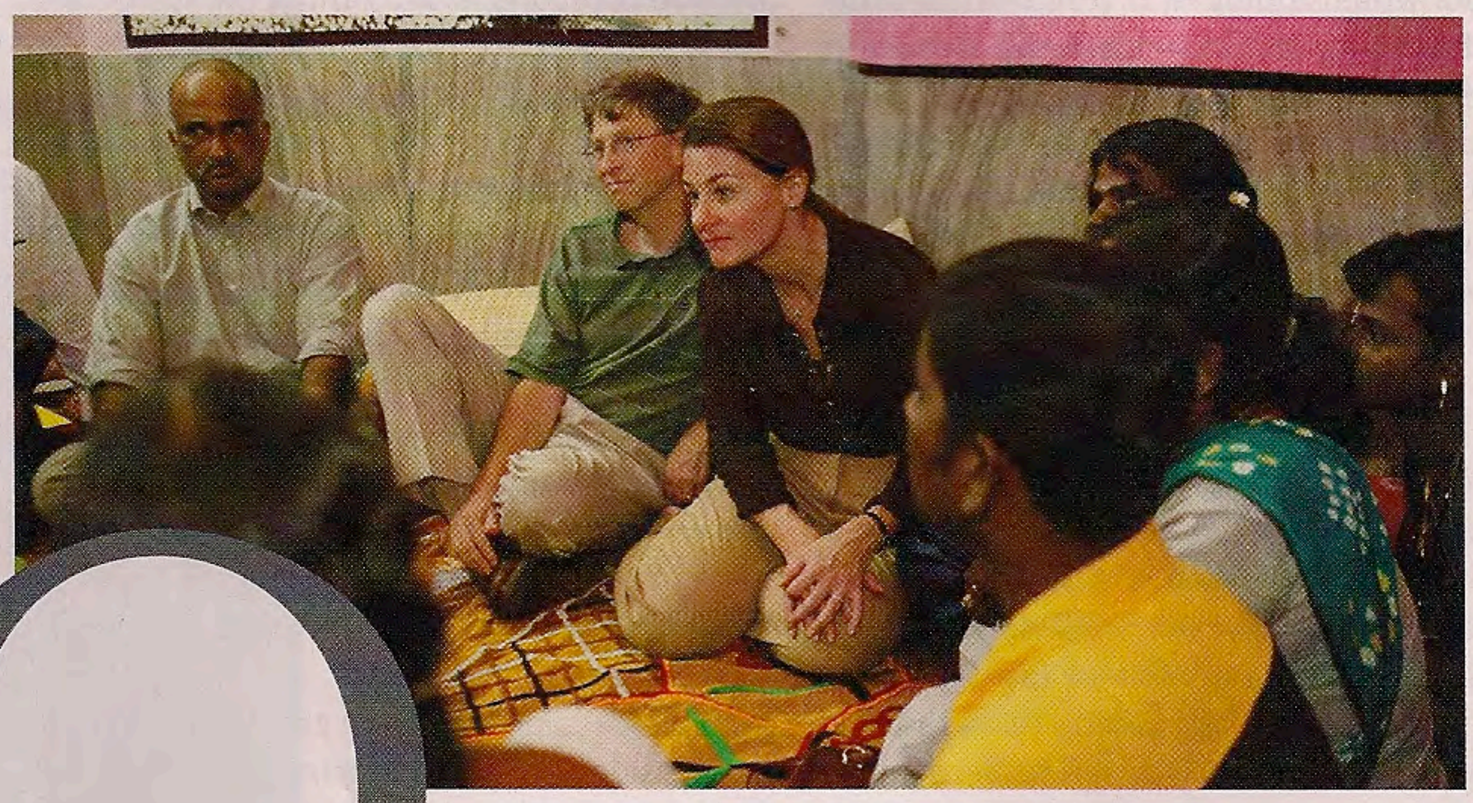
WASHINGTON CEO



Bill and Melinda Gates on a 2005 global health learning mission in India.

A WORLD WITH NO DISEASE?

Science, business and philanthropy join to fight disease worldwide

By Sally James

The key to fighting malaria might come from Westlake, where the Seattle Biomedical Research Institute has one of the world's largest malaria laboratories. The center for the worldwide testing of HIV vaccines is in Eastlake's 1600 building, above a bakery. But that's not all. Add the University of Washington, which just created a new department of Global Health; the Fred Hutchinson Cancer Research Center; the nonprofit PATH, in Ballard; and a constellation of other laboratories that are all working on research from Burkina Faso to Beijing.

Once you know what goes on inside these buildings, Seattle may never seem the same. When you are stopped at a light on Westlake Avenue, you might close your eyes, tune in to an imaginary wavelength and hear a high-pitched whine from a colony of mosquitoes, whose cousins bring malaria to millions. Not far away, on Eastlake Avenue, your antennae might sense the weary frustration of workers fighting the HIV epidemic that threatens to orphan children in much of southern Africa. And when you are stopped at one of Eastlake Avenue's lights, you may hear Ghanian drummers and the plucking of Indian sitar strings.

Last summer, a Harvard global health expert told a National Public Radio interviewer that we have entered a golden age in global health research, where problems once thought intractable are now considered solvable. The dramatic turnaround was stimulated in large measure by the philanthropy of the Bill and Melinda Gates Foundation, which the Gateses founded in 2000 and now has assets of about $32 billion. That amount does not include the $31 billion Warren Buffett committed to the foundation last summer. Of course, by the time Buffett made his surprising announcement, the Gates Foundation was already one of the most powerful agents for change worldwide, and it had made global health a top priority from the beginning.

Yet many Seattle institutions have been working on global health issues since the 1970s, including a strong department of infectious diseases at the University of Washington and two nonprofits: PATH (originally called Program for Appropriate Technology in Health) and SBRI, the Seattle Biomedical Research Institute. Moreover, many Seattle scientists had major careers studying infectious diseases before Bill Gates became famous.

All this rich history, combined with fuel from the Gates Foundation money, has meant that Seattle now joins a handful of cities where global health policy is made.

In the 1970s King Holmes began working at the University of Washington doing research on sexually transmitted diseases and viruses. In those days, sex and viruses were not linked to the AIDS epidemic. Holmes became an expert on the human immunodeficiency virus (HIV), and he was recently named the chair of the new Department of Global Health, created last year as a joint effort of the UW's School of Public Health and School of Medicine. The new department has received seed money from the Gates Foundation.

Chris Elias came to Seattle just six years ago. He is now the president of PATH. Global health "has been around, underfunded and politi-

TOP: COURTESY BILL AND MELINDA GATES FOUNDATION / PRASHANT PANJIAR; OPPOSITE: CLOCKWISE FROM TOP LEFT: BILL AND MELINDA GATES FOUNDATION / COURTESY FRED HUTCHINSON CANCER RESEARCH CENTER; COURTESY UNIVERSITY OF WASHINGTON; COURTESY FRED HUTCHINSON CANCER RESEARCH CENTER

SEATTLE INSTITUTIONS ADVANCE WORLD HEALTH

VILLAGE REACH www.villagereach.org

- Saves lives in developing countries like Mozambique by improving access to vaccines and other essential health services.

PATH www.path.org

- An international nonprofit created in 1977 that works with communities worldwide to develop sustainable solutions to break cycles of poor health. With 450 employees, it has its main offices in Ballard and branches in 14 other countries.

- Christopher J. Elias, M.D., M.P.H., president
The leader of PATH for six years, during which the organization has almost tripled in size. He formerly worked for the Population Council.

SEATTLE BIOMEDICAL RESEARCH CENTER www.sbri.org

- A nonprofit founded in 1976, the center has more than 200 staff members working in labs in Seattle and in Tanzania. One of their main projects is understanding and trying to combat malaria.

- Kenneth Stuart, Ph.D., president
Stuart co-founded the original lab in 1976 in Issaquah. His own research centers on understanding single-celled organisms that cause disease.

UNIVERSITY OF WASHINGTON DEPARTMENT OF GLOBAL HEALTH http://depts.washington.edu/deptgh

- A work in progress, it is a shared venture between the existing School of Medicine and the School of Public Health, kick-started by a $20 million grant from the Bill and Melinda Gates Foundation. The department will focus on identification and evaluation of health problems in underserved populations and develop ways of reducing the burden of disease.

- King Holmes, M.D., Ph.D, chair
Before becoming Global Health chair, Holmes was founding director of the Center for AIDS & STD at the UW, which grew to one of the world's leading AIDS research and training institutions.

INSTITUTE FOR SYSTEMS BIOLOGY www.systemsbiology.org

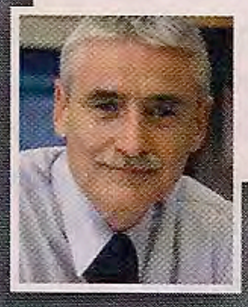
- The Institute takes a revolutionary approach to analyzing biological complexity and understanding how biological systems function. Promising technologies have spun off into start-up businesses, such as VLST Corp. and NanoString Technologies Inc.

BILL AND MELINDA GATES FOUNDATION www.gatesfoundation.org

- The Gates Foundation has an endowment of $31.9 billion and a long-term commitment from investor Warren Buffett that will at least double the size of the foundation's giving over the coming decades. One of the Gates Foundation's major goals is to eliminate such killer diseases as malaria, AIDS and tuberculosis. It is a major source of funds for other Seattle organizations.

FRED HUTCHINSON CANCER RESEARCH CENTER www.fhcrc.org

- A nonprofit biomedical-research institution opened in 1975, and one of 39 National Cancer Institute-designated comprehensive cancer centers. Three Nobel laureates are among the estimated 2,300 employees.



- Lee Hartwell, Ph.D, president
The leader of the Hutch for about a decade, Hartwell won the Nobel prize for his discoveries about genetics.

INFECTIOUS DISEASE RESEARCH INSTITUTE www.idri.org

- IDRI, founded in 1993, identifies scientific leads for vaccines, diagnostics and therapeutics, and develops those leads into products that can be produced in countries that need them. IDRI has developed a tuberculosis vaccine in partnership with GlaxoSmithKline. The vaccine is currently in trials.

At build-out, the future Gates Foundation headquarters near Seattle Center, a 15-year project, may include some 800,000 square feet of floor space and house as many as several thousand employees.

cally ignored for years," says Elias. But the way the public sees it has changed, and, perhaps more important, the notion that problems are too big to solve has changed. Elias adds that approaches to global health are "joining a cutting-edge business model with science and applying it to sustainable solutions. The challenge is reframing it so it isn't charity."

Nobel Prize winner Leland Hartwell, president of the Fred Hutchinson Cancer Research Center, sees a big change in how the public sees the world, which, eventually, might mean a change in how the world sees Seattle. "I don't know quite how to get my finger on the pulse," he says, "but ... there's a groundswell of interest and commitment to public health." Calling it a quiet revolution, Hartwell says that younger scientists in particular seem very committed to working toward worldwide goals in fighting disease.

An increasing number of the Hutch's own research projects are aiming overseas. The center joined other organizations to conduct the second annual Pacific Health Summit in Seattle in June 2006, which gathered U.S., British and Asian political and health leaders to discuss mutual challenges, such as the avian flu threat.

One world health leader who knows Seattle very well is Helene Gayle, who is now the president and CEO of CARE, but once worked at the Gates Foundation. Gayle says that Seattle is not the equal of Atlanta or Boston in the sheer number of people working in global health, but that it is quickly catching up. "Over the next decade," predicts Gayle, "the city will rise in importance. The Gates Foundation will be a magnet, and other partners will develop." She called the change a subtle "shift in the center of gravity on the West Coast," as more and more policy influence resides in Seattle.

Tom Paulson, who has witnessed many of the changes, is a science writer for the *Seattle Post-Intelligencer*. He complains that much of what's happening remains largely invisible to the public. "It's goofy that Buffett's gift made people pay attention," remarks Paulson, pointing out that the Gates Foundation was the largest single donor to global health before the additional money drew headlines. The European press often covers global health issues more completely than the American news media, Paulson says. As an example, he cited British Minister of Parliament Gordon Brown's November effort to raise additional money for GAVI, the children's vaccine initiative, which had its origins in Seattle with the Gates Foundation. The announcement hardly made a blip in post-election U.S. headlines.

Money is a confusing part of the overall research picture. Money comes to institutions like the Fred Hutchinson Center and the University of Washington from hundreds of sources, including the National Institutes of Health and private foundations, such as the Gateses'. Measuring a city's research wealth is a complex equation.

U.S. research money, for the most part, doesn't get spent on diseases that are threats outside the country, such as malaria. So scientists working on those diseases need private foundation money. For example, in 1999, the Gates Foundation gave $5 million to SBRI to set up its malaria lab. Today, that lab has about 70 people, including scientists from Africa, Europe and Asia, who have come to learn the latest research techniques. The lab continues to receive Gates Foundation money. So besides the money coming in to Seattle research, money also matters as it flows out to others around the world in the form of new approaches to global health.

By some measures, according to Fred Hutchinson's Hartwell, Seattle's research funds rank with those of San Francisco and Boston. He says each city takes in roughly $2 billion per year in federal research grants. To illustrate Seattle's stature in research, an article in *The Scientist* magazine listed Seattle scientist Lawrence Corey as one of the top 20 recipients nationwide of National Institutes of Health monies in 2005. Corey is in charge of the largest HIV vaccine project in the world – one that encompasses 27 cities on four continents, coordinating clinical trials of experimental vaccines. Corey is affiliated with both the Hutch and the UW.

But Seattle does not yet equal Boston or San Francisco in the transfer of capital and entrepreneurial zest from the labs to new biotech companies. The city also does not have the aggregation of universities, endowments and alumni that exist in Boston and San Francisco. The only large pharmaceutical company presence in town is Amgen, which purchased the hometown biotech Immunex.

Alan Frazier of Frazier Healthcare Ventures calls Seattle one of the "dominant places in the research of diseases."

Last fall, one of Seattle's largest hometown biotechs, Icos Corp., laid off hundreds of employees as the giant pharmaceutical manufacturer Eli Lilly moved to take over the company.

For his part, venture capitalist Alan Frazier of Frazier Healthcare Ventures, which has offices in Seattle and Palo Alto, Calif., says he gets tired of people asking about the transfer of scientific assets from labs to new biotech companies. "People focus on the tech transfer," he said in an interview. "But the research itself is huge in this town. We are not a leader in biotech or devices, but we are one of the dominant places in the research of diseases and what to do about them."

Imagine the Space Needle with a giant spotlight pointed at the night sky. Every night, the brightness is calibrated according to how much grant money the Gates Foundation has given out.

TOP: COURTESY BILL AND MELINDA GATES FOUNDATION

When Buffett's gift was announced, it doubled that annual number from about $1.3 billion to $3.5 billion. But if the light is already too bright to look at, what impact does it have at twice the brightness?

To add perspective, National Public Radio producer Richard Knox related the Gates Foundation's annual giving to other global health expenditures. "That's $3.5 billion," Knox wrote in a report aired last June, "more than three times what the World Health Organization spends. But it's only a small fraction of the $80 billion the world devotes to drug and vaccine research and development, and it's a tiny fraction of the $400 billion the world's poor and middle-income countries spend on health."

During that same radio report, Knox asked Harvard's Chris Murray, an expert on global health, about the future. Murray said he worries that failure to deliver some big successes in global health in the next few years might result in a disappointment strong enough to close doors in the future. The next few years will show whether the brightness of its light changes how the world sees Seattle.

In one concrete way, the Gates Foundation is creating a symbol by building a headquarters near Seattle Center. The buildings are designed to provide some 800,000 square feet of floor space, and to house as many as several thousand employees (The Foundation currently employs about 320). One of the Foundation's most important recent hires is Tadataka Yamada, who was named president of its Global Health Program. Yamada is a former chief of research at the pharmaceutical giant GlaxoSmithKline. His experience is considered essential to speeding up vaccine development for diseases like malaria.

Seattle scientist Lawrence Corey is in charge of the largest HIV vaccine project in the world.

According to Hartwell, Corey and others, there is a difference between doing science here and elsewhere. In this city, scientists are perceived as part of a village, rather than as competitors, and their approach to problems is to comprehend them as equations, as codes, as challenges that can be analyzed and conquered. Seattle's medical research community includes Leroy Hood, who made his name as the inventor of technology that helped sequence DNA quickly. Hood, a superstar with 14 patents, won the 2003 Lemelson-MIT prize for innovation. Currently, he runs the Institute for Systems Biology in Seattle, where he hopes to redesign the way we think about biology.

If you were mixing Seattle science as a fragrance, it would have some of the cool calculation of software code and the woodsy notes of pioneer explorers. Mix in imagination and the paper smell of crisp new money.

Case in point: Hood, along with Leland Hartwell, joined with researcher and entrepreneur Stephen Friend in the 1990s to create the local start-up Rosetta Inpharmatics. Rosetta is now a subsidiary of Merck & Co. Friend remembers the 1990s as a particularly heady time in Seattle. He left Boston and joined the Hutch before moving on from there to Rosetta. "In Boston," he says, "the context in which new ideas were heard began with skepticism. In Seattle, the question was 'Why not?' instead of 'Why?'"

Rosetta created gene analysis hardware and software to give researchers a quicker way to evaluate vast data and find out key information for drug development. Friend remains president of Rosetta while he works for Merck in Pennsylvania, helping to set the strategy for cancer research and applying many of the Rosetta technologies to that work. From his inside-outside-insider view, he sees the giant pharma company as something he will slowly change.

"I thought how precious it was to have the chance to change the momentum in a place where the flywheels are so enormous," Friend says of his decision to join Merck. Thinking big, in medicine as well as in the public's view of the world, is a transition he considers new in the past five years. "Before then, I don't think people were allowed to dream at the global level," he said.

Maybe dreaming big is part of living in the shadow of Mount Rainier and the Olympic range. Many scientists say the beauty just outside the lab door is another reason they chose Seattle. Hartwell's bicycle occupies part of his office. Helene Gayle remembers fondly her hours in a kayak on the waters here.

Perhaps the most obvious question, when surveying the work that the Gates Foundation has supported in vaccine development, is whether our region needs some kind of vaccine-manufacturing facility. Chris Elias at PATH says something small, just the size to produce research-level amounts, might be nice. But he didn't say it was likely to happen, although Washington Gov. Christine Gregoire has staked some of her political capital on the Life Sciences Discovery Fund, which was created in 2005 and is supported with taxpayer money. The fund aims to make grants available within the state to grow the life sciences industry. Gregoire calls Seattle "one of the epicenters of global health research."

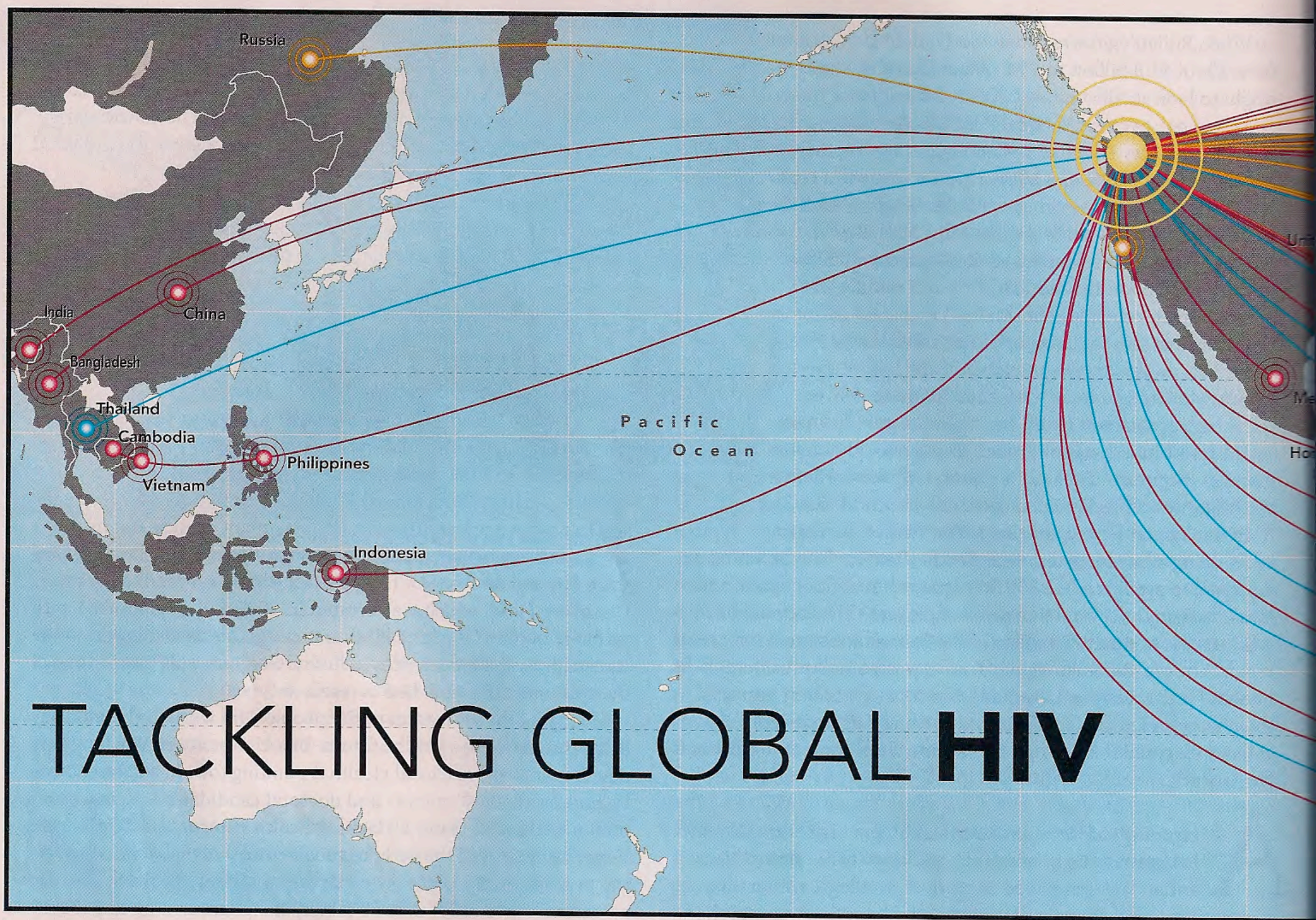
Changing the education of the people who work in the industry is another move toward the future. The University of Washington's new Department of Global Health is pointing toward a different way to educate medical doctors and doctoral candidates in science and public health. Jim Kim, a Harvard health expert, told *The Seattle Times* last year that the fledgling department might eventually raise the prestige of the UW above Harvard or Johns Hopkins. The department hopes to grow to 50 faculty members and up to 500 students. They also hope to organize work spread across many places in the city. One example from a planning document says 15,000 square feet of space is devoted to different HIV research projects all over Seattle.

Real estate, and the realities of business, are part of the special petri dish mixture of Seattle where global health research grows. People like multibillionaire Paul Allen have taken off on ventures that complement the research. Allen had a bold vision for a map of the human brain and financed an institute to create that in Seattle. He also has a bold vision for a map of a refurbished south Lake Union as a research center. Making money is one of the realities of American business, and that self-interest is just where professor Anne Marie Kimball finds the subject of her new book, *Risky Trade: Infectious Diseases in the Era of Global Trade*. She teaches in the UW School of Public Health. "Our health and safety here in Seattle," Kimball says, "depends on the health and safety of every country we trade with or travel to. If Indonesia has weak public health systems, whatever erupts there will be on a plane to Seattle very quickly."

In this gray winter, the tropical heat lingers in laboratories beside our city's rain-soaked streets. There is a bit of Indonesia in Ballard, a bit of India at SBRI, a bit of South Africa in the vaccine trials network. And the hopes of millions of children ride on the research that bubbles and hums all day and all night in the metro-global science center of Seattle.

Sally James is a Seattle-based reporter.

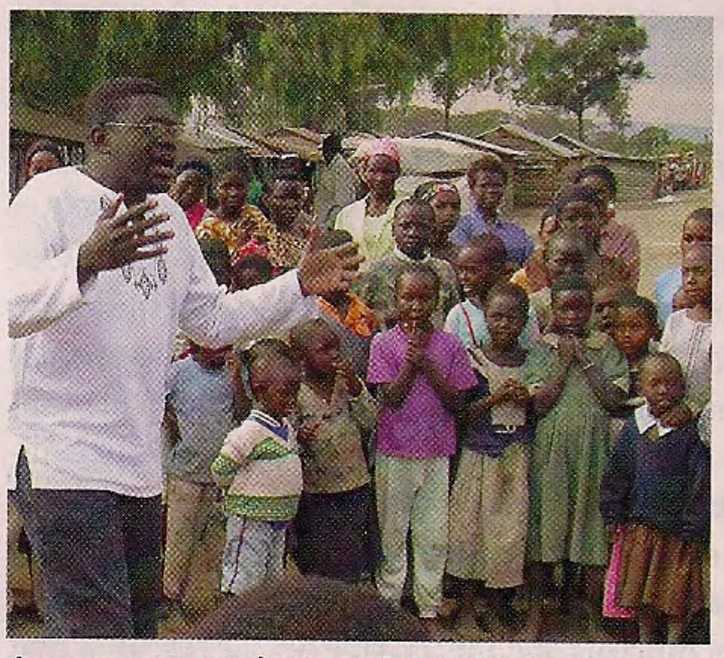
COURTESY: FRED HUTCHINSON CANCER RESEARCH CENTER



TACKLING GLOBAL **HIV**

Seattle institutions are playing a central role in the worldwide effort to fight HIV, focusing primarily on AIDS prevention and on work to develop an AIDS vaccine.

An estimated 15,000 square feet of office and laboratory space in Seattle is dedicated to fighting HIV/AIDS.



Actors at an outdoor market in Kenya dramatize HIV/sexual intimacy issues while the audience responds with questions, suggestions, and debate, in hopes of viable solutions.

PATH

PATH has a budget this year of $170 million, of which a portion goes toward operating HIV prevention programs in 44 countries: Bangladesh, Belgium, Bolivia, Botswana, Brazil, Cambodia, Chile, Colombia, Dominican Republic, Ecuador, Egypt, Eritrea, Georgia, Guinea, Guyana, Haiti, Honduras, India, Indonesia, India, Kenya, Mali, Mexico, Mozambique, Namibia, Nepal, Nicaragua, Nigeria, Pakistan, Paraguay, Peru, Philippines, Romania, Russia, Rwanda, Senegal and South Africa. The map does not include links to every country in which PATH does HIV work, nor does it include all regional offices.

FRED HUTCHINSON CANCER RESEARCH CENTER

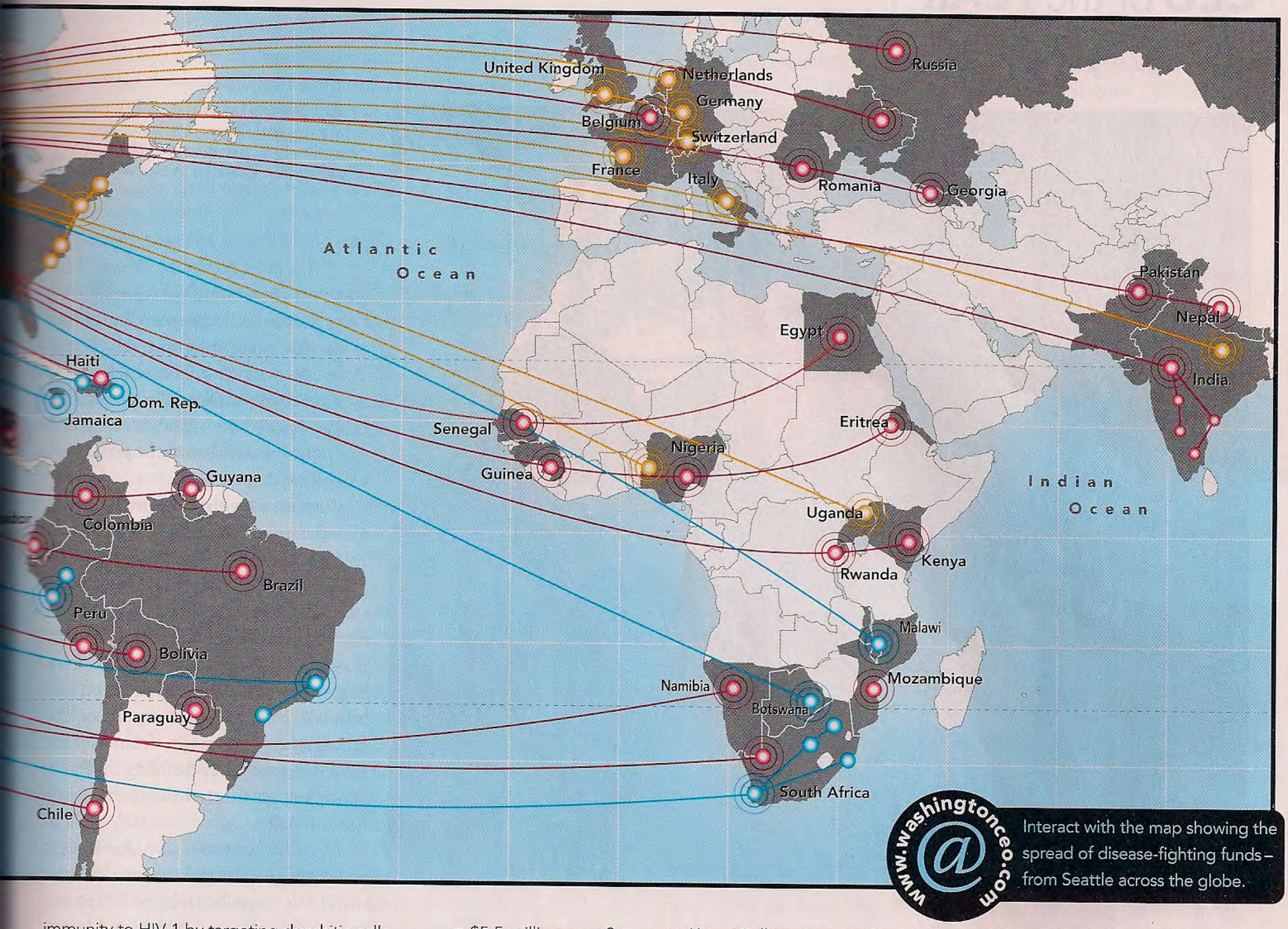
Fred Hutchinson Cancer Research Center manages a network of trial sites dedicated to the development and testing of preventive HIV vaccines. The sites are in Botswana, Brazil, Dominican Republic, Haiti, Jamaica, Malawi, Peru, South Africa, and Thailand. The Hutch has received $30 million over 5 years from the Gates Foundation to develop HIV vaccines.

THE BILL AND MELINDA GATES FOUNDATION

AIDS-related grants in 2006 included the following:

- $500 million to the Global Fund to fight AIDS, TB and Malaria based out of Geneva, Switzerland.
- $258 million for a community-driven HIV prevention program in the India states of Andhra Pradesh, Karnataka, Tamil Nadu, Maharashtra, Manipur and Nagaland.
- $33 million over 5 years to the Foundation for the National Institutes of Health, Bethesda, Md. to create a consortium of immune testing laboratories.
- $31 million over 5 years to Duke University, Durham, N.C., to establish a global laboratory network to benefit AIDS vaccine development.
- $23.7 million to the International AIDS Vaccine Initiative, New York, over 5 years to design HIV/AIDS vaccine candidates.
- 24.6 million over five years to The Aaron Diamond AIDS Research Center, New York, to develop a vaccine that elicits durable cellular and humoral

PATH



immunity to HIV-1 by targeting dendritic cells.

- $18 million to Beth Israel Deaconess Medical Center, Boston, over 5 years to develop vaccines for HIV-1.
- $15 million to Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, to develop a potential vaccine strategy to stop the HIV pandemic.
- $10 million over 5 years to the UW to define the qualities of an HIV vaccine that will make it sufficiently immunogenic to elicit protective responses in humans.
- $9 million over 5 years to Imperial College of London to use novel recombinant adenovirus vector technologies to develop an HIV vaccine.
- $8.4 million over 3 years to New York University to determine whether certain substances can induce antibodies that protect against HIV.
- $8 million over 3 years to Global Solutions for Infections Diseases, Brisbane, Calif., to acquire and disseminate information that will further the development of a safe and effective AIDS vaccine.
- $7.5 million over 3 years to the Fraunhofer Gesellschaft Institute for Biomedical Engineering of Ingbert, Germany, to develop a Global HIV Vaccine Cyrorepository.
- $5.5 million over 3 years to Kings College London to develop a safe, effective and affordable vaccine for the prevention and control of HIV/AIDS in developing countries.
- $4.4 million to support Global HIV Vaccine Enterprise.
- $1 million to International AIDS Society, Geneva, for global conference in Toronto of those committed to responding to the HIV/AIDS epidemic.
- $357,000 to Academic Medical Center, University of Amsterdam for AIDS Vaccine conference in 2006.

SEATTLE BIOMEDICAL RESEARCH INSTITUTE

SBRI is developing novel computational and biological approaches for the design and evaluation of HIV vaccine candidates. It has received $19.3 million over 5 years from the Gates Foundation to support the work.

UNIVERSITY OF WASHINGTON

The UW is conducting research to help define the qualities required of an effective HIV vaccine.

GLOBAL HIV VACCINE ENTERPRISE

An alliance of independent organizations around the world from India, France, South Africa, Italy, Uganda, Russia and the U.K., dedicated to accelerating the development of a preventive HIV vaccine.

In addition to its contribution to HIV research and prevention, the Gates Foundation has also given $104 million over 5 years for TB drug development; $32 million over 5 years to the Schistosomiasis Control Initiative in Africa; $28 million over 5 years for research in India, Peru, Uganda and Vietnam to reduce cervical cancer; $22 million for clinical trials in Congo, Sudan and Angola for an oral drug for early stage African sleeping sickness; $21 million for researchers in U.S., Europe and Kenya to develop drugs to treat typanosomiasis and leishmaniasis; $21 million to the International Vaccine Institute in Seoul, South Korea, to accelerate the introduction of cholera vaccines that will be field-tested in Dhaka, Bangladesh; and $14 million to the Sabine Vaccine Institute in Washington, D.C., to develop a vaccine for hookworm in cooperation with Europe, Australia and Brazil, to be tested in Brazil.