India, Japan launch HIV vaccines to match local strains

When the first HIV-positive case surfaced in the southern Indian city of Madras—now called Chennai—18 years ago, the Indian Council of Medical Research (ICMR) declared that the virus had been introduced by visitors from the decadent West. The agency advised the government that screening foreign tourists was all that was required to curb the virus' spread. Now, with nearly 5 million HIV cases, India is set to test a vaccine tailored to its citizens.

The search for an HIV vaccine has been fruitless thus far (see Commentary, page 221), and nearly 30 candidates are still in phase 1 clinical trials. The only candidate to reach phase 3, VaxGen's AIDSVAX, failed in both the US (*Nat. Med.* **9**, 376; 2003) and Thailand, but a third controversial trial will soon begin in Thailand.

Creating a vaccine for HIV is challenging in part because different strains are prevalent in different parts of the world. Countries such as India and Japan are now trying to match vaccines to the local strain to maximize the chances of success. "It's become clear in the last three to four years that we must tailor the antigen to the population," says Max Essex, chairman of the Harvard AIDS Institute.

India had refused to test any vaccine unless it targeted subtype C, which is prevalent in the country. Most vaccines are based on subtype B, predominant in the US and Europe. India's current candidate is a live attenuated vaccine that carries six HIV-1 subtype-C genes.

"Our vaccine has a better chance of success than AIDSVAX because it is tailor-made for Indians and more immunogenic," says Lalit Kant, a deputy director-general at the ICMR. "Even if it is only 50% efficient, it would help in curbing the spread of the virus."

EPA Photo/EPA/Piyal Adhikary

Scientists are preparing to test a vaccine against HIV subtype C, the strain most prevalent in India.

Because the recombinant virus expresses multiple viral proteins, adds Sekhar Chakrabarti, a researcher at the ICMR, it has a better chance than AIDSVAX, which carried a single surface protein, gp120.

Others are not as optimistic, saying there is little reason to believe the current candidates will succeed. "I think it would be very surprising if this vaccine will generate broadly cross-reactive neutralizing antibodies against HIV," says Michael Lederman of the AIDS Clinical Trials Unit at the University Hospitals of Cleveland.

Meanwhile, in Japan, where the number of new infections is rising sharply each year, Aikichi Iwamoto and his colleagues at University of Tokyo are testing a subtype-B vaccine tailored for Japanese patients. The vaccine targets *HLA-A24*, the human leukocyte antigen present in 70% of the Japanese population.

Iwamoto's team created a cocktail of peptides that specifically bind to *A24*, using wild-type peptides and mutated versions from Japanese patients. Preliminary results are expected later this year.

The Japanese vaccine highlights the enormous difficulty in designing affordable delivery methods. The researchers culture each patient's cells with the peptides and inject them back into the patient. Because the vaccine is tailored so precisely to both patient and viral strain, it's an unlikely candidate for wider-scale application.

Targeting specific viral strains may be sensible, but what's ultimately needed is a vaccine that provides more general immunity, say some experts. Even in places like India where one subtype is dominant, other subtypes are present, and the HIV virus is constantly mutating and hybridizing. Hybrids are appearing in places such as Thailand and Uganda, notes Wayne Koff, senior vice president for research and development at the International AIDS Vaccine Initiative. "There's a virus problem because reverse transcriptase is so prone to errors and selection pressure," says Koff. "And then there's a people problem—people move around."

The solution may be to create cocktails of different vaccines or to focus on common ancestral sequences among strains. The failure of the AIDSVAX trials demonstrates that a subtype-specific approach may not be enough, says Bette Korber, a researcher at the Los Alamos National Laboratory. "We are going to have to be cleverer than that," she says.

I-han Chou, Tokyo; K.S. Jayaraman, New Delhi

Cambridge slammed for axed primate center

Research organizations are condemning Cambridge University's decision to shelve plans for a multimillion-dollar primate center.

The center was designed to bring together neuroscientists from Cambridge and lure researchers from elsewhere. But the project was dogged by controversy from the start. A public inquiry in late 2002 recommended against building the center because it was not of "national importance," but deputy Prime Minister John Prescott last November granted the university permission to proceed.

The South Cambridgeshire district council twice turned down permission to build the site on grounds that protests by animal-rights campaigners would disrupt traffic and become a nuisance to local residents. The proposed site was close to Huntingdon Life Sciences, a research company that tests pharmaceutical products on animals, and that has repeatedly been targeted by animal-rights activists.

On 27 January, the university announced that spiraling costs had forced it to shelve the project. Even though the university had secured a projected US$44 million cost from public and private sources, several factors including extra security expenses had contributed to a rise in costs of $14 million.

"This is a serious blow for British medical research," says Mark Matfield, director of the UK Research Defence Society. "These delays and security concerns were caused by orchestrated threats and intimidation," Matfield says. In a statement, the Association of the British Pharmaceutical Industry called for legislation "so that action can be taken against the [animal-rights] terrorists."

Xavier Bosch, Barcelona