

Breaking through the HIV vaccine 'logjam'

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When biomolecular engineer Phil Berman began his postgraduate work in the 1980s, he had no idea he would spend the rest of his career searching for a way to stop a deadly virus that was then almost entirely known. But around him, as if from nowhere, hundreds of people began to die. He has spent the past three decades looking for an effective vaccine against the AIDS epidemic that would claim more than 20,000

lives in the coastal metropolis alone.

"It was a plague," Berman said during a recent visit to his lab at the University of California, Santa Cruz. "People were dying left and right."

Berman and his team have been searching for a way to make HIV vaccine production faster and more affordable—and, he said, they've found it.

"There are dozens of good ideas for vaccines that are sitting on the shelf because there has been no way to produce them quickly and economically," he said. "We think the technology we developed will break that logjam and allow those brilliant ideas that have been mothballed, basically, because there hasn't been a way to produce them."

The new production method takes advantage of technologies to reduce the time, improve the yield and lower the cost of [vaccine development](#). A process that used to take two years now takes about two months, while simultaneously producing yields 100 or even 200 times higher.

A potential vaccine needs specific proteins to trigger an immune system response, Berman said. The proteins are produced by [cell lines](#) derived from the ovaries of Chinese hamsters, with many thousands of potential cell lines needing screening to find those that with a high enough yield.

Screening the cell lines manually in the lab used to take months, Berman said, but the team spent most of the past two years customizing a colony-selection robot to do the job in a matter of days.

The team is able to use those protein-rich cell lines to produce the vaccine in vats much smaller than the beer-vat-size fermenters they would otherwise need. The advance means that the type of large-scale manufacturing facility that would have cost \$500 million when Berman

first began working on the problem could now be made for about \$25 million.

"You can make the drug much cheaper, and much more affordable by the people that need it," Berman said. "It's huge. It's a huge improvement."

Along the way, Berman and graduate student Gabriel Byrne used the gene-editing technology CRISPR to create a cell line that mimics proteins found on the HIV virus, improving the potential protection of the only HIV vaccine to succeed in a human trial.

These days, because of advancements in a regimen of treatments in the 1990s, infection with HIV for most people with access to health care does not mean death, but perpetual treatment. About 1.8 million people a year are infected with HIV, according to statistics compiled by the United Nations.

Berman and a number of researchers worldwide have continued to search for an effective way to immunize the next generation and halt the virus' spread. Berman himself has chased the project from its early days at Genentech in the late 1980s to its spinoff VaxGen, and, finally, to his lab at UCSC's Baskin School of Engineering. At VaxGen, he oversaw an early HIV vaccine trial that failed.

The UCSC lab is ready to begin producing two HIV vaccines on a large scale, Berman said. Their improved version of AIDSVAX—the only [vaccine](#) to go through clinical trials and demonstrate protective effects—is one, with a second candidate coming from a strain of the virus more commonly found in Southern Africa and India that accounts for a majority of new infections.

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