



BIOTECH, HIV, VACCINES

## Antibodies for HIV, Long Dismissed, Show Signs of Comeback at Seattle's Theraclone

Luke Timmerman 4/7/09

One of the great riddles of modern medicine is why a few rare individuals who get infected with HIV retain a strong enough immune defense to naturally fight off the virus in all its nefarious strains. Some of these people are prostitutes in Africa, they never take an expensive cocktail of antiviral drugs, and they never need them because they never get sick.

What if scientists could pinpoint exactly what's going on in their immune system that keeps the virus at bay, put it in a bottle, and market it as a treatment for the vast majority of people who aren't so genetically gifted? That's exactly what Seattle-based Theraclone Sciences (formerly known as Spaltudaq) is attempting to do at its lab on First Hill. This effort is still in its very early days, but CEO David Fanning told me about some intriguing progress in recent months, just a few steps away from our Xconomy Seattle office.

Theraclone's effort has a lot stacked against it from the get-go. There are already 33 FDA-approved drugs for HIV, according to [this list](#) compiled by the agency. These various cocktails of antivirals have basically turned HIV in wealthy countries from a death sentence into a chronic disease to be managed. The drugs have made fortunes for companies like Gilead Sciences and GlaxoSmithKline. But one drawback is these pills need to be taken diligently every day. Patients, some of whom are indigent or drug users, sometimes struggle to stick with this disciplined medication schedule for life. In doing this, they run the risk of letting the virus develop resistance to these treatments. So Theraclone's idea is to develop a potent genetically engineered antibody drug that could be given intravenously under a doctor's supervision once a month, or maybe even less frequently.

No one has come close to doing this, partly for the same reason nobody has been able to develop a successful HIV vaccine. The virus, a wily character, has always been able to mutate into multiple strains that have dodged these kind of antibody-based attackers in past studies. No companies are pursuing a neutralizing antibody approach to HIV, according to the International AIDS Vaccine Initiative, or IAVI. But Theraclone, along with partners at IAVI, thinks it may have found a rare type of antibody in the blood of people innately immune to HIV with superb viral-killing ability. If they're right, it could lay the groundwork for a promising new alternative form of therapy, and maybe even a vaccine far in the future. The implications of that are obvious—more than 30 million people around the world are [estimated](#) to be living with HIV, and it is still thought to kill 2 million people a year.

"We'd like to investigate two or three complementary antibodies to put sufficient pressure on the virus, so you don't enable it to escape," Fanning says. "That's the key."

Theraclone [reported](#) some intriguing data on its program a week ago at the HIV Immunobiology Meeting in Keystone, CO, sponsored by the Bill & Melinda Gates Foundation. Based on blood samples from these rare HIV neutralizer patients, obtained from IAVI, Theraclone scientists discovered two new antibodies that were able to neutralize a broad array of HIV strains in the lab.

Theraclone made these antibodies using standard genetic engineering techniques, and showed in a lab dish that they can kill HIV in a much more potent, or lower dose, than the other four antibodies scientists have identified over the past 15 years against HIV.

This sort of exploration for novel antibodies is right up Theraclone's alley. The company's scientists look at blood or tissue samples from patients, and identify antibodies that are made by people's immune systems against foreign invaders like viruses or bacteria. Mother Nature has evolved pretty efficient defenses against these infectious invaders, so the company's philosophy is to follow these clues, and make genetically engineered copies of these antibodies as drugs. The company, founded in 2005, raised \$29 million to continue developing the technology in March 2007 from Arch Venture Partners, Canaan Partners, HealthCare Ventures, Amgen Ventures, MPM Capital, and Alexandria Real Estate Equities.

Most scientists I know would shake their heads at the idea of antibodies as treatments for HIV, because the virus is supposed to be able to mutate and outflank these kind of treatments. I asked Fanning how he plans to combat that. The key is finding what he called "highly conserved epitopes" found across multiple strains of HIV. This is like finding the backbone of the virus, parts that are so essential that they just can't be mutated.

If you can find these "highly conserved" regions of the virus, then these could also be useful targets for an HIV vaccine, although that's the domain of IAVI, and not something Theraclone has a commercial interest in, Fanning says.

The hypothesis still has a lot to prove. The Theraclone approach hasn't even shown an ability to neutralize HIV in animals, so it's still a long way from its first test in people. This sort of work requires money, and Theraclone, like a lot of small biotech companies, can't afford to fritter it away in a downturn. The company plans to continue hunting for a few more of these HIV neutralizing antibodies, and it hopes to find a big drugmaker to join it in a discovery collaboration, Fanning says.

Theraclone has about 22 employees now, after a small layoff, Fanning says. It has enough cash to last through 2010. If it can get enough financial backing, possibly from a partner, it envisions taking forward a combination of antibodies, a so-called "polyclonal" brew that could attack the HIV virus from a variety of angles. I tried to press Fanning on a lot of questions about timelines for development, when we can expect to see results from this HIV program, but he wasn't going for it. "We're excited," he says. "But we're still pretty early as a company."

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