

From Diagnostic To Vaccine: The Fight Against Tropical Disease Continues

TechLab

University of Virginia

University of Virginia Patent Foundation



Each year, more than 3 million children around the world die of diarrhea and other gastrointestinal ailments, primarily in developing countries.

Scientists at the University of Virginia (U.Va.) and TechLab, a medical diagnostic manufacturer based in Blacksburg, Va., are working together to make a dent in the disease and, if all goes well, come up with a vaccine against amebiasis, or amebic dysentery.

The story begins in 1989, when Dr. William Petri, a trombone-playing researcher at U.Va. received a National Institutes of Health (NIH) grant to study a protein on the surface of *Entamoeba histolytica*, a parasite that causes dysentery. Petri is the chief of the Division of Infectious Diseases and International Health at U.Va. in Charlottesville.

With the help of colleague and longtime friend, Dr. Barbara Mann, they were able to successfully clone the surface

protein so it could be used to develop antibodies that would result in an accurate diagnostic test. This test, which has been cleared by the U.S. Food and Drug Administration (FDA), identifies the *E. histolytica* organism in children and adults suffering from diarrhea and dysentery. It was licensed by the U.Va. Patent Foundation to TechLab in 1992.

The company is now collaborating with Petri to develop a low-cost dipstick-like device similar to a home pregnancy test that changes color when used to analyze infected fecal matter. The dipstick, which is being tested in Bangladesh, uses TechLab's diagnostic technology. But it will deliver it in a simpler form, Petri says.

Providing such a low-cost kit would allow the most impoverished nations to have greater access to the technology, thereby allowing for proper diagnosis and treatment of dysentery.

Petri says he believes FDA clearance of the dipstick test may occur by the end of 2008. The current form of the test is a bit more complicated, but can also be used in the field, he says.

Debi Hudgens, a licensing associate at the U.Va. Patent Foundation, calls the collaboration between her school and TechLab "extremely productive."

Joel Herbein, who heads TechLab's parasitology section, says working with Petri is important because he has collaborators all over the world and can set up clinical evaluations in places where gastrointestinal diseases are endemic.

"We want our products to be used in very simple settings to diagnose disease without a lot of supplemental expensive equipment," says Herbein, who earned his Ph.D. in cell biology from Duke University in Durham, N.C.

"There is always a push for these tests to become simpler and cheaper, faster to run and more sensitive."

TechLab came into being in 1989, when it was spun out of the Virginia Tech Anaerobe Laboratory in Blacksburg, Va. It was founded by microbiologists Tracy Wilkins and David Lyster, whose work had focused on *Clostridium difficile*, a bacteria that can also cause gastrointestinal illnesses. The company now has 72 employees and more than 15 products on the market, including the *E. histolytica* test. Lyster said TechLab is always trying to push basic research to improve its products.

"We go to the top institutions in the country," he says. "That's why we started the collaboration with U.Va., because it is a top-notch university doing work that dovetails perfectly with what we do here."

A Chance Meeting Leads to Collaboration

Petri and Wilkins crossed paths in 1992 when Petri made a presentation at an American Society of Microbiology chapter meeting held at Virginia Tech.

"Very fortunately for me, Tracy happened to be there," says Petri. "The presentation was about our attempts to make a better diagnostic test for amebiasis. We'd had some limited success doing that, but Tracy and his company were and still are today, the world's experts in how to make diagnostic tests for intestinal infectious diseases."

The pair spoke during the meeting and decided to work together.

"There were no research grants or anything," he recalls. "We agreed to take some of the antibodies that we had made against this parasite and turn it into a diagnostic test that would work and could pass muster at the FDA."

Petri calls the importance of the collaboration between the two "enormous for the field of tropical medicine and

amebiasis. There still is no other diagnostic test specifically for *E. histolytica*. Since then, it has gone through three generations of FDA approval, with each one better than the last generation.”

Petri says the importance of the collaboration goes well beyond simply having a good diagnostic test.

“We have been able since 1999 to work with a cohort of 500 children in Dhaka, Bangladesh, who have been monitored every other day for diarrheal illness,” he says. “With their tests, we have been able to quickly ascertain when the children have diarrhea if it is due to amebiasis, which often leads to malnutrition. And malnutrition in turn is the most common cause of death in children in the developing world.”

Before there was a good diagnostic test for amebiasis, Petri says no one knew how common it was or if those who had it were resistant to being reinfected.

“A number of very fundamental questions were unresolved,” he says. “If you don’t have a good way of reliably diagnosing an infection, there is no way to study it in humans. All this was made possible by the TechLab test.”

Petri and his colleagues in Bangladesh learned that amebiasis is quite common in the children they are following.

“About 40 percent of Bangladeshi children we are following are infected with this parasite every year,” he says. “We also discovered that the infection is linked to malnutrition. So if you are malnourished, you are four times more likely to become infected.”

Hope for a Vaccine

Petri and his team learned that when the body creates antibodies against this parasite, reinfection is less likely. In other words, they discovered that these intestinal antibodies can lead to immunity to the infection.

“We can use this information to try to rationally develop a vaccine against the infection,” he says. “All because of the TechLab test. Without that, none of this work would have gone forward. This has been the perfect collaboration where both parties benefit equally. This has been win-win from the very beginning.”

Petri said his current work with TechLab is being supported by the National Institutes of Health through cooperative research agreements that are part of the Vaccine Initiative and with Small Business Technology Transfer program funding.

But the work Petri is most devoted to is the amebiasis vaccine.

Petri said he believes the vaccine will be tested on humans by 2011.

“If I can help achieve a vaccine against amebiasis, I will be overjoyed,” he says. “That will be a huge accomplishment by many people working together.”

“The biggest winners, I think, are going to be children in the developing world,” he says.

“*Malnutrition is the biggest killer of children in the first five years of life. What is coming out of all this is a better way of understanding what contributes to malnutrition in the developing world.*

Dr. William Petri

What we have discovered so far from this work is the contribution of cryptosporidiosis, amebiasis and giardiasis to

malnutrition. Having a better way of diagnosing means you have a better way of treating it to try to help prevent malnutrition.

“And it’s malnutrition that makes children so susceptible to the other diseases like pneumonia that kill so many of them around the globe.”

This story was originally published in 2008.

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