

Diagnostic Breakthrough Unmasks A Killer In Sub-Saharan Africa

Immuno Mycologics

University of Nevada, Reno



It's no secret that sub-Saharan Africa is being ravaged by HIV/AIDS. An estimated 22.5 million people in the region are living with HIV, accounting for about two-thirds of the world's total. Some 1.8 million died from AIDS in 2009, and an estimated 2.6 million became infected with HIV that year, according to the World Health Organization (WHO). WHO also estimates that 11.6 million children in the sub-Saharan region have been orphaned as a result of HIV/AIDS.

What is not so well-known is that another vicious killer — a fungus — is stalking those suffering with HIV/AIDS. Called *Cryptococcus neoformans*, it causes cryptococcal meningitis, an infection of the membranes covering the brain and spinal column. Found in various sites in the natural environment around the world and inhaled by victims,

Cryptococcus neoformans opportunistically attacks immunocompromised individuals — like people living with HIV/AIDS, rheumatoid arthritis patients and transplant recipients — whose immune systems are either compromised or suppressed. Left untreated, cryptococcal meningitis can cause swelling of brain, fever, sensitivity to light, stiff neck,

headache, nausea and vomiting, confusion, disorientation, hallucinations and death. A study reported in the journal, AIDS, estimates that cryptococcal meningitis kills 500,000 people a year in sub-Saharan Africa. In sub-Saharan Africa, cryptococcal meningitis is estimated to cause more deaths among those living with HIV/AIDS than tuberculosis.

The Crux of the Problem

Fortunately, there is a tool in the works that will help shrink this epidemic. “With early diagnosis cryptococcal meningitis can be treated with readily available and inexpensive medicine, although individuals with HIV/AIDS require long-term treatment to prevent reoccurrence. The question is: How do we rapidly diagnose cryptococcosis in sub-Saharan Africa?” says Sean Bauman Ph.D., CEO of IMMY (Immuno-Mycologics Inc.), an Oklahoma company founded in 1979 to produce fungal diagnostic products.

“*For over 30 years, IMMY has been manufacturing diagnostic kits for cryptococcal meningitis. The current technology is simple but requires refrigeration and additional equipment to work.*”

“I was in Tanzania almost a year ago doing product training, and it became clear to me that our current *Cryptococcus* test was not the right technology for the developing world,” Bauman says. “So we set out to do something about that.”

Bauman had known Thomas Kozel, Ph.D., of the University of Nevada School of Medicine, part of the University of Nevada, Reno (UNR), as a leader in the field of *Cryptococcus* research since 1995. “So I gave him a call.”

The Key to the Solution

With funding from the National Institutes of Health, Kozel has been investigating *Cryptococcus neoformans* for over 30 years, doing basic science studies on how the organism produces disease.

“We were interested in antibodies as a way to probe the structure of the yeast and for reversing the anti-immune-cell action of the capsule,” says Kozel. “So when Sean called and asked if we had an antibody that could be used for a point-of-care immunoassay for the diagnosis of cryptococcal meningitis in the field, I thought, ‘I know we do.’”

“I was sure because we had recently gone through our collection of antibodies, trying to develop a very sensitive laboratory based assay that would pick up all forms of the diagnostic target globally. We had just completed that work when Sean called,” he continues.

It turned out that Kozel did indeed have an antibody that would fulfill IMMY’s requirements. Kozel had an antibody that increased and broadened the sensitivity of the test, brought it closer to the point of patient care and dramatically reduced the cost. “It’s an almost perfect antibody that can be made in tissue culture using techniques for producing hybrid cell lines so that it is always the same,” he says.

Kozel sent samples of the antibody to Bauman. When IMMY tested it, they had a “eureka!” moment, and, not long afterward, Bauman was applying to the UNR for licensing the antibody.

Rapid Licensing

“The entire licensing process went very quickly — about four months from beginning to end,” says Michael Birdsell, director of Intellectual Property Marketing and Business Development at UNR. “The key to successful licensing is having the right partner,” he adds. “Although we generally like to work locally with licensing partners, IMMY had all the right stuff: key expertise including years of working with *Cryptococcus*, current access to markets, capital and a high level of commitment. With lives in the balance, we had an obligation to seek the quickest way to market for this

technology.”

IMMY has been busy with the antibody developed by UNR. “We have already developed a test kit that will be useful in existing labs,” Bauman says. “It has recently been cleared by the FDA, has been approved in Europe and is already in use in sub-Saharan Africa. Kits are going out across the world, and momentum is starting to build for this product in the marketplace.” The kit has been evaluated or is in the process of being evaluated in the United States, South Africa, Thailand, Vietnam, India, Kenya, Uganda, Rwanda, Zimbabwe, Tanzania, Guatemala, Argentina, Brazil and Mozambique. Further, the test meets the WHO ASSURED criteria: affordable, sensitive, specific, user-friendly, rapid, equipment-free and delivered to those who need it.

A Simple Test

IMMY is in the final stages of putting together a field kit that has all the necessary components to run the test in the back of a truck or in a crude rural clinic in sub-Saharan Africa. The test is almost as simple as a pregnancy test: (1) place a drop of diluent that comes with the kit into a tube, (2) add a drop of patient specimen (urine, plasma or whole blood from a finger stick), (3) add the dipstick containing the antibody to the tube, (4) wait 10 minutes and (5) read the results: two lines, positive; one line, negative.

Delivering the test to places where it is needed is also easy to do, says Bauman. “We can FedEx stuff nearly anywhere in the world,” he says. “In addition, we look for distributors in country to partner with. Some countries also have ministries of health where material is warehoused, and they are responsible for making sure it gets to where it needs to be.”

Bauman says, “It’s a really simple test, and the simpler the test, the lower down the health care chain we can go with it. You have to realize that in many areas of Africa, health care infrastructure is very limited.” He notes that the new test will appeal to health care providers in developed countries as well because it is so easy to use.

Of the licensing process, Bauman says, “UNR has been wonderful to work with. We had a common vision — to help cryptococcal victims in the developing world. Big profits are not what IMMY is after. We are a privately held, family-owned company, and we are not beholden to shareholders, which enables us to develop and market products that meet the needs of both the developed and developing world.”

Ryan Heck, director of UNR’s Technology Transfer Office agrees: “One of the stipulations in our agreement for the licensing of the antibody with IMMY is to have this crucial test available at low cost. Dr. Bauman has already begun to make this happen.”

A Big Impact

The upshot of this new technology promises to be very significant. “With the new point-of-care diagnostic test, a health care provider can give the test, observe the results and administer the first dose of oral medication, all within a few minutes,” says Kozel. “Studies have shown that early identification and treatment are essential to beat cryptococcal meningitis. A late diagnosis means that antifungal therapy will likely fail in resource-limited countries. Most patients in that setting are not diagnosed until they are very sick, and then it’s too late.”

Bauman adds, “Antifungals used to treat cryptococcal meningitis are available for free or at low cost in regions such as sub-Saharan Africa. In countries with limited infrastructure or resources, as many as 1 in 10 AIDS patients may develop crypto. If we can diagnose early and begin treatment, we can save an amazing number of lives.”

Bauman estimates 1,700 people die every day from cryptococcal meningitis. Thanks to Tom Kozel's research and rapid technology transfer from the University of Nevada, Reno, the new diagnostic test from IMMY promises to help sub-Saharan Africa respond to the adversity of the AIDS epidemic by significantly reducing the death toll from cryptococcal meningitis and preventing thousands of sub-Saharan children from becoming orphans.

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