New approach to combat intractable bacterial infections

January 23 2012, By Nicole Miller

(Medical Xpress) -- Bacteriologist Marcin Filutowicz specializes in developing antimicrobial technologies that one day may help replace antibiotics—and save lives—as the power of our antibiotics arsenal wanes. But he doesn't stop there. Filutowicz has founded or co-founded three biotech companies to help ensure that his technologies actually make it into the world's hospitals. The idea for his newest venture, Amebagone, founded this year, sprung from his work investigating a collection of soil-borne amoebas assembled decades ago by UW

bacteriologist Kenneth Raper, who is best known for helping ramp up penicillin production in time to save thousands of soldiers wounded during World War II.

Grow Magazine: Let's start with the basics. What's an amoeba?

Amoebas are unicellular organisms. They are not animals or plants or bacteria. They are protists, which is a whole separate group. And what they do, their sole purpose in life—as much as we can say—is to feed on bacteria. So this is their primary source of sustenance, and once they eat all of the bacteria in their environment they yell at each other—using chemical signals—and gather together.

On the Petri dish, you can see them swarming when they decide to aggregate. Initially, they form something that looks like a slug. It's a community of a million or so amoebas that are packed together into a sack. The slug moves around looking for more food. If it can't find anything to eat, the slug transforms into stalks and spores that get distributed by the wind. When the spores land on moist soil, they germinate and start eating the bacteria in the soil, and the process repeats itself.

How did you start working with these organisms?

For one of my companies, PlasmiGon, we needed access to libraries of small molecules to be successful. After screening a few libraries that were available to me, I started thinking about other potential sources of small molecules, and I realized that Ken Raper, who established the whole field of amoeba studies, had left a huge collection of amoebas in our department. This collection involves over 1,000 different amoebas gathered from five continents and several island nations. So it's

extremely diverse in terms of the geographical locations. It represents a huge resource of diversity of small molecules.

So my take was, why don't we start reviving these amoebas and come up with techniques to look for useful small molecules produced by them? So we started opening those samples, some of them 70 years old. And then the issue was, well, how do you propagate them? Because, to be honest, I knew nothing about amoebas.

I went to a colleague and asked, "How do you grow these beasts? Do you grow them like bacteria?" And he said, "You feed them with bacteria." The moment he said that—"You feed them with bacteria"—I went back to my office and I quickly computed all of the information I had learned over the past few days. I realized that this could be a new biotherapy because the particular amoeba we wanted to grow, Dictyostelium discoideum, is benign. There was no single report of it having adverse effects on humans, animals or plants. It's an organism that you simply put alongside bacteria, and they do nothing else but eat it. I disclosed this to WARF in 2009, but they turned my disclosure down.

That's surprising.

Not really. At the time, we didn't have any proof-of-principle, no data, nothing. It was just an idea. But I decided that I could not let it die. I decided to form Amebagone and let that company patent the technology.

How do you picture amoebas being used in medicine?

Right now we're focused on methicillin-resistant Staphylococcus aureus (MRSA). This MRSA is a major agent of nosocomial infections in hospitals. It kills a lot of people. And it happens that two billion people on this planet carry staph in their nostrils. It is part of our natural biota.

They inhabit a very narrow area in our nostrils that has just the right temperature and salinity, so they are not all over. They are compartmentalized in a band or section of the nostrils.

And we all touch our noses. We can't help it. As we touch, there's moisture in there, and so we contaminate our fingertips. And after surgery, it's natural to want to see the wound, and in many cases people accidentally self-contaminate the surgery site just by lifting up the dressing to look at it.

But if we can deliver amoebas to the nostrils pre-surgery, we can essentially decontaminate the nostrils of undesirable microbes. We did proof-of-principle experiments with MRSA, and amoebas eat MRSA like crazy. So even though antibiotics cannot kill MRSA, amoebas can.

Is it safe to use amoebas this way?

In the literature, there is no reported evidence to support virulence of Dictyostelium discoideum, but obviously once we have a product ready for clinical trials, the FDA will scrutinize that. And keep in mind that amoebas are all around us in the environment—in the soil, in the air we breathe, on our food and in and on our bodies.

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Are there other applications for this technology?

Yes, it's just a matter of finding the right amoeba—or combination of amoebas—to combat a particular infection. Already, we have beautiful data showing that amoebas can eat Erwinia amylovora, the fire blight pathogen that infects orchards. We also have amoebas that can eat the

bacteria that cause pneumonia.

Now we are starting to look at biofilms, which are thick aggregates of bacteria that are virtually impervious to antibiotics. Amoebas can eat biofilms, so they must produce something that dismantles biofilms and releases individual cells for them to access. One potential application for this is diabetic ulcers. The rise of diabetes in the United States is alarming, and one of the consequences of advanced diabetes is skin ulcers, which lead to amputations. The ulcers are incurable with antibiotics because they are seeded with biofilms. Currently, some doctors prescribe maggot therapy—where they apply maggots directly to the ulcer—as a treatment of last resort for this. That's because the maggots "debride" the site, meaning they eat away the dead tissue, removing the bacterial biofilms as they go, which allows topical antibiotics to work.

When I came up with the idea for treating diabetic ulcers with amoebas, I talked to an infectious disease expert, and he said it would be a marvelous alternative to maggot debridement therapy. He would rather prescribe amoebas, which are too small to see, to his patients than have them witness maggots eating their flesh. So this could be huge application.

We're also going to hunt for new kinds of antibiotics produced by Dictyostelium discoideum and other amoebas, as genome analyses indicate they have the capacity to make a lot of compounds that may function as antibiotics.

More information: This Q & A was originally published in the fall 2011 issue of Grow magazine.