Fund-fest

Startup Entopsis gets money from Breakout Labs for 'crazy ideas'

By Diana LaChance

Funding doesn't come easy to most biotechnology startups. Investors aren't interested unless a profitable product can be brought to market with breakneck speed. Federal institutions, meanwhile, require such rigorous testing that a product's release can be delayed by years or even decades. That's the challenge Entopsis co-founder and CEO Obdulio Piloto was facing as he struggled to get his new company off the ground. Enter Breakout Labs, a program overseen by the Thiel Foundation to financially support early-stage science and bridge the gap between private and federal funding.

"I tried getting funding from many other places, but they all said no. We heard a lot of 'That's not going to work' or 'I don't see how that's going to pan out.' It made me feel kind of like, what are we going do?" says Piloto, who learned about Breakout Labs and their focus on radical research from fellow Entopsis co-founder Ian Cheong. "Ian said 'There are these fun crazy folks that fund only crazy ideas,' and I said we fit the bill! So I contacted Breakout Labs via their website and submitted a proposal."

It was time well spent. Entopsis, which is based at the HudsonAlpha Institute for Biotechnology, was chosen by Breakout Labs to receiving funding last May, becoming only the seventh company to obtain financial support from the Thiel Foundation and the first one located in the Southeast region. That should come as no surprise, however, to those who know of HudsonAlpha's reputation for engendering highly successful spin-off companies and startups. And indeed, Piloto credits the Institute for much of his success in launching Entopsis in the first place.

"There are tons of small companies here, so they provided good examples and a good environment to try starting our own company," says Piloto. He also learned a lot while working at another HudsonAlpha company, Conversant Bio. "I served as their chief science officer, mainly running the R&D effort for the company, and that really helped a lot in terms of figuring out how to run a small business, what to do, what not to do." Just as influential has been the assistance he has since received from the Institute's fellow occupants. "The people here have been incredibly helpful," he says. " [HudsonAlpha co-founder] Lonnie McMillian provided us with seed money to get things started, and Microarrays Inc. lets us use their lab space to get projects off the ground."

PERSONALIZED PLATFORM

So just what makes Entopsis such an excellent candidate for inclusion in the Breakout Labs family? Piloto says it's their goal of creating a superior, non-invasive, and low-cost diagnostic/prognostic platform for personalized medicine. "A platform is basically a system to address various diagnostic or prognostic questions, like, 'Does this person have breast cancer?' or 'Is this disease expected to respond well to a given therapy?'" Current platforms are limited in the amount of information they can provide, often answering only one question at a time. "What we want to do," says Piloto, "is have one platform that answers various questions, so that we can better capture a larger range of patients who have the same disease but caused by different factors."

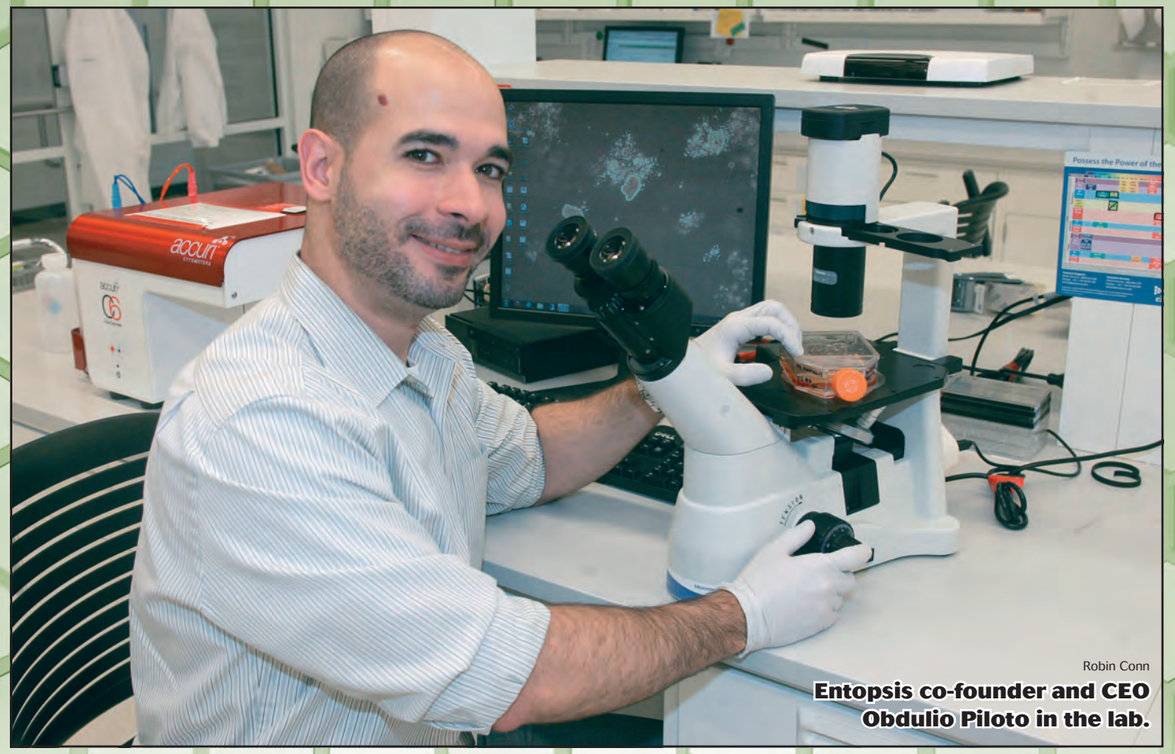
Take as an example five women who have breast cancer. "A traditional test might indicate that these five patients have breast cancer and also how aggressive it is, or what stage it is," says Piloto. But a more advanced platform could tell you that four of them were genetically pre-disposed to breast cancer, whereas the fifth "has a type of breast cancer driven by a different set of mutations; that is, an atypical type of breast cancer." With that knowledge, a doctor may then be able to tailor that fifth patient's treatment to more effectively treat her specific type of breast cancer.

The foundation of the platform is a patient's health status signature. As Piloto explains, diseases alter the protein composition of a patient's biofluids, which can be anything from saliva or urine to amniotic or spinal fluid. "These changes can be captured through the use of a sensitive proteomic microarray that results in unique protein binding patterns, or health status signatures," says Piloto. Those signatures are then analyzed for known biomarkers, patient-derived antibodies, and protein labeling through amine or thiol groups and compared with signatures obtained from previous patients and non-diseased donors. That allows a doctor to not only make an accurate diagnosis but perhaps even detect more than one malignancy.

In short, the new platform shows "what's there and what's not there," says Piloto, who compares the signature to a pattern. "Most people are looking at what's there in terms of a yes/no answer – you know what you're looking for and you try to find it. But we're using combinations of known and unknown biomarkers to make a diagnosis." That removes the bias associated with traditional platforms, wherein a known antibody or protein is used to try to determine the presence of a particular biomarker. "With ours, we don't use any antibodies or peptides that would bias," says Piloto. "Instead, we compare the binding patterns of a few hundred proteins from healthy and diseased samples."

Piloto conceived the idea for an advanced platform during his tenure at Conversant Bio, after meeting with clients in the biotechnology and pharmacology fields who were developing diagnostic assays. "From listening and talking to a lot of these folks, I grew more and more interested in the diagnostics area and I figured there wasn't one general platform that allowed someone to create various assays quickly," he says. "We started thinking about what kind of platform we could come up with that would be novel, low cost, and versatile, and that could create various assays quickly."

To do that, he and Cheong teamed up with Microarrays Inc. to create a special slide whose surface is characterized to the nanometer scale. Ultimately, says Piloto, "we're planning to create a number of unique, synthetic slide surfaces in a reproducible fashion." Those unique surfaces will add another dimension to the analysis – literally – by allowing features to be represented as two and three dimensions as opposed to the traditional two dimensions. Then, properties will be added to the slide surface to enable binding by proteins or other biologically relevant material from the patient sample. What



Robin Conn

Entopsis co-founder and CEO Obdulio Piloto in the lab.

binds, and what doesn't bind, will then allow clinicians to make a fast and accurate diagnosis and allow researchers to identify new biomarkers.

"Even though we don't always know what biomarkers we're looking at, we can do follow-up studies to figure out what proteins we are examining," says Piloto. "So the clinician can use the platform to find out whether a person has A, B, or C. But the researcher can say 'This protein is showing up in people with A, B, and C. Let's see what role it plays in this disorder.' They can use this platform to find new biomarkers and see what pathways might be involved in a given disorder."

OPPORTUNITIES ABOUND

And while he says that cancer is "the sexiest" example, Piloto sees opportunities for many other, less-common disorders, like scleroderma. "It's not that people don't care; it's that there aren't as many patients and it's less pressing," he says. "But you could push research forward a lot faster in these areas if you could figure out the pathways." It's that particular aspect that Piloto says makes him very excited. "I just wish I could do more," he says. "I even dream about it at times! It's a bit of an obsession, but it's a healthy obsession."

Then there are the savings to be had, first by being able to identify multiple diseases simultaneously rather than just one at a time, and then by using biofluids to make diagnoses rather than resorting to costly and invasive procedures, like mammograms, pap smears and colonoscopies. "This falls into the molecular diagnostics category, which, though not currently the standard of care, is a growing field," says Piloto. "It's a faster, less-expensive way of quickly screening patients."

That would also make outreach efforts to low-income populations much more affordable and effective. "Women could be quickly screened for breast cancer by giving a drop of blood instead of getting a mammogram, which isn't always accurate," he says. "Then you can take them to the next step if they're positive for the low-cost test. Because if you catch it early, cancer is very curable. But if you don't know, and you have it for a long time, it's hard to treat."

At the moment, Piloto says he's about a year from having a late-stage prototype that could be used to test patient samples – and even then, there's no guarantee. "Part of it is that things take time to work out in the lab," he says. "And part of it is regulations. You need to jump through a lot of hoops and it's expensive to get things approved." And that, again, is where funding becomes critical. "I could do a lot more with more money," says Piloto. "We spend a lot of time getting money to be able to do the test to be able to get it approved. Raising money is a lot of work!"

Fortunately, the funding Entopsis will receive from Breakout Labs will alleviate some of those difficulties. "Their support enables us to carry out some of the early studies to improve the idea and push it forward," he says. After that it's anyone's guess, though Piloto is hoping by that point the platform will essentially sell itself. "If it's a really good test, we think we'll do well," he says. "It will be a clear sale." ■