TORONTO STAR
www.thestar.com

A lab mouse's friend

DAVID BRUSER
March 13, 2006

Last year, the University of Minnesota sent professor and paediatric cardiologist Dr. Liz Braunlin to chase down the latest technology for the school's stem cell research labs.

Her search started and ended in Toronto, on the sixth floor of a bland office building at Yonge St. and Lawrence Ave., above the subway station.

For $200,000, Braunlin brought home the Vevo ultrasound for mice from VisualSonics, a company founded in 1999 by scientist and industrious tinkerer Dr. Stuart Foster.

"It was clear that it was a totally unique machine," says Braunlin, who tracks how various stem cells affect the heart of a mouse. "It's going to be the way everybody does their studies in the future."

That's the hope driving the young company that grew from Foster's lab at Sunnybrook and Women's College Health Sciences Centre, where he jury-rigged his first micro-ultrasound with off-the-shelf parts and exposed wires, to a firm employing 70 with annual sales of $24 million.

Just as many hospitals and clinics carry ultrasound machines for sonograms and other human applications, VisualSonics expects most labs where small animals suffer for human disease research will need such a micro-ultrasound.

"There's at least 6,000 mouse houses around the world; at least 3,000 in North America. (That's) 40 million mice per year used in life science research," says company CEO Tom Little. "It's a huge potential."

VisualSonics pegs the market at $2.9 billion.

Little, 44, with a background in venture capital, and brought in to head the firm in 2002 by a major investor, runs the company. Foster, 54, serves as chair and chief science officer, spending about 20 per cent of his time where he is on this day, in the VisualSonics boardroom.

Across the hall, a small work force takes parts supplied from throughout the GTA and assembles the finished product, a 400-pound machine about the size of a mini-fridge. Packed and stamped boxes await shipment to Asia, Chicago, Michigan, North Carolina, the Netherlands.

"At the University of Toronto (alone), there are hundreds of research labs that are knocking genes in and out of the mouse genome, and saying: `What does this do?' " says Foster, also the associate chair of medical biophysics at the University of Toronto. "Some affect heart development, some affect development of cancer, and they want to follow those in real time with simple imaging equipment.

"That's what our machine does. No other (ultrasound) machine does that."

LUCAS OLENIUK/TORONTO STAR
A duo - VisualSonics CEO Tom Little, left, and Dr. Stuart Foster - flanked by a trio of the ultrasound machines their company makes in Toronto.

Paradigm Medical Industries, Inc. of Salt Lake City, Utah, says it also makes a micro-ultrasound device that can be used on mice, though the company's website emphasizes the machine's ability to view the human eye.

The difference between human ultrasound and the VisualSonics version for mice, according to Foster, is scale: What works on a 80 kilogram person cannot on a 40 gram mouse.

"A typical image of ultrasound would be a kidney scan, or something like that, or liver scan. Fifty thousand of these are done every year in Toronto hospitals, probably more than that," Foster says. "The resolution of those images are on the order of half-millimetre to a millimetre. We created the technology that allowed us to make the resolution less than 100 microns."

And in real time. At the beginning, when Foster and his staff of researchers and graduate students at Sunnybrook made the prototype and then a few more for local scientists, the device snapped four frames per second. Now, thanks to millions of venture capital dollars spurring development, the Vevo takes 200 frames per second.

The first Vevo to leave Foster's lab went to physiologist Dr. Lee Adamson, who studies pregnancies and placenta development in mice at Mount Sinai Hospital.

Until then, analysis of mice embryos proved difficult: "A mouse embryo is a couple millimetres in size or less, earlier in development," she says. "We hadn't had the tools to see how they're developing because they're so small. Until VisualSonics came along. It has absolutely revolutionized our field."

Now Adamson says she can non-invasively monitor blood flow, placenta development and chart the effect of a particular gene on a pregnancy, all without killing the mouse and putting its parts under a microscope.

The mice are sedated and spread out under the watchful eye of the transducer, a handheld tool scientists can press against any area of a mouse.

“When they’re done, they just wake up, and we put them back in the cage with their mouse cage mates,” she says. “And the pregnancy continues. (Without the Vevo), think of how many mice you’d have to kill to do that kind of time-course study.”

That’s why Foster, who also co-founded Toronto’s Mouse Imaging Centre (MICe) five years ago, built the machine.

“We were aware that the human genome project was making huge progress, especially around the end of the 1990s. All of a sudden people were asking, `What is the phenotype of my mouse? And I don’t want to sacrifice my mouse that it took two years generating. I want to look at it. I don’t want to kill it,’ “ Foster recalls.

“I said, `Well, here’s an interesting technology.’ “

He founded VisualSonics in 1999, “with one employee — myself. Not even an employee, because I couldn’t pay myself.”

Soon, he says, word of his machine had spread and calls came from researchers in Germany, Montreal and Texas.

Foster remembers thinking, “I’m not trained to do this, and I’m not going to do it. I’m a research scientist, not a business person. It had to (be) something that could be made in a cost-effective fashion. Not at Sunnybrook. You can’t buy a whole bunch of off-the-shelf parts and glue them together with cables and wires.”

His entrepreneur brother tapped Foster into the finance community, “just to meet people who knew how to build a business, because I certainly didn’t. I recognized that very early.”

VisualSonics says Hargan Global Ventures invested $1.5 million, moved the company to Yonge and Lawrence and in 2002 brought in Tom Little. ***Later that year, Little helped attract VenGrowth Capital Partners, which invested $12 million.***

Foster’s colleague and the other co-founder of the Toronto mouse house, Dr. Mark Henkelman, says Foster avoided a typical, costly mistake by admitting he’s not a businessman.

“I’ve actually seen a number of start-up businesses come out of labs. The person who makes the first invention wants to own it, wants to sit on top of the company,” he says. “You just know if the guy won’t let go, he’s going to kill it.”

There are other machines Henkelman uses at MICe that allow for viewing at the micro level, including a micro MR (magnetic resonance) and micro CT (computed tomography).

But he says his CT machine is best for looking at bones or dead mice because it’s “moderately slow,” and even a sedated mouse moves too much for it to work properly. Plus, upping the resolution means intensifying radiation rays and “eventually we ensure that it’s a dead mouse.” VisualSonics says Vevo does not use harmful radiation.

Henkelman’s micro MR does not pick up bones or other solid tissue. And, two hours elapse before the first images are ready for viewing.

It’s also 10 times more expensive than the ultrasound. But the machine can take images of up to 19 whole mice at the same time.

A downside to micro-ultrasound, he says, is that it sometimes takes up to an hour to prep each mouse for the procedure, which, like a human ultrasound, involves moving the scanner around until getting the optimum angle. Foster adds that an ultrasound does not work as well as an MR machine in penetrating the skull to view the brain.

Meanwhile, Foster and Little have high hopes for the firm that has sold more than 200 units since commercializing the Vevo in 2003.

“Those (original investors) are still in the company and obviously they’re hoping that after some continued success, perhaps we could go public and then they would get to sell their shares for billions of dollars,” Little says.

But if such wild success comes, Foster expects to remain largely aloof from the corporate world.

“I think I’m best suited to being a scientist,” he says with a laugh. “I enjoy it a lot. I’m just thrilled to see VisualSonics so successful. But at the end of the day, I’m a scientist, and that’s what I’ll do.”

Reprinted with permission from the Toronto Star.