

Lab to Life

September 22, 2017 1:30 PM

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Nick Pashos, Mei Wang and Jason Ryans are recipients of National Science Foundation Innovation-Corps grants. They, along with other Tulane doctoral students and faculty mentors, were awarded \$50,000 grants during the past few years to look into the marketability and viability of their “bench science” as they develop new products to improve lives. (Photos by Rick Olivier)

Editor's note: This article appeared first in the September 2017 issue of *Tulane* magazine.

The world of bioinnovation is the science that propels mere mortals known as scientists into visionaries who solve the most complicated medical conundrums today. In the relatively new field that constantly strives to solve the perplexing puzzles at the nexus of mechanics and biology, Tulane University is producing dynamic solutions to some very complex problems. If curing lung disease and cystic fibrosis, for instance, seems like it could be decades away, there is one researcher who has a decidedly different notion of that timetable.

“Think organogenesis,” said Bruce Bunnell, director of Tulane’s Center for Stem Cell Research and Regenerative Medicine and professor in the Department of Pharmacology in the School of Medicine. “The days of having to sign up organ donors, probably in the next decade, will come to an end, in theory. We’ll be able to grow the organs in laboratories.”

This medical breakthrough is particularly important when it comes to replacing human lungs. A matching donor can give up a kidney and still survive, and liver cells regenerate, so whatever tissue

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is donated grows back, but living people cannot donate a whole lung. That's why Bunnell is working so diligently to produce lungs in the lab.

One of Bunnell's PhD students, who has been working with him on the stem cell research to generate new lungs, recently came to him with an idea straight out of the box.

SCAFFOLDING OF SKIN

"It was 2014, and I had one of my sleepless nights," said Nick Pashos, a doctoral student in bioinnovation.

"I was watching a documentary on Netflix called 'Becoming Chaz,' about Sonny and Cher Bono's daughter Chastity transitioning to male Chaz Bono. Chaz was sitting with his girlfriend in the pre-op area, talking to the breast surgeon who was telling him that post-operatively he might not have nipples any longer.

I remember thinking, wow ... is this an issue? I hadn't realized that having a mastectomy meant removing the nipple and areola [the darker surrounding tissue]. Or, that if you keep it, you stand the chance of it becoming necrotic [cell death due to a lack of blood supply], which would mandate that it has to be removed. I stayed up the rest of the night researching this."

Pashos walked into Bunnell's office the next day and presented him with his newfound thoughts on breast reconstruction.

"I said I had an idea," said Pashos. "I told him it was basically the same concept as the lungs, but I wanted to transfer those procedures over to the nipple and areolar area. His initial response was, 'Come again?'"

But Bunnell was aware of one important factor, which encouraged him about the musings of Pashos.

"One of the problems we were running into with lungs was that they're very complex organs with different cell types. They have to function in different ways, and getting the appropriate cell ratios in there at the right time and in the right position to function properly can be difficult. But skin is a much simpler organ. ... It's just a couple of layers. I thought Nick's ideas made sense."

Bunnell required that Pashos do some fieldwork, to check the viability of his idea with those who would actually be intimately involved with his innovation— surgeons and patients.

"We met with two plastic surgeons. First, we discussed the intricacies of the procedure with Dr. Abigail Chaffin [assistant professor of surgery at Tulane]. Next, we took it to Dr. Scott Sullivan [physician and co-founder of the Center for Restorative Breast Surgery in New Orleans. Sullivan earned a Bachelor of Science in biomedical engineering from Tulane in 1987]. Both surgeons thought it was an idea whose time had come," said Pashos.

THE RACE IS ON

With the eventual knowledge that both doctors and patients were interested in this new biotechnology, Pashos began to put the pieces into place.

Since one in eight women will develop invasive breast cancer, and many require mastectomies or opt for preventive ones either to prevent the cancer's spread or to avoid the possibility of cancer altogether, the race for Pashos was on to make reconstruction more complete.

"I spent time with Dr. Sullivan at his Breast Restorative Center in New Orleans," said Pashos, "and learned the intricacies of breast reconstruction. After observing multiple surgeries, I knew I needed to tweak my original idea. With a National Science Foundation grant, and winnings from a number of competitions, I set out to build a graft that would not only be cosmetically pleasing but functional

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as well.”

Current procedures to reconstruct the nipple/areolar complex involve everything from tattooing nipples and areolas on to the patient’s chest to fashioning a raised nipple out of the patient’s own underarm or thigh tissue. But tattoos fade, and raised nipples eventually lose the structure that supports the protrusion, making the procedure impermanent.

“This is why we construct a scaffold,” said Pashos. “It’s a personalized transplant model, if you will, made from human tissue or from prophylactic mastectomy tissue. Then we remove all of the cells and the donor’s DNA from it, and what you’re left with is a collagen structure, which I call scaffolding. Think of it as the two-by-fours, which hold something together, but instead of filling it in with brick and mortar, in this case it’s cells.”

Pashos now leads his own company, BioAesthetics. A biotech accelerator program—IndieBio in San Francisco—has now picked up his project.

Representatives from that group came to New Orleans earlier this year, met with Pashos for one hour, and explained that they would give him \$250,000 if he would agree to come to the Bay Area for four months, where they would give him the tools he would need to get his product to the marketplace. Once through FDA registration and ready for clinical use, Pashos and his mentor Bunnell (now an adviser to the company) hope that the project Pashos has been working on for years will be more than his PhD dissertation, but will bring a positive change to those undergoing breast reconstruction.

“If everything works perfectly the first time,” said Bunnell, “we could see this being done on humans in the next two to three years. We may not need clinical trials, just human application, since there are already a lot of de-cellularized human skin products that have been transplanted in humans.”

Ultimately, the FDA regulators will make that call. In the meantime, it’s been a whirlwind from the very inception of this idea.

“Compared to academia, the world of technology runs at lightning speed,” said Bunnell.

“When Nick met with IndieBio, and they expressed an interest, they told him the class started in nine days, and they wanted him in San Francisco. He had nine days to change his entire life ... and he’s done it.”

BIOPSY AT THE SPEED OF LIGHT

In another arena, Tulane doctoral candidate in biomedical engineering and bioinnovator Mei Wang is solving a different problem related to cancer, with her colleagues from Instapath.

The Instapath team’s work with improving biopsy evaluations won this year’s grand prize in the International Business Model Competition in Mountain View, California, in April. (They also earlier this spring won the Tulane Novel Tech Challenge sponsored by the Office of Technology Transfer and Intellectual Property Development. Pashos also won the Novel Tech Challenge, sponsored by the Burton D. Morgan Foundation, in a previous year.)

Apart from Wang, members of the Instapath team are Tulane students Sam Luethy, Peter Lawson and David Tulman and faculty adviser Quincy Brown, an assistant professor of biomedical engineering.

Their work with structured illumination microscopy to examine fresh tissue is being heralded as the wave of the future in rapid biopsy evaluation.

“Right now, 20 percent of biopsy analyses are inadequate,” said Wang. “This is because you’re only looking at some of the cells falling off the biopsy, and that’s not enough for a complete evaluation.

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To have biopsy procedures redone is painful, and there's a waiting period of six weeks for a repeat procedure.

So, if the surgeon determines there are red flags everywhere, the patient is put on some form of treatment, but predicting the exact targeted treatment required has to wait."

Clinical studies for Instapath using real tissues are running over 90 percent accurate, and new evaluation methods will give physicians the tools to make a better, quicker diagnosis, where time is of the essence in many aggressive cancers.

"In our current procedure, the whole biopsy is stained with fluorescent stain," said Wang, "and using a special light, we take a picture from the structured illumination. So, there's no need for actual cutting in this technique. ... It's cutting with light. When all is said and done, a box will be next to the patient's bedside or in the O.R. [operating room], the biopsy will go into a computer system, and a pathologist from anywhere in the world can read this remotely, and respond over the internet or with a phone call."

Patents have been filed, FDA approval will be needed, and industrial-consulting firms will take the Instapath invention from prototype to the final design.

Ultimately, quick and accurate diagnosis of biopsy tissue, in order to expedite treatment, can be the difference between life and death for the patient dealing with cancer.

CHANGING LIVES

Bioinnovation is not only applicable for the human species, but often crosses over into the animal kingdom. For Jason Ryans, who will receive his doctorate from Tulane this fall, a serendipitous class on microdevices changed the trajectory of his lifetime focus. In the biomedical engineering program, he has worked extensively in lung and fluid mechanics. But in a bioinnovation class, Ryans was required to come up with a new technology, and apply to the Bill and Melinda Gates Foundation, which contributes to making lives better in developing countries.

"In this case it was working with mosquito borne viruses," said Ryans. "We came up with a device that would change color when a drop of blood was put on it, if the patient was positive for malaria. My partner Ashwin Sivakumar [also a biomedical engineering graduate student] and I came up with a prototype.

We ended up winning the New Day Challenge, the Spark Award and a business competition at Johns Hopkins." (They also received supported from the Tulane Novel Tech Challenge.)

But venture capitalists saw no opportunity to get their investment back for malaria testing in developing countries, although they lauded the Tulane partners for their work. It was at this point that the two doctoral students looked to solve a problem in the lucrative cattle industry.

"We discovered there was a bovine diarrheal virus, which has a large impact on cattle production," said Ryans. "Profit margins in the cattle world are based on the weight of the animal and how well it reproduces, but this virus was interfering with that. Worse yet, the virus was being passed from mother to calf, and the viral shedding at feedlots was spreading the disease like wildfire. This can affect roughly 15 to 20 percent of cattle."

Conventional testing for the virus has been cumbersome, and not user-friendly for farmers, who have been required to get blood samples from their livestock. This new innovation in viral detection of BDV can glean results from saliva or nasal swabbing, and the sample needs no refrigeration.

"This virus is not transmitted to humans, and therefore does not need the go-ahead from the FDA (Food and Drug Administration), but rather needs regulatory approval from the USDA (U.S. Department of Agriculture), which is a much faster process," said Ryans.

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And what started out as a side project for Ryans has taken on a life of its own.

“You know, initially I wanted to be in academia and research, and now I’m interested in the entrepreneurial side, combining business and science. I might want to do consulting, or go to work for the FDA to get some experience in the regulatory industry, and maybe eventually a private company.”

So for Nick Pashos who began college wanting to become a dentist, or Mei Wang who dreamed of being a physician, and Jason Ryans who saw himself spending his life in a lab, the prospect of changing the world through bioinnovation has changed their lives, and ultimately all of our lives, for the better.

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