

CAREERS

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Cleveland, Ohio, is experiencing a thriving biomedical-science ecosystem.

MEDICAL TECHNOLOGY

Ohio's bio boom

Life-sciences research and innovation are saving a state struggling with a flailing industrial base.

BY NEIL SAVAGE

Back in 2010, officials from the US Air Force Research Laboratory at Wright-Patterson Air Force Base outside Dayton, Ohio, paid a visit to Jason Heikenfeld. They were looking for someone who could devise a way to continuously monitor pilots' well-being in flight.

"My initial response was, 'I don't know how to do that,'" says Heikenfeld, an engineer who runs the Novel Devices Lab at Ohio's University of Cincinnati. But after some thought, he was soon working to develop wearable sensors that could measure biomarkers in human sweat. These would, in turn, provide information similar to that from a blood test — but in a continuous and non-invasive way.

By 2013, he had progressed to a point at

which he was able to create a company to commercialize the sensors. To launch his business, which he dubbed Eccrine Systems, he raised US\$1.5 million in early-stage venture capital from CincyTech, a local seed fund supported by the state of Ohio, his university, the Cincinnati Children's Hospital Medical Center and various local corporations and individual investors. In August 2016, Eccrine won a \$4-million contract from the Air Force to develop the sensors. Today, it boasts a 7-member executive team and; in March, the company was designated in a Bloomberg article as one of the year's 50 best start-ups, having raised almost \$9 million in capital.

Between 2001 and 2009, Heikenfeld had founded two other electronics companies, but didn't have quite the same luck. Although he was able to sell the technologies to other

businesses, the original companies have since dissolved, owing, he thinks, to a paucity of early- and mid-stage support for consumer-electronics ventures in the state. But life-science launches, he says, are another story: plenty of researchers and investors are focused on the sector. "Consumer electronics is not something Cincinnati is known for," he says. "But biotech in Ohio — you're able to find really great people."

A THRIVING MARKET

Life-sciences research and innovation are indeed flourishing in the state. The bioscience sector employs 68,500 people across 2,391 companies, with a total payroll in 2014 of \$4.8 billion, according to a 2015 report from BioOhio, an association of research institutions and companies in the state (see go.nature.com/2nxa168).

Ohio, whose major cities include Columbus, Cleveland and Cincinnati, is home to between 150 and 225 hospitals — depending on how they are categorized — and at least 360 post-secondary institutions, including universities, community colleges, vocational schools and specialized job-training centres, of which at least 108 offer bioscience degrees or certificates, the report shows.

In 2015, Ohio's institutions and companies attracted some \$701.6 million in research funding from the US National Institutes of Health (NIH) — exceeding the US average of \$470.7 million per state — plus another \$14.7 million from the US National Science Foundation (NSF). The cities can also point to local venture-capital groups, private foundations and university offices that help technologies developed at those institutions to spin out into new businesses.

Private investment in life-sciences companies in 2016 totalled about \$374 million, according to BioOhio. That's a sliver of what the hottest areas of the country for life-sciences start-up companies can tally. The Boston region of Massachusetts, for example, received \$1.1 billion in investments in biotechnology and medical-device companies in the third quarter of 2016 alone, according to a report by the international accounting firm PricewaterhouseCoopers (see go.nature.com/2nxj46v). The San Francisco Bay Area of California raked in \$663 million in investment in the same quarter.

But the state of Ohio is also investing in the field. One chief factor that helped to expand its life-sciences ecosystem is Third Frontier, an organization created by the state government ▶

► in 2002 with a collective \$2.3-billion bond issue approved by voters. “If it wasn’t for that state investment, I don’t think I would be doing Eccrine Systems,” Heikenfeld says.

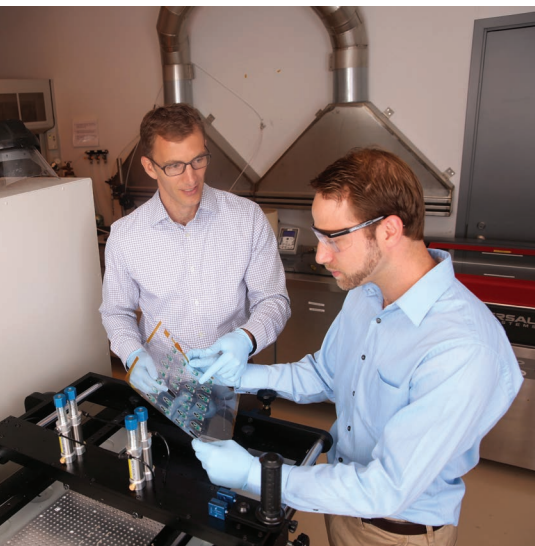
With the combination of Third Frontier, a strong community of investors, growing interest among Ohio’s universities and a good manufacturing base, scientists who want to develop their biotechnology research into a business have plenty of resources from which to draw. And there are other advantages, too: Ohio remains a much less expensive place to live than coastal cities such as New York, Boston or San Francisco. The *US News and World Report* ranks it as the most affordable state in the nation (see ‘A state in the middle’).

AN INDUSTRIAL BOOST

The seventh most populous US state, Ohio is part of a region known as the Rust Belt, which stretches roughly between western New York and Wisconsin, and whose industrial base has largely declined since the 1980s, although automotive and aerospace manufacturing still have a presence. Ohio’s industrial background, however, supports the areas of life sciences in which the state is most successful, particularly in medical devices and diagnostics, says John Lewis, president of BioOhio.

That manufacturing base proved useful to Wayne Poll, a urologist and surgeon who founded Minimally Invasive Devices (MID) in Columbus, the state’s capital, in 2007. The company makes FloShield, which uses a carbon dioxide spray to keep the lens of an endoscope, an instrument used to look inside the body, clear during surgery. MID also has a manufacturing plant in Dayton. “Southwest Ohio has a very rich network of toolers, injection moulders. There’s a real talent base there,” says Poll.

Poll was a surgeon and chief of staff at Riverside Methodist Hospital in Columbus, and spent three years as medical director of clinical innovation for OhioHealth, the area’s non-profit



Eccrine Systems creates wearable sweat sensors.

TECHNOLOGICAL FIX

A state in the middle

Ohio’s governor, John Kasich, wants the state to shed its ‘Rust Belt’ moniker. Speaking to a forum in February sponsored by the Associated Press, Kasich said that the state should embrace new technologies.

The belt gained its name in the 1970s, when economic changes eradicated hundreds of thousands of manufacturing jobs and left abandoned mills behind.

The state has not yet fully recovered. In February this year, its seasonally adjusted unemployment rate was 5.1%, a tick higher than the national average of 4.7%. A recent list of “Best States” by the *US News and World Report* gave Ohio an overall ranking of 35 out

of 50, on the basis of factors including health care, crime and the economy.

It was, however, judged to be the most affordable state, with the cheapest housing and the ninth-lowest cost of living.

In other categories, it came in below the median. It ranked 40th in infrastructure, for example — bridge and road quality and commuting time all ranked 18th. Renewable energy use came in at 45 and Internet download speed at 46.

Health-care quality ranked 17th, but health-care access was ranked at 26, dragged down by its low numbers of children’s dental and wellness visits. **N.S.**

health-care system. But after 22 years as a physician, he decided he was ready for a career change. He has found the start-up environment in Columbus to be congenial, with plenty of financial and mentoring support. Companies that might be too small to garner much notice in a place such as California’s Silicon Valley, he says, do much better in Ohio. “Little MID gets a lot of attention in Columbus,” Poll says. “Here, if you’re even a struggling tech start-up, you feel special, like you’re part of a club.”

Resources to support spin-offs of university and hospital research have been growing. “It’s very different than eight or ten years ago,” says Dorothy Air, head of entrepreneurial affairs and technology commercialization at the University of Cincinnati. “The Midwest is a growing presence in terms of the investment environment and the overall number of start-up companies.”

When she began her position in the early 2000s, there was little support for start-ups. But starting about five years ago, her university decided to focus more on promoting entrepreneurship, looking at new technologies and inventions with an eye towards commercialization. As part of that shift, the university combined its technology-transfer, commercialization and intellectual-property offices into the Technology Accelerator for Commercialization. Now, instead of automatically seeking patents for anything that a researcher develops, the office evaluates its commercial potential first. It then provides researchers with seed funding and introduces them to experts who can help them to launch a business.

Also jumping on the commercialization bandwagon is the Ohio State University (OSU) in Columbus. After hosting only a handful of start-ups in past years, it oversaw the creation of 38 companies between 2012 and 2015. One is Core Quantum Technologies, founded by two OSU professors and an alumnus to develop fluorescent nanoparticles for medical imaging and diagnostics. It raised money

through an NSF Small Business Innovation Research grant and Third Frontier.

“The pieces seem to be falling into place,” says Matt McNair, vice-president of OSU’s Office of Economic and Corporate Engagement, which was created in 2015. OSU also set up a \$100-million investment fund to support start-ups. “Between that and Third Frontier, there’s quite a bit of money available,” he says.

A SAFETY NET OF FUNDS

Third Frontier is widely considered to have been the catalyst for start-up success in Ohio over the past decade. Its Technology Validation and Start-up Fund helps to support new companies as they nurse technology from proof-of-concept and begin to woo venture capitalists. One advantage, says Lewis, is that Third Frontier was funded through the sale of investment bonds specifically for that programme, rather than through general tax revenues. So, when the recession hit and many states stopped spending tax dollars on new technology, the state couldn’t take away its money. The programme has around \$214 million left to spend, and Lewis and others hope that Ohio will renew the funding when it runs dry.

Private venture funds around the state are also on board — among them, Ohio Tech-Angel Fund in Columbus, North Coast Angel Fund in Mayfield Heights, near Cleveland, and Queen City Angels in Cincinnati. And private philanthropic foundations are trying to help companies to bridge the gap between a scientific discovery and a potential drug that would interest investors — a period called the valley of death, during which time the academic papers supporting a project have already been published, but the drug hasn’t been developed enough to prove that it’s marketable.

The Harrington Discovery Institute in Cleveland is one such non-profit foundation, and supports research into new therapies. Its commercial arm, BioMotiv, funds companies

founded on those discoveries. The institute hopes to build a supportive ecosystem in the area that, if not as big as Boston or Silicon Valley, could become at least as active as smaller regions such as the Research Triangle of North Carolina. “The chances of success occurring in a region increase enormously if you can increase the number of companies,” says Baiju Shah, head of BioMotiv, which he calls a ‘bio-science accelerator’.

In Cleveland, meanwhile, the Wallace H. Coulter Foundation has teamed up with Case Western Reserve University — the leading patent-producing university in the state — to form the Case–Coulter Translational Research Partnership, which invests \$1 million each year in helping companies to take their inventions to the investment stage. “We just want to get technology out of the university and into the patient population,” says Steve Fening, director of the programme.

To that end, the partnership collaborates with entities such as BioEnterprise — a Cleveland-based group that provides both money and guidance and has helped more than 350 bioscience companies to raise more than \$2 billion in funding since its 2002 inception.

Cleveland has seen a boom in the past several years, Fening says. “They can’t build apartments fast enough for people living downtown. Ten years ago, nobody wanted to live there.” One new resident is Siemens Healthcare, which, in December 2015, moved its regional base from Pittsburgh, Pennsylvania, to Cleveland’s Global Center for Health Innovation.

Ohio was an attractive environment for Shaun Young, who in 2015 founded a start-up in Columbus called Ardina. The company provides health-care referral and insurance-gap coverage, which pays for expenses not covered by private insurance, such as patient co-payments for visits to a physician. Young, a pharmacist from Hawaii who has lived in California, Arkansas and Massachusetts, likes the affordability and culture of the city. “Columbus has been very family-friendly,” he says. The local infrastructure was a huge help in starting Ardina, he says — particularly Rev1 Ventures, a seed-funding group.

For his part, Heikenfeld is happy in Ohio — it’s a great place to turn research into a company, he says. “It’s the universities, it’s the venture-capital community, it’s urban revitalization, it’s the regional strategy — it’s everything you need,” he says. “We’re changing perceptions, and the proof is in the success.” ■

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COLUMN

A growing phobia

If you are terrified to meet with your supervisor, start with small doses, says **Eleftherios Diamandis**.

Supervisor phobia, as I call it, is an irrational fear that I have seen often among trainees in my 30-plus years as a faculty member.

Yes, some principal investigators are harsh and unsupportive. But in my experience, this phobia is unrelated to a supervisor’s behaviour — or even to a graduate student’s or postdoc’s initial promise. Instead, it describes junior researchers’ fear of meeting with their supervisors and discussing their own research.

The phobia usually develops during the first or second meeting. The supervisor, with the best of intentions, provides constructive criticism — and then it all goes pear-shaped. I remember remarking on the slow progress of one PhD student’s research project at our second review meeting (typically held six months after their project launch). Three months later, I repeated my concerns, which were mainly about how slowly the student was learning essential techniques such as mass spectrometry, the workhorse of our lab. But instead of addressing those concerns, the student stopped scheduling meetings. I was too busy to notice for another six months.

In the meantime, the student also started to avoid my colleagues and was silent at lab meetings. After two years of this behaviour, and in the absence of a single publication or review, I suggested that the student consider pursuing a master’s degree rather than a PhD.

I was horrified when my suggestion elicited tears. The student and I decided to give the programme another try, with the proviso that we would hold mandatory monthly meetings. I also ensured that the student could get technical support from my lab manager. After three years, the student published in a good journal, and 18 months and two research papers later, was ready to write a thesis.

This may be an extreme case, but it happens. When challenged, such a trainee will typically defend themselves by saying that they have to finish an experiment in two weeks; they have a broken instrument; a critical reagent hasn’t arrived. I’ve watched students duck into another lab when they see their supervisor walking down the corridor.

Eventually, the trainee becomes isolated from the supervisor and the research group, and hides the problems that they may be having with experiments, rather than seeking help to resolve them. The fallout can compromise a



student’s efforts to complete their degree, publish papers or present at conferences.

So, how to deal with this? I find that ‘interoceptive exposure’, in which the trainee confronts their fears in controlled, limited doses, works best here. If you are struggling with this phobia, it’s up to you to resolve it. Ideally, your supervisor will be empathetic until you can acclimatize to feedback and criticism — but you must schedule regular meetings with your supervisor, and openly discuss your projects and progress. Start with 15-minute meetings once a week or biweekly, and then extend the duration and reduce the frequency as necessary. Try also to chat with your supervisor about topics unrelated to your work — the weather, or a film.

If you’re a mentor, keep these meetings short until the student feels more comfortable and comes to understand that constructive criticism is extremely valuable. Let your student reveal their sensitivities to you, and give them the option to walk away at any point. Knowing that there is an escape will help the student not to panic. Interoceptive exposure worked for me with four out of four students with this problem.

But if you are the student, understand that these meetings benefit you, and that it is your responsibility — not your supervisor’s — to set them up. You need to be able to organize your thoughts, rethink experiments, present experimental results and interpretations and consider your next steps. These skills will make supervisor meetings less frightening and more useful.

So take a deep breath — and head to that office more frequently. ■

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