TO MARKET, TO MARKET

AT BRANDEIS, WHAT GOES ON IN THE LABORATORY DOES NOT NECESSARILY STAY IN THE LABORATORY

BY LAURA GARDNER

If you've ever buttered your toast with Smart Balance spread, you may have noticed the fine print on the bright yellow tub that tells how Brandeis University researchers enhanced the ratio of good to bad cholesterol. This year, the license from the Smart Balance brand of products will bring in the lion's share of more than $1 million in royalties for the university and its Office of Technology Licensing (OTL).

University technology transfer—the movement of knowledge and discoveries from the academy to the general public—was embryonic at Brandeis a decade ago when "Brandeis butter" was licensed to GFA Brands, Inc. (now Boulder Specialty Brands, Inc.). Today, Smart Balance buttery spread, a patented blend of natural vegetable oils that improves the HDL/LDL cholesterol ratio, is only Brandeis's most famous and visible tech-transfer project to date. In the last few years, following an extreme makeover of the tech-transfer office here, licensing of technology to third parties has gained remarkable momentum across a range of innovations in the life sciences, physics, computer science, and education.

By all accounts, the growing visibility and sophistication of tech transfer is generating excitement in many circles, both within and beyond the university.

"I think Brandeis stock is undervalued—I see the stock going up," quips physician Laurence Blumberg '83, a member of the Brandeis University Science Advisory Council (BUSAC) and a prominent biotechnology investor. "Brandeis is a top-ten science university, and it's hard to keep the lid on that."

From tortilla chips to 3-D mammography

As at any top-ten science university, inventions at Brandeis cover a range of technologies. Biologist and veteran lipid expert K. C. Hayes, who developed Smart Balance, more recently discovered with his colleagues a way to produce tortilla chips that actually reduce your cholesterol while you eat them. And they taste good, too. So good that last year California-based

ILLUSTRATION BY JAMES STEINBERG
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Corazonas Foods licensed the phytosterol technology that makes the chips cholesterol-lowering. Today, the company is building a family of snacks around it.

Other Brandeis faculty inventors include computer scientist Jordan Pollack, whose online interactive educational video games help kids learn spelling, math, and other subjects, and synthetic chemist Li Deng, whose chemical catalysts are used in the pharmaceutical and biotech industries.

But that's not all. In the fields of drug development and medical diagnostics, faculty inventors are developing a range of technologies that promise to benefit humankind in profound ways. Some examples: Larry Wangh and his team of scientists in the biology department are developing DNA tests to detect infectious diseases as well as assays to test for cancer and bioterrorism agents. Biologist Neil Simister and his colleagues at Brigham and Women's Hospital and Children's Hospital Boston have created technologies that deliver drugs by inhalation and extend the efficacy of drugs in the bloodstream, reducing dosing frequency.

Above, cancer detection, prenatal diagnosis, forensics, and animal infectious diseases are all potential applications for Larry Wangh's platform technology, LATE-PCR.

On facing page, OTL executive director Irene Abrams says Brandeis is now attracting more first-time inventors, industry-sponsored research, and venture capitalists.

Scientists at Brandeis spin-out Dexela Corporation are testing a prototype for low-dose 3-D digital mammography. The biochemistry team of Greg Petsko and Dagmar Ringe has developed a pharmaceutical technology that could be instrumental in finding new treatments for Gaucher's disease, and Brandeis, along with Brigham and Women's Hospital, has entered into an option agreement with New Jersey–based Amicus Therapeutics to license it. In addition, chemist Jeff Agar has provisionally patented a promising method to treat the familial form of amyotrophic lateral sclerosis (ALS), also called Lou Gehrig's disease.

It's not just about money

While the Office of Technology Licensing has achieved impressive revenue growth, filling the university's coffers is not the primary goal of tech transfer**,** says Irene Abrams, OTL executive director. Blockbuster licenses that bring in many millions a year are the exception rather than the rule; only a handful of universities can boast such a revenue stream, while the cost of obtaining global patent protection for a single invention can easily reach $250,000.

"People like to focus on the money, but I would like to put forward a broader view of technology licensing," explains Abrams. "If we can increase Brandeis's visibility and faculty opportunities to interact with industry, there will be many other benefits to the university."

Those benefits include attracting and retaining top-notch faculty; disseminating research to make a positive social impact; fostering corporate investment in basic research, industry collaborations, and consulting relationships; providing access to better technical facilities; and cultivating job opportunities for graduates and postdocs.

"Brandeis has taken the lead in facilitating my engagement with faculty, and I expect that, over time, there will be opportunities to identify graduates and postdocs we could hire," says Reid Leonard '80, executive director of licensing and external research at Merck Research Laboratories in Boston. "It is equally likely that we could identify some collaborative research opportunities down the road."

Collaborating with a global leader

"Scientifically, it's a fabulous deal, and commercially, too," asserts Larry Wangh, describing his lab's relationship with Smiths Detection, a world leader in threat detection and screening technology for military, transportation (such as airport screening systems), and homeland security applications. Over the last three years, the U.K. corpora-

tion has invested substantial resources in Wangh's research program to develop a platform technology for DNA testing.

"Not only has Smiths invested in Larry Wangh's lab, but the company is continuing to expand its relationship with Brandeis, increasingly relying on the university to supply the creative research fueling their investment in life-science technology," says Abrams. "When an industry leader like Smiths is committed to an ongoing relationship with Brandeis, it shows tremendous confidence in our science."

Agar, whose ALS research has also caught the attention of industry, seems to reflect the general sentiment about commercializing basic research at Brandeis: "I do basic research, but I'm not happy until it actually does something. Curing ALS in a dish is a good start, but treating it in humans is the ultimate goal."

Patent prowess

The number of invention disclosures (internal confidential documents describing patentable intellectual property), patents, and licenses an institution tallies is the first measure of tech-transfer prowess. In this regard, Brandeis is beginning to leverage its considerable faculty and student talent. So far this year, OTL has received twenty-five invention disclosures, and Abrams projects several more before year's end. Last year saw nineteen invention disclosures, up from six in 2004. Abrams projects twelve new patent applications this year, up from one just three years ago.

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Several factors have contributed to this wave of activity. The Science Advisory Council was instrumental in rescuing the university from the tech-transfer shoals, where lack of funding, visibility, and experienced leadership had stranded the office in the nineties, despite the Smart Balance deal. At the council's inaugural meeting in 2000, member Margery Feldberg '74 says, the board decided then and there to "get the tech-transfer function up and running, promote it, and make it profitable." Feldberg helped lead the transformation of the office, says Alex Barkas '68, BUSAC chairman and a member of the university's board of trustees.

While invigorating tech transfer, the university also retained a clear commercial incentive for faculty and students with patentable intellectual property: 40 percent of any revenues or royalties resulting from licenses goes to the inventors. A 25 to 30 percent revenue-sharing arrangement between a university and its inventors is much more typical. The office came into its own under the guidance of tech-transfer white knight Larry Steranka and his successor, Abrams, who spent seventeen years honing her skills at the icon of tech transfer, MIT, before joining Brandeis last year.

"We've hit the ground running, really, since we started at almost ground zero," says Barkas, who holds a PhD in biology and is cofounder and managing director of California-based Prospect Venture Partners. "We're really capturing the potential licenses now, and it's partly because the faculty believe they have advocacy and support."

"For a small research university with, really, a newly professional tech-transfer office, Brandeis is negotiating a record number of patents and licenses, and we're now able to attract more first-time inventors, industry-sponsored research, and the attention of venture capitalists," says Abrams.

Reinventing tech transfer

If academic tech transfer is maturing nicely now, it's because of a historic act of Congress more than two decades ago. The Bayh-Dole Act of 1980 turned the status quo on its head by allowing universities and other nonprofit institutions to own the discoveries resulting from federally funded research. Before then, federal agencies owned the patents that grew out of tax-supported university research, though by and large the government allowed patents to wither on the vine. The potential public benefits of tech transfer—economic development and a positive impact on society—just didn't materialize.

"It's very difficult to develop the early-stage technology that comes out of universities without a lot of championing, and the federal government really wasn't able to provide that," says Abrams.

The Bayh-Dole Act stipulated that universities must protect their discoveries through patents and pursue commercialization. Most

Above, biologist Neil Simister cofounded Syntonix, the first Brandeis spin-out to be acquried by a biotechnology giant.

Facing page, Chemist Jeff Agar is developing a novel strategy to treat Lou Gehrig's disease.

important, the legislation said all revenues must go to the university and be shared with the creators, thereby providing a powerful incentive to inventors. Stanford boasts the oldest tech-transfer office in the country, organized in the wake of the Bayh-Dole Act and followed a few years later by MIT. But it was closer to 1990 when the field of technology licensing really began to come into its own, according to Abrams. "Now, virtually every university has some form of technology licensing," she says.

The mother of invention

According to a national survey by the Association of University Technology Managers (AUTM), universities and other nonprofits signed almost 5,000 new licenses in 2005. That same year, 527 new products came on the market, 628 spin-out companies were created, and more than $42 billion was invested in U.S. academe. Indeed, the tech-transfer movement gave rise to the biotechnology industry, whose lifeblood is early-stage technology originating at the lab bench of basic research.

As a leader in life-science research, Brandeis is fueling innovation in biotechnology in a number of areas where there is unmet need for more effective treatment or diagnosis. Syntonix, a biopharmaceutical spin-out formed by Brandeis with Brigham and Women's Hospital and Children's Hospital Boston to commercialize novel drug-delivery methods, was bought earlier this year by Biogen Idec, becoming the first Brandeis spin-out to be acquired by a biotech giant. Syntonix was started by Brandeis's Simister, along with Wayne Lencer of Children's Hospital; Richard S. Blumberg of Brigham and Women's; and Blumberg's brother Laurence, who was the business founder.

Better health care

Syntonix's technologies harness the human body's natural immunological pathways to provide novel methods of drug delivery. Many pharmaceuticals consist of molecules too large to be absorbed through the mucous membranes, meaning that patients with chronic conditions like hemophilia, anemia, multiple sclerosis, and autoimmune disorders must take drugs either intravenously or by injection. Frequent dosing is typically needed, because the drugs break down quickly in the bloodstream.

In the early- to mid-1990s, Simister, Lencer, Blumberg, and their colleagues discovered that the molecular receptor that carries immunoglobulin G antibodies from mother to fetus across the placenta is also found in the mucous membranes lining the intestines, airways, and lungs. This discovery led to the idea that the receptor, known as FcRn, could be used to carry large-protein drugs across mucous membranes into the bloodstream, suggesting the possibility of replacing these injection drugs with inhaled or oral versions.

Then the scientists discovered that the FcRn receptor also prevents antibodies from breaking down quickly in the bloodstream, the normal fate of other molecules. This rescue capability made FcRn part of a so-called salvage pathway. To take advantage of this pathway, Syntonix scientists designed pharmaceutical proteins that bind to FcRn, extending the lifetimes of these drugs in the bloodstream.

"We founded Syntonix with the hope of translating our basic discoveries into improvements in health care. The company developed and expanded our technologies to the stage where they have preclinical drug candidates for treating hemophilia and infertility," says Simister, adding, "Biogen Idec's acquisition is an excellent outcome because they have the expertise in manufacturing and development to bring these drugs to the clinic."

Under the deal, Biogen Idec paid $40 million for Syntonix, with the potential for up to

another $80 million in payment if certain milestones are met. "It's a very good outcome; the underlying biology is sound, and in three to four years we could have a life-saving drug on the market," says Laurence Blumberg. "It's all about innovation."

Which takes time, money, patience, perhaps the spark of genius, and probably more money.

Larry Wangh should know. After teaching in Brandeis's genetic counseling program for years, he and his colleagues sought to improve preimplantation genetic diagnosis for couples at risk of having children with severe hereditary x-chromosome-linked disorders. His research, in collaboration with two other labs, did lead to better *in vitro* genetic diagnosis using real-time polymerase chain reaction (PCR), a molecular biology technique that replicates DNA from a single gene or gene fragment. Wangh's early focus on PCR's limitations, particularly for samples as small as a single DNA molecule, fueled a research direction that today promises to open a whole new landscape to DNA testing.

"Even after twenty years of research, there are only a handful of PCR-based tests, and the reason is that there are inaccuracies in the standard methodologies," says Wangh. "We have reduced and eliminated those inaccuracies."

The new and improved method developed in the Wangh lab, known as Linear-After-The-Exponential PCR (or LATE-PCR for short), is substantially more reliable and sensitive than conventional PCR. "From now on, anywhere there is DNA or RNA that you want to study, or make more of, LATE-PCR will be the technology to use," says Wangh.

Cancer detection, prenatal diagnosis, forensics, and human and animal infectious diseases are all potential targets for this testing technology. For its part, Smiths Detection is focused on military-threat detection and homeland security issues and is planning to leverage this platform technology in the areas of biodefense and first response.

"In all of these fields, LATE-PCR will make it possible to construct highly informative, rapid, affordable assays, replacing or supplementing current tests that take days or weeks to generate answers and cost the users millions of dollars," says Wangh.

A daring dream

Ever since he was a boy, chemist Jeff Agar was certain he wanted to cure disease in humans. Later, as a graduate student, he realized he wasn't seeking to defeat just any disease, but a truly cruel killer whose progression is swift and unstoppable. "ALS is the place where I thought I could make the biggest difference," he says.

Agar's scientific verve has brought him much closer to achieving that daring childhood dream. At thirty-four one of Brandeis's youngest inventors, he has developed a novel method to treat Lou Gehrig's that he believes is unlike any other approach in neurodegenerative research. Moreover, he has developed a portable kit using mass spectrometry, an analytic technique that measures the composition of physical samples, such as tumors and tissue, to detect disease, including ALS. Both are in the patent pipeline, and Agar is hammering out the final details of an agreement with ExSAR, a New Jersey drug-development company interested in commercializing his ALS research. Agar says the entrepreneurial culture here played no small role in bringing him to Brandeis, where he works not only around the clock, but against the disease's own deadly timeline.

The fatal neuromuscular condition typically starts by affecting walking and ends by causing loss of respiratory function, all within the course of three to five relentlessly devastating years. Motor neurons transmit the command to move from the brain to the skeletal muscles, but in a person with ALS those motor neurons are weakened and ultimately destroyed by a toxic protein. Underlying Agar's research is the key discovery that changes taking place in proteins, such as oxidation, are toxic to motor neurons. His strategy is to commercialize a novel class of pharmaceuticals, called AGE inhibitors, that prevent modified proteins from killing motor neurons.

"I am sticking with ALS research until there's a treatment," Agar says with quiet determination. "The first time I'll ever feel joy in my research is the moment it extends the life of a patient."

Laura Gardner is the university science editor.

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