

# America's BIOTECH heartland



Although not the first location that comes to mind, Wisconsin is making its influence felt.

BY RANDALL C. WILLIS

**S**ilicon Valley—the high-tech region outside of San Francisco. Genetown—the biotech mecca that is the Boston area. Beertown and Mad City—not exactly what one thinks of when conjuring up images of a biotech hotspot. Nonetheless, Milwaukee and Madison are just two of the centers of scientific excellence in the northern state of Wisconsin. Brought together by the confluence of state, local, academic, and corporate efforts, this region is rapidly expanding its role in America's biotech industry, turning technological dreams into commercial reality.

## After-school specials

To a great extent, the success of Wisconsin's biotech initiatives rests squarely on the shoulders of its academic institutions and their desire to license technologies developed at the schools to local companies. According to the recently released *Wisconsin Bioscience 2004* report from the Wisconsin Association for Biomedical Research and Education, the University of Wisconsin–Madison is one of the largest research organizations in the United States and is ranked in the top 20 institutions worldwide for NIH funding. With its affiliated medical school, hospitals, and clinical centers, UW–Madison employs hundreds of physicians and thousands of professional clinical staff.

Likewise, the Medical College of Wisconsin in Milwaukee, a private institution, is the state's largest medical school and is similarly affiliated with several hospital and clinical research centers, such as the Children's Hospital of Wisconsin and the Blood Research Institute. Other schools with a strong foundation in research include UW–Milwaukee, which is highly ranked in neu-

rosience; Marquette University, which is heavily involved in biochemistry, biology, and physiology; and the Milwaukee School of Engineering, which has a growing bioengineering program.

"The university offers many resources to entrepreneurs to help them in forming companies," says Susan Pschorr, director of finance and human resources at Platypus Technologies. The company, which specializes in nanostructured surfaces for technologies such as arrays, is located in the MG&E Innovation Center, a business incubator in the University Research Park of UW–Madison.

"Platypus benefited from the UW–Madison School of Business's Weinert Center for Entrepreneurship and the WAVE Program, which partners M.B.A. students with young companies to develop business and strategic plans," Pschorr explains. "The Small Business Development Center (SBDC) offers a number of courses and other resources giving scientists access to education in fundamental business areas to prepare for starting businesses. Two of Platypus's founders attended SBDC courses. In addition, the Office of Corporate Relations offers valuable resources to Wisconsin businesses."

Aside from being premier learning institutions, the universities and colleges of Wisconsin are also good sources of basic technologies that local companies can harvest and develop.

"A tradition of educational excellence has contributed to an environment of intellectual curiosity, exploring spirit, and intuitive vision—together they create a rich business development climate," explains Bill Linton, president and CEO of Madison-based Promega. "World-class institutions, such as the University of Wisconsin and the Medical Colleges of Wisconsin, not only offer strong spin-off

and collaborative business opportunities but also contribute a wealth of diversity and interest culturally.”

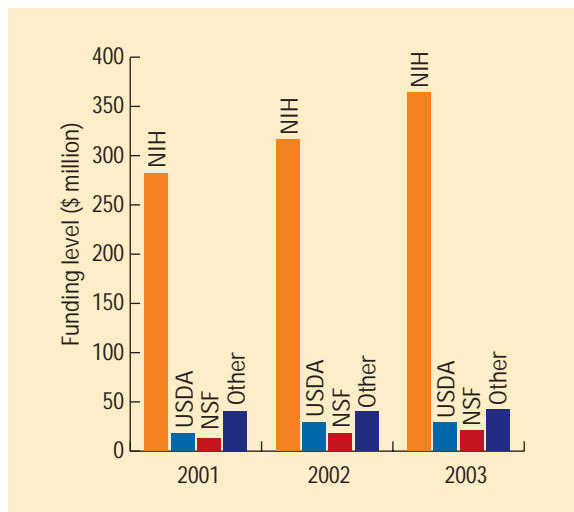
“Although the majority of our R&D work is performed within the company, we also license technology and optimize it in our R&D department so that our customers can readily use these new methodologies,” says Katherine Kramer, technical communication manager at EPICENTRE, a molecular biology reagents supplier. “Two good examples of this are our CopyControl Systems, which were originally developed in Waclaw Szybalski’s lab, and our EZ::TN Transposome Kits, based on the hyperactive Tn5 transposition system from William Reznikoff’s lab, both at UW–Madison.”

The schools are also good sources of staff, and many university departments have long-standing relationships with the local companies.

According to Susan Byram, business director for Bruker Nonius Crystallographic Systems, a branch of Bruker AXS, the company recruited its CTO and global head of its Single Crystal Diffraction team, Roger Durst, and its chief detector scientist, Tim Thorson, from UW–Madison. Similarly, it recruited two senior applications scientists, Cary Bauer and Matthew Benning, from the Rayment and Holden research groups at the university; and some of the company’s scientists have adjunct appointments at UW–Madison, which, Byram suggests, helps it retain top people.

“We think there are several factors contributing to the success of companies spinning off from UW–Madison,” offers Joleen Rau, director of marketing communications at microarray technology specialist NimbleGen Systems. “UW is a highly respected research facility and draws talent from across the nation. In the end, this talent really doesn’t want to leave Madison, due in part to the relationships people have formed with a wide range of like-minded people and the attractive standard of living they experience. In addition, the university has even created a research park that is ‘start-up friendly,’ and many of the biotech companies in Madison start or spend time there.”

The interaction between industry and academia is not, however, solely one-way. In March, officials at Bruker Nonius announced the formation of a collaborative effort with the UW–Madison Structural Genomics Consortium. In partnership with Discovery Partners International, Bruker Nonius delivered a Crystal Farm imaging system, BruNo robotic sample handler, and PROTEUM/MICROSTAR X-ray and light



**Federal support for Wisconsin bioscience R&D comes largely from the NIH.** (Based on numbers from *Wisconsin Bioscience 2004*.)

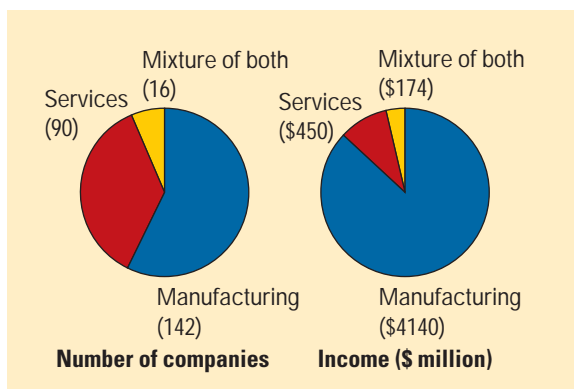
it established and is the sole corporate sponsor of two nonprofit entities. It created the BioPharmaceutical Technology Center Institute to extend lifelong learning in the sciences and culture to a broader community, both locally and globally. Likewise, Promega realized its commitment to children and their quality care by establishing the Woods Hollow Children’s Center, a daycare center for infants and school-age children that is accessible to both Promega parents and the larger community.

### Moving at WARF speed

As an adjunct to the technical and personnel support that companies receive from the universities, they can also find business and financial support through venture capital (VC) firms and the Wisconsin Alumni Research Foundation (WARF).

“Venture capital in Wisconsin, like anywhere, has certainly had its ups and downs during the past 20 years,” says Tom Schwei, vice president and general manager of DNASTAR, a sequence analysis software firm. “We have been fortunate to have a couple of local players who have had a strong dedication to our market for many years, including Robert W. Baird and Venture Investors of Wisconsin. More recently, Mason Wells and Frazier Technology have joined the mix in our area.”

These funds serve companies directly and collaborate with other VC firms to fund ideas in the Madison area, Schwei explains. In



**Wisconsin bioscience is dominated by the manufacturing sector.** (Based on 2002 numbers from *Wisconsin Bioscience 2004*.)

addition, Wisconsin has seen a growing number of angel investors to help companies get to the VC financing stage. “Even though it is still challenging for new ideas to get funded, there are more funding options today than there have ever been, and the prospects for new spin-offs from UW are better than ever,” he adds.

Established in 1925, WARF is a private, nonprofit organization designed to support scientific research at UW–Madison by patenting inventions arising from university research, licensing technologies to companies for commercialization, and returning this income to the university. From its first licensing agreement in 1927 with the Quaker Oats Company for a process that fortified breakfast cereals with vitamin D, the organization has been instrumental in the commercialization of products and processes. These have included coumarin, a blood thinner used to treat cardiovascular disease; a pharmaceutical tablet coating method used to control drug release; and innovations in magnetic resonance imaging (MRI) technology to facilitate disease diagnosis and treatment. Similarly, WARF-sponsored technology for isolating human embryonic stem cells has been critical in the stem cell debate and led to a WARF subsidiary, the WiCell Research Institute, being named one of three Exploratory Centers for Human Embryonic Stem Cell Research in the nation by the National Institute of General Medical Sciences in September 2003.

“The most critical steps for a new company are finding funding and space,” NimbleGen’s Rau offers. “Both of these were relatively easy for NimbleGen in the early days.” WARF put the founding scientists in touch with local VC money, which provided the initial funds to start the company, she explains, while the state of Wisconsin provided a technology development loan and the MG&E Innovation Center supplied an incubator site for the fledgling company. WARF also assisted in managing the company’s intellectual property (IP) in the early days. “All of these factors combined made it relatively easy to get the company off the ground,” Rau adds.

“WARF was and continues to be instrumental in the establishment of NeoClone,” says Deven McGlenn, in speaking of the antibody specialist company of which he is CEO. “They funded the patents and licensed the technology to NeoClone. In exchange, they have an equity stake in the company and receive royalties from NeoClone on product sales.”

### A selection of Wisconsin-based biotech companies

Company	URL
Aldrich Chemical	www.sial.com
Bruker AXS	www.bruker-axs.com
Cedarburg Pharmaceuticals	www.cedarburglabs.com
ConjuGon	www.conjugon.com
Covance Laboratories	www.covance.com
Deltanoid Pharmaceuticals	www.deltanoid.com
DNASTAR	www.dnastar.com
EMD Biosciences–Novagen	www.emdbiosciences.com
EPICENTRE	www.epicentre.com
EraGen Biosciences	www.eragen.com
Gala Biotech	www.gala.com
GenTel BioSurfaces	www.gentelbiosurfaces.com
Gilson	www.gilson.com
Infigen	www.infigen.com
Lucigen	www.lucigen.com
NeoClone	www.neoclone.com
NimbleGen	www.nimblegen.com
OpGen	www.opgen.com
Pel-Freez Clinical Systems	www.pel-freez.com
Pierce Biotechnology	www.perbio.com
Platypus Technologies	www.platypustech.com
Prodesse	www.prodesseinc.com
Promega	www.promega.com
Quintessence Biosciences	www.quintbio.com
Schwarz Pharma USA	www.schwarzusa.com
Scientific Protein Laboratories	www.spl-pharma.com
Takara Mirus Bio	www.takaramirusbio.com
Tetronics	www.tetronics.com
Third Wave Technologies	www.twt.com

For an expanded list of companies, see [www.wisconsinbiotech.org](http://www.wisconsinbiotech.org).

The story is similar at biochip producer GenTel BioSurfaces. “WARF took an equity position in GenTel in lieu of up-front licensing fees,” explains company President Alex Vodenlich. “They were able to help us assemble a good IP portfolio around which we could start the company. More recently, WARF has helped us restructure our licensing agreements to better fit our future commercial and financial needs.”

### Government

Aside from the generous contributions of organizations like WARF and to help offset the general lack of VC money, the local, state, and federal governments are active in supporting Wisconsin’s biotech initiative. In part, this support is promoted through the lobbying activities of groups like the Wisconsin Technology Council and the Wisconsin Biotechnology and Medical Devices Association (formerly the Wisconsin Biotechnology Association; WBA).

According to James Leonhart, executive vice president of the WBA, the primary functions of his group include acting as a purchasing consortium, organizing networking opportunities, lobbying federal and state governments, and helping with regulatory and branding issues.

“We have an excellent working relationship with Wisconsin Gov. Jim Doyle, who has become a strong proponent of the biotechnology industry,” Leonhart explains. “We also have strong ties to the Economic Development Commission of the City of Madison and the Spirit of Milwaukee, branding the industry

in the biotech and medical device centers of the state.”

Perhaps the biggest impact the federal government has on Wisconsin biotech comes through basic research funding, setting the groundwork from which groups such as WARF and the universities can spin off technologies. According to the *Wisconsin Bioscience 2004* report, the NIH alone accounts for 70–80% of federal funding for Wisconsin research, which approached \$500 million in 2003.

The state government is similarly committed to finding ways to develop and nurture a strong biotech industry in Wisconsin, according to EPICENTRE’s Kramer. In-state funding in 2003 for

biotech research neared \$40 million, with another \$20 million coming from WARF.

For example, according to NeoClone's McGlenn, his company was recently awarded a \$150,000 loan on extremely favorable terms to support its research efforts. Likewise, in September 2003, Governor Doyle announced the Grow Wisconsin Initiative, which among other things created a \$300 million fund providing seed and early-stage capital, and another \$10 million for a free training fund for companies looking to invest in new, high-paying jobs.

At the local level, in June 2003, the Madison City Council adopted an ordinance amendment altering the zoning restrictions for companies looking to set up biotech research facilities.

### Location, location, location

As much as any other factor, the lifestyle of the northern Midwest attracts many people to Wisconsin's universities and biotech community. Largely devoid of the hustle and bustle of the California and New England coasts, Wisconsin represents something of an idyllic setting that appeals to both family and friends.

"Madison offers a very rich cultural and intellectual environment, as well as a highly skilled workforce," Platypus's Pschorr says. "We are surrounded by natural beauty and have access to great recreational activities. The size of the city means there are not a lot of traffic headaches or long commute times, but it is located close to Milwaukee and Chicago, so we have easy access to big-city amenities. Madison also has an excellent school system."

"The main drawback is Madison's location in relation to interacting with companies on the coasts," she adds. "There are direct flights to only a very limited number of destinations, and there also seems to be a psychological barrier that hinders companies on the East and West coasts from working with companies in the Midwest."

"I have been part of the company both in northern California and here in Madison," Bruker Nonius's Byram offers. "We moved our manufacturing capability to Madison in 1984, and the improvement was striking. The Midwest work ethic really helps."

"In Silicon Valley, at that time, there was so much competition from electronics businesses that it was not uncommon to see our manufacturing workforce turn over completely in the space of several years," she says. "After moving to Wisconsin in 1984, some of our key people have been with us ever since and contribute measurably to the quality and on-time delivery of our instruments."

### Supply-side economics

Interestingly, whereas other biotech clusters throughout the United States and around the world typically focus on the drug discovery arena, the Wisconsin biocluster seems to lean toward supplies and services. According to Lucigen's Harry Burrill, this is the result of several factors involving financing and the industrial legacy of companies such as Aldrich Chemical, Gilson, and Promega.

"Many of the entrepreneurs starting biotech companies in the Madison area are 'graduates' of Promega, so the research products market is what they are familiar with," he explains. "Perhaps more

importantly, compared to the wads of cash needed to start a drug discovery company, you can 'bootstrap' starting a research products company with much less money, then get products on the market relatively quickly to generate a revenue stream for survival and growth. This is an important consideration given the relative scarcity of capital for biotechs in Wisconsin."

Recently, the importance of the area's industrial legacy was highlighted with the formation of Takara Mirus Bio, a joint venture of Japan's Takara Bio and Wisconsin native Mirus Corp.

"Takara was just in the process of closing down a U.S. subsidiary when contacted by Terry Sivesind, who was then with PanVera," explains Leslie Miller, the marketing and sales specialist for the new company. "Terry and his colleagues were able to convince Takara that their background at Promega would allow them to also be successful with selling the Japanese products, which were similar, in the United States. They were persistent and had no competing products, so Takara decided to give them a try."

Alternatively, it might be a question of local sensibilities.

"Perhaps the nature of companies located in the Madison area is reflective of the conservative Midwest culture of Wisconsin," DNASTAR's Schwei echoes. "While 'tools and services' companies may never hit a home run from a company and shareholder valuation perspective, they can certainly provide a very comfortable return for shareholders and be a great place to work for employees for many years. They offer a business model that has much less risk than a diag-

nostics or therapeutics company, but still with solid returns when properly managed."

This situation, however, does not mean that companies working the supply side today will not move into a drug discovery mode tomorrow. Over the last few years, there has been dramatic growth in the antibody-based therapeutic market, which has caught the eye of NeoClone.

"Our research focus is to tailor our technology to develop therapeutic monoclonal antibodies (mAbs)," McGlenn says. "We continue to make significant progress in this area and hope to be in a position to generate therapeutic mAbs within one to two years."

Likewise, GenTel BioSurfaces' Vodenlich points to several other firms beginning to push into the Wisconsin therapeutics market, including Quintessence Biosciences, ConjuGon, and Deltanoid.

### Room to grow

"Several of the companies in the Madison area have been in existence more than 20 years and have contributed significantly to the local business community," Schwei says. "Numerous others have grown up in the past 5 to 15 years. While Madison is not yet the largest biotech community in the nation, it is certainly a dynamic place where many interesting things are going on."

"There is virtually unanimous agreement that technology-based companies are critical to ensuring a strong economy," he adds. "And we have a growing number of businesspeople who understand what it takes to be successful with technology businesses." ■

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