

Nanotechnology Entrepreneurs: Creating the Foundation for an Amazing Future

By Jed Weiner, Editor, BioLogical Quarterly

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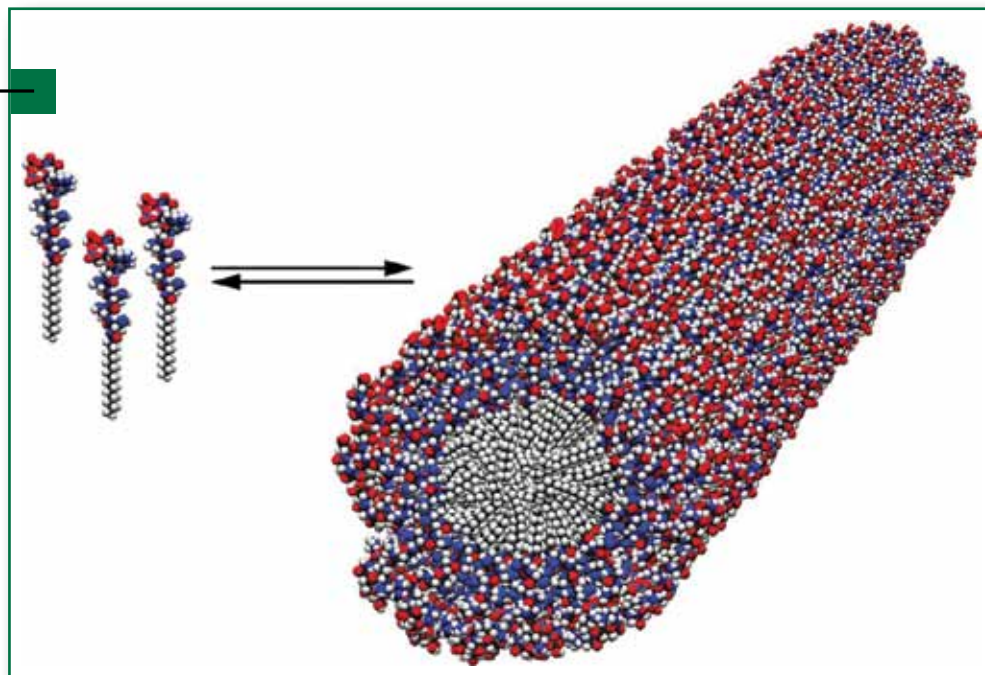
In the winter 2008 issue of BioLogical Quarterly, we covered the Illinois research institutions that are actively exploring nanoscience and nanotechnology, a world that exists between 100 nanometers and one nanometer (a billionth of a meter). In this final installment of a two-part series, we highlight some of the start-up companies working diligently to translate academic discoveries into commercial products. Space constraints preclude BQ from reporting on all of the state's more than 30 nanotech companies. Instead, we have selected several companies to represent the groundbreaking and promising work emerging from the entrepreneurial enterprises headquartered in Illinois.

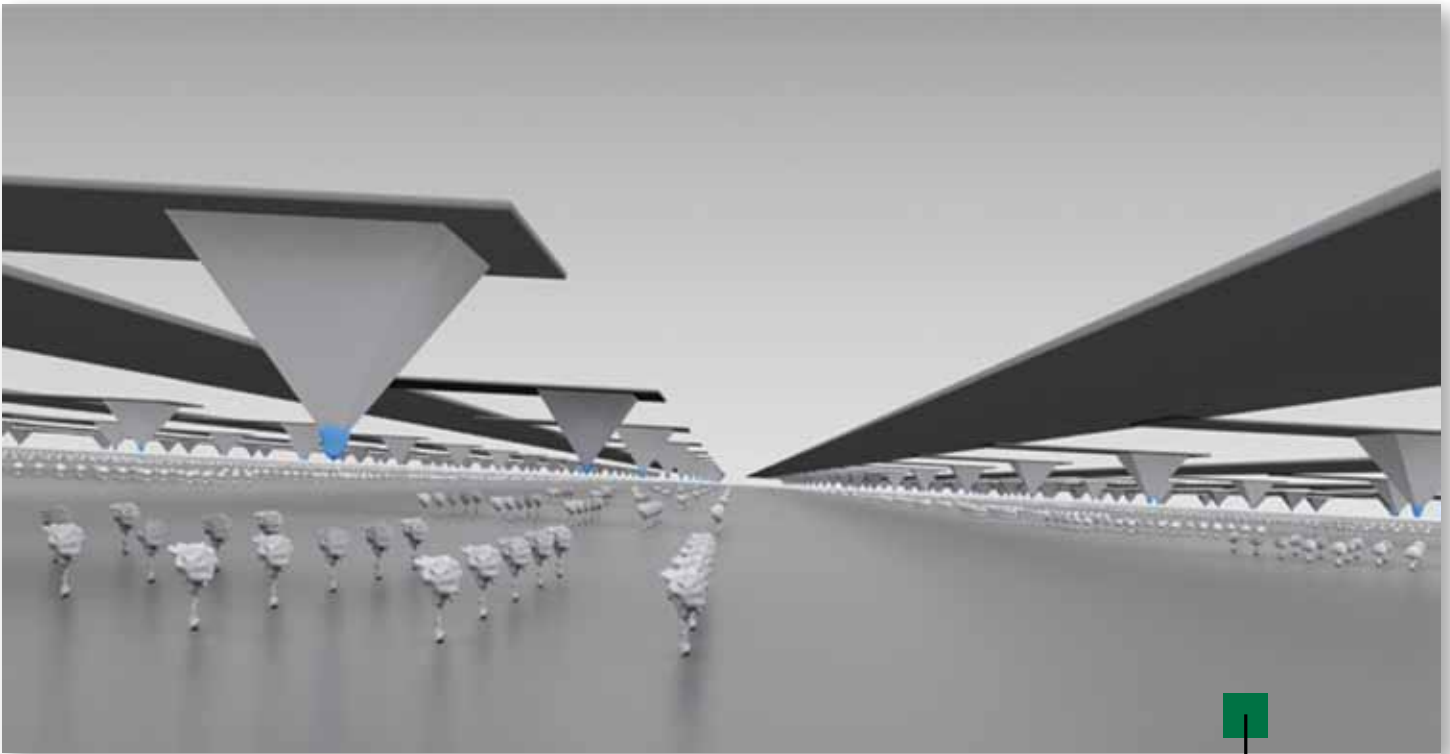
Michael Rosen, an iBIO board member and a seasoned executive in the pharmaceutical and biotech industries, currently leads the strategic

marketing efforts for Forest City's Science + Technology Group, a developer of science and technology parks across the country. One of those sites is in Skokie, about 13 miles north of Chicago on the former G.D. Searle campus. "When people ask what sets Chicago and Illinois apart from other regional life science clusters, nanotechnology is clearly one of those points of differentiation," Rosen said. "Building a nanotech cluster at the Illinois Science + Technology Park has been and will continue to be one of our prime areas of focus over the next five to 10 years."

In 2009, the Skokie facility already is home to four Northwestern spinout nanotech companies and the national trade association for the nanotech industry, the NanoBusiness Alliance. Two of the companies, Nanotope and Nanolnk, are among the highest-profile examples of Illinois' global leadership in the nanosciences.

Nanotope is developing injectable, self-assembling nanofibers that can encourage the cellular repair or regeneration of human tissue.





Nanotope – Pioneers in Regenerative Medicine

Nanotope is developing a technology platform that it hopes will make it a leader in regenerative medicine. Its lead products target neuron regeneration for prevention or reversal of paralysis associated with spinal cord injury, and angiogenesis (creation of new blood vessels) for advanced wound healing.

The products, currently in preclinical testing, are injectable compounds that initiate and support tissue regeneration and growth. The underlying technical basis is a customizable chemical matrix, or gel, of nanofibers that provides three-dimensional bioactive scaffolding in which cells and tissues may grow and differentiate. "What we think is innovative about Nanotope is that we have a technological platform that can be customized for a wide range of different tissue targets," said James Hulvat, PhD, Nanotope's vice president of research and development. "Unlike many drug development companies that are betting their future on a 'one-off' product,

we have a number of different ways to develop our technology."

Nanotope's technology platform was first developed by Dr. Samuel Stupp, the director of Northwestern University's Institute for BioNanotechnology in Medicine (IBNAM). Today Nanotope is conducting longer-term animal studies as preparation for initiating research with human subjects, perhaps as early as next year. Future R&D programs will investigate regenerating bone, cartilage, heart tissue, and peripheral blood vessels.

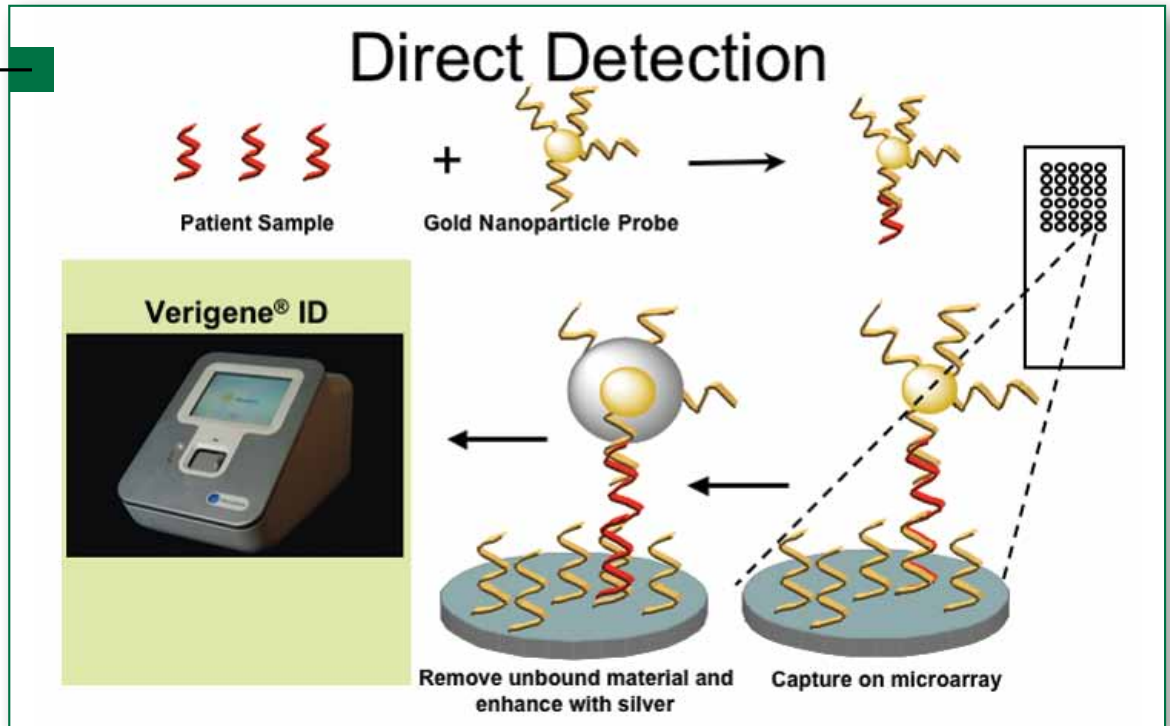
Nanolnk – Manufacturers of a Mighty Pen

While Nanotope seeks to apply its platform to a variety of therapeutic areas, Nanolnk has identified multiple and diverse pathways for commercializing its Dip Pen Nanolithography® (DPN®), a patented and proprietary nanofabrication technology for the life science and semiconductor industries. Northwestern University's Chad Mirkin, PhD,

DPN features the massive parallel capability of cantilevers and tips that create nanoscale features with various materials. DPN arrays contain as many as 55,000 tips in an area less than two-tenths of a square inch.

Resizing Technology

The specificity and sensitivity of the Verigene System's nanoparticle-based direct detection system enables high count multiplexed assays, providing clinically relevant panels of tests in a low cost, easy-to-use format.



*Nanolnk offers
biochips for
stem cell
research,
and systems
for protein
detection and
discovery.*

director of the school's International Institute for Nanotechnology (IIN), founded Nanolnk in 2001 based on his research team's development of the DPN technology. Eight years later, DPN enables depositing a variety of nanoscale substances onto many different materials.

"Using nanotechnology is a great way to prevent counterfeiting of pharmaceutical products," said Tom Levesque, vice president of Nanolnk's NanoFabrication Systems Division. "We offer the world's only on-dose, multilayered, brand protection technology. But that's just one part of Nanolnk. In 2009 we're also offering nanoscale biochips for use by stem cell researchers, new systems and services for nanoscale protein detection and discovery, and customized DPN solutions configured precisely for our customers' needs."

Nanolnk has more than 160 patents and applications filed worldwide and has licensing agreements with several U.S. and European universities, including Northwestern, the University of Illinois at Urbana-Champaign, Stanford, and the California Institute of Technology. Levesque expects Nanolnk's

next wave of customers will come from researchers in cell culture and tissue engineering, as well as diagnostic companies looking at detecting proteins and visualizing protein binding. "We can provide great value to scientists involved in the early stages of disease detection and therapeutic discoveries," Levesque said.

Nanosphere – Similar Origins, A Different Path

Like Nanolnk, Nanosphere is another company founded by Dr. Mirkin. Northwestern's Robert Letsinger, PhD, and Dr. Mirkin created Nanosphere in 2000 based on their research into the power and function of gold nanoparticles. Seven years later, in a move highly publicized throughout the biotech community nationwide, Nanosphere took the "going public" path with an initial public offering in November 2007. Despite Wall Street's turmoil over the past 18 months, Nanosphere may be positioned for long-term growth. It has transformed itself into a fully integrated healthcare company with in-house expertise in R&D, manufacturing, sales & marketing, and customer service and support.

We think we can be one of several examples of successful companies that our region will produce in the coming years.

Nanosphere's nanoparticle probe technology, available through the company's Verigene[®] System and assays (tests), is designed to simplify molecular diagnostics, making it accessible to virtually any clinical laboratory, including hospital-based labs. Its ultrahigh-sensitivity capabilities could lead to earlier and more precise detection of cancer, heart disease, and neurodegenerative disorders. The Northbrook-based company also has developed a new bio-security system and could develop food safety systems for the rapid identification of biological pathogens. If successful, Nanosphere technology would not only contribute to national security, but also help protect public health.

"We have mastered the functionality of these extraordinarily tiny gold particles," said Nanosphere CEO Bill Moffitt. "As a result, we have created biological probes that are exquisite in their power *and* ease of use. By the end of the year we expect to bring to market our second-generation Verigene System, which will enable a hospital to draw a blood sample, place it into an on-site Verigene SP System, and then get the results quickly. Offering the combination of ultrasensitive molecular assays and rapid speed at costs lower than currently available is a great source of pride to our Nanosphere team."

According to Moffitt, 2009 should also bring FDA clearance for several important new tests for the Verigene System. New assays would enhance the diagnosis of cystic fibrosis, along with a variety of respiratory illnesses, and detect a gene linked to a potentially fatal iron overload disorder, which could dramatically alter the treatment of a long list of diseases, including cirrhosis of the liver, liver cancer, pancreatic and thyroid cancer, hypothyroidism, diabetes, kidney failure, and heart disease. "I think it's going to be a significant year for the company," Moffitt said. "We're going to demonstrate to the market the real breadth and horsepower of this platform."

Perhaps of greatest long-term consequence, Nanosphere's plans for 2009 include the commencement of an international, multisite trial investigating an ultrasensitive protein assay designed for the early detection of heart attacks

and other cardiovascular conditions. With a new ability to detect a protein called troponin shortly after a patient arrives at a hospital emergency room, cardiologists might be able to treat heart patients more quickly and effectively, leading to better health outcomes.

Many observers expect Nanosphere to be the leading nanotechnology company in the state. "We hope we don't let them down," Moffitt said. "Time will tell, but we think we can be one of several examples of successful companies that our region will produce in the coming years."

Northwestern University – Chicago's Catalyst for Nanotech Start-ups

It's no coincidence that some of the most well known and well respected nanotech start-ups in the country originated with research conducted at Northwestern. For more than a decade, Northwestern has invested heavily in developing a world-class faculty in the various fields that comprise nanoscience, and has made significant efforts to nurture a culture of technology transfer unmatched in the Midwest. To date, Northwestern has spawned 14 nanotech start-ups, and two more currently are under development. According to Chad Risko, PhD, scientific officer and industrial liaison on Dr. Mirkin's IIN team, the start-ups have attracted more than \$360 million in venture capital financing.

A key instrument to facilitate start-ups is the IIN's Small Business Entrepreneur's Evaluation (SBEE) program. Through the SBEE, Northwestern researchers present their technology and commercialization concepts to students from Northwestern's Kellogg School of Management. The output of this group effort often is a well-constructed business plan, the critical step for an entrepreneur to attract the financing necessary to start a company.

In addition, the IIN's Nanotechnology Corporate Partners (NCP) program provides a mechanism to directly link IIN researchers with industrial partners. "Eighteen companies are participating in the NCP program, and we have the capacity

to expand to much larger numbers," Dr. Risko said. "The NCP program provides a formal structure for ongoing collaboration between IIN researchers and our industrial partners. It's a partnership that benefits both sides."

Beyond Evanston – Other World-Class Research Leads to Illinois Start-ups

As reported in Part One of this *BQ* series, researchers at the University of Illinois (Urbana-Champaign and Chicago campuses), the University of Chicago, Argonne National Laboratory, and the Illinois Institute of Technology also have been advancing the field of nanotechnology for many years and will continue to do so in the future. Following are a few more examples of Illinois-based companies that have grown out of discoveries made at the state's academic and research institutions (headquarter locations and ties to research institutions in parentheses).

Arryx, Inc. (Chicago, University of Chicago) uses focused light to form microscopic optical traps to grab small objects. These optical traps (also known as laser tweezers) can manipulate hundreds of microscopic and nanoscopic objects. Haemonetics, a global leader in the design, manufacture, and worldwide marketing of automated blood processing systems, found this technology intriguing enough to enter into a formal collaboration with Arryx in 2004. Arryx became a wholly owned subsidiary of Haemonetics in 2006.

Autonomic Materials, Inc. (Champaign, University of Illinois at Urbana-Champaign) offers innovative self-repairing technologies that extend the lifetimes of industrial coatings. In a process that resembles a biological response from a person's immune system, when a scratch is produced in an industrial material, microcapsules inside the new protective coatings disassemble and their contents flow to the damaged zone, forming a polymer that "heals" the injury, or scratch.

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Resizing Technology

The Verigene System performs both genomic and ultra-sensitive protein tests in an "on-demand" format, simplifying the testing process and optimizing responsiveness to the physician and patient.



BioSante Pharmaceuticals, Inc. (Lincolnshire, ties to multiple universities) has developed what it believes are important formulations for delivering protein-based therapies via its biodegradable calcium phosphate nanoparticles. BioSante has completed preclinical tests showing that its nanoparticle vehicles enhance and extend the beneficial effect of proteins when administered under the skin, inside the cheek, or through nasal inhalation.

NanolIntegris, Inc. (Skokie, Northwestern University) was founded in 2007 to capitalize on a scientific breakthrough pioneered by Northwestern Professor Mark Hersam, PhD. Today, NanolIntegris produces unique, high-quality carbon nanotubes that the company refers to as "the building blocks for the next generation of nanotechnology applications." NanolIntegris sells its products to developers of nanotech-based products.

Nanophase Technologies Corporation (Romeoville, University of Chicago and Argonne National Laboratory) produces engineered nanomaterial products for a variety of diverse markets, including personal care,

abrasion-resistant applications, environmental catalysts, antimicrobial products, and a variety of ultrafine polishing applications. End-use applications of Nanophase's technologies include wood preservation; protection from ultraviolet rays; antimicrobial and scratch-resistant coatings; production of fuel cells and catalytic converters; and deodorants, antiperspirants, and shaving and hair removal products.

Polyera Corporation (Skokie, Northwestern University) is a leading supplier of materials technology for the printed and flexible electronics industry, an emerging commerce of materials made from organic, carbon-based compounds. While the materials, most notably semiconductors and insulators, function similarly to their traditional counterparts, their ability to dissolve into a solution or ink creates new opportunities for end-use products. Polyera's customers are developing radio frequency identification (RFID) tags to identify, track, sort, and detect persons and items; new technologies for electronic display panels; solar panels for generating electricity; and sensors to detect changes in temperature, pressure, radiation, and chemical identity.

Despite Wall Street's turmoil over the past 18 months, Nanosphere may be positioned for long-term growth.

Words of Caution – Without Adequate Funding...

Much of the success of the state's roster of nanotechnology start-ups can be traced directly to the willingness of Illinois-based investors to support these groundbreaking entrepreneurs. As the companies mature, they have secured funding from the east and west coasts, traditional strongholds for venture capital (VC) financing. Ultimately, more companies might follow Nanosphere's lead and attract investments from the public through stock offerings.

As mentioned by many at the 2009 iBIO IndEx annual conference, access to additional funding is critical to the ongoing growth and success of the state's nanotech industry, yet that funding is in peril. Forest City's Michael Rosen offers a perspective shared by many members of the community. "There doesn't seem to be the breadth in VC support and activity for nanotech as you've seen at similar stages of biotech's evolution. On the other hand, there seem to be very early stage investors who are interested in

the technology, perhaps because of key angel investors' links to universities.

"One of the challenges we face is that there is not as broad a VC base for nano as there is in biotechnology. However, major multinational corporations, including those outside the life sciences, are jumping in earlier than you would see in biotech, and that's because the applications of nanotech go beyond drugs and extend into devices, material fabrication, and industrial applications."

In the spring of 2009, even as the world grapples with the global economic crisis, nanotechnology entrepreneurs must obtain the financial support critical to fulfilling their visions of a safer and healthier world. There's no shortage of breakthrough science or human capital in Illinois. If investors and public-private partnerships are willing to sustain those nanotech companies most likely to produce commercially viable products, the benefits to society, and the returns to the investors, will be plentiful. **BQ**



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