Forbes/Wolfe Emerging Tech REPORT

Volume 6 / Number 12 /December 2007

Technology Trends to Watch in 2008

Things we know about 2008: It will be a leap year, the U.S. will elect a new president and Beijing will be hosting the Olympic games. Beyond that, making predictions for the next 12 months can be risky business.

One other prediction, however, is that my team will be watching developments in some very specific emerging technology markets next year. We explore a select few in this issue, including converging developments in molecular biology, **Honda's** [HMC] fuel cell gambit, and the approaching battle for GPS chipsets targeting 3G cellular networks.

Some of the technologies we explore in this issue will probably see significant breakthroughs over the next twelve months. But space limitations prevent me from exploring all of the sectors worth tracking in 2008. Among the notable absences below—like emerging display technologies, biopolymers and nano-enhanced medical imaging—may appear as feature topics in future issues.

Molecular medicine

Independent advances in molecular biology, nanotechnology and genetics over the past decade began to converge this year, signaling some notable breakthroughs in medical diagnostics and treatment.

Most notable among the successes was the recent IPO of molecular diagnostics company, **Nanosphere** [NSPH] (*see "A Tale of Two Nanotech IPOs", November 2007*). The company's Verigene system leverages nanotechnology to move genetic and protein testing to the point of care, thereby overcoming the time—and cost-intensive limitations of conventional polymerase chain reaction (PCR) tests.

Nanosphere's current menu of diagnostic tests is limited. I am optimistic long-term. Piper Jaffray initiated coverage earlier this month with a BUY rating and $17 price target. Meanwhile, analysts for both Credit Suisse (target price: $22) and Leerink Swann (price range of $16-$18) gave Nanosphere outperform status.

The company is a pure-play in the global molecular diagnostics market that, in 2006, measured $2.3 billion according to Boston Biomedical Consultants. The market is projected to grow more than 15% over the next five years.

And the momentum is pushing even more proactive solutions based on sequencing individual genomes. The 0.1% difference between our DNA is what determines why some of us develop certain diseases and others do not. Electrophoresis can sequence individual strands of DNA today. But it would take the technology decades to sequence enough genomes necessary to begin isolating the genetic root of many diseases.

Companies like **Helicos Biosciences** [HLCS] and **Illumina** [ILMN] are among the companies vying to develop new technologies to accelerate and simplify the sequencing of single DNA strands.

Reverse genetics

Interest in personalized medicine hasn't been lost on incumbent biotech giants, like Roche, **Abbott Laboratories** [ABT] and **Siemens AG** [SI]. Many of them are launching initiatives that combine in vitro diagnostics with therapeutic solutions in one procedure, according to Cheryl Barton, founder of U.K. consultant firm PharmaVision.

Many of those solutions are likely to include targeted drug delivery —another trend worth watching in 2008.

While many current drugs provide effective therapies, more precise delivery to target sites can increase net potency and reduce toxicity. One approach incorporates ligands into drug formulations to enhance their selective uptake in target tissues. Another approach effectively steers magnetic nanoparticles toward disease sites where they dump their therapeutic load or else destroy cancerous tissue with heat (*see MagForce Technologies, Companies to Watch, November 2007*).

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Targeted carrier systems represented about half of the $6.5 billion market for advanced drug delivery in 2006, reported Barton. By 2015, the sector could see nearly thirty new commercial therapies focusing on treatment for cancer, cardiovascular and infectious disease.

The convergence of diagnostics and therapy is natural, even organic. Intersecting advances in cloning, genetics, instrumentation, and molecular and structural biology have allowed researchers to see beyond the exterior morphology of cells and tap their component molecules for solutions.

That spells breakthrough developments in another medical sector: the development and production of new vaccines.

Traditionally, vaccines were manufactured from the complete organism, such as an inactivated flu virus. Today, advances in molecular biology

are enabling researchers to isolate subcelluar components of viruses to develop vaccines through cloning, said Adel Mahmoud, a senior molecular biologist at Princeton University. The approach, called reverse genetics, is similar to reverse engineering.

The acceleration of vaccine development through cloning has broken down the sector's traditionally high barriers to entry, which has attracted the attention of pharmaceutical companies. It has also opened the possibility of single dose vaccines with a long term immunity response.

One concrete development to watch for in 2008 is how the TroVax vaccine, made by **Oxford Biomedica** [OXB.L], performs in its Phase 3 clinical trials. Designed to treat kidney cancer, TroVax works by encouraging the immune system to attack a protein found in solid cancers.

Fuel cells roll out

Next year won't be the end of the gas-powered vehicle. But Honda Motor Company's release of 500 hydrogen fuel-cell powered FCX Clarity's in California in 2008 could be the beginning of the end.

What makes Honda's gambit significant is the corresponding release of its Home Energy Station Unit. Set the unit up in the yard, and it will use natural gas to produce enough Hydrogen to power your FCX Clarity and your home at around 50% of the normal cost and with a 30% reduction in emissions.

Its approach addresses the Catch-22 confronting every alternative-powered vehicle that's come down the pike: Without the fueling infrastructure, there's no incentive to buy a hydrogen-powered vehicle, and until hydrogen-powered vehicles become available there's no incentive to build the infrastructure.

By offering both, Honda could jump start demand for the Clarity, which is based on Honda's own V Flow fuel cell. The cell stack combines hydrogen with atmospheric to form chemical energy, which is then converted into electric power. The road to mass commercialization still stretches ahead, and hydrogen fuel cell vehicles are not the only alternative vying for attention.

Even so, getting the technology rolling on California highways will build important momentum for the fuel cell industry. And California is a strategic proving ground. In addition to $4/gallon gas prices, the state is willing to subsidize fuel cell energy stations to keep pressure off its electrical grid. That may give the Clarity an edge over plug-in hybrids.

GPS chipsets

Personal navigation devices (PNDs) are a hot gift to give this holiday season. Unit sales of GPS systems rose 488% over last year, according to the latest point-of-sale information from market research firm NPD Group.

GPS chipset provider, **SiRF Technology Holdings** [SIRF] is the company to beat in the personal navigation device space, with over 50% market share. The company is one of several gearing to battle it out for a piece of the next-generation cellular handset market.

Mobile phones are only starting to emerge as a high-growth market for GPS chipsets, which include the basic radio-frequency (RF) and GPS base-band chips. True, most handsets already incorporate the technology, but it goes largely unused because most network operators have been slow to roll out location-based services with broad consumer appeal.

The other reason GPS chipset suppliers have ignored the current generation of mobile handsets is **Qualcomm** [QCOM], which has been packaging GPS capability into its mobile phone chips for the last seven years.

The industry, however, is shifting from today's GSM and CDMA network standards toward 3G, or W-CDMA standards, and next-generation-compatible handsets are forecast to see a CAGR of 22% over the next five years.

Although Qualcomm is still a strong contender for that market, its dominance is not sealed in stone, said Gemma Tedesco, an analyst for In-Stat. The key may be integrating base-band and RF chips into a single module. These single-chip solutions will be critical to getting onboard cellular handsets, since they offer reduced power, size and components.

Not surprisingly, single-chip structures are being fielded by all the players vying for the W-CDMA handset market, including SiRF, Qualcomm, **Texas Instruments** [TXN], **Broadcom** [BRCM] and a host of smaller and international players.

The Insider

What a year 2007 has been! And what a year we think 2008 will be. This issue, we look at the top trends going into 2008. These key trends will evolve in future issues just as quickly as the technologies themselves do. In Best Buy the other day, I asked the customer service department what the most returned item was. The answer? GPS units. Surprised that would be so, I dug deeper. It turns out the vast majority of people were gifted low-end models of GPS units and were returning them for higher-end more expensive models. It's only a single data point from a single store—but it merits watching closely as the chipsets, touch screens, batteries and hardware coatings all incorporate nanotech and other emerging technologies to drive demand for GPS enabled devices.

In due time, the media and investors will shift priorities. The zeitgeist of global warming pales in comparison to vaccines. You have a choice: worry about a 100 year problem that can be solved in 50 years, or a 20 year problem that needs to be solved in 10 years. Vaccines are an underappreciated segment of life science sector and new innovations in this arena and the massive market sizes have gotten me very excited. Be sure to read our story Next Generation Vaccines, page 3, on this area and the key emerging players. And be sure to read our exclusive interview with Janine Benyus on biomimicry—technology inspired by Mother Nature. As always, here's to thinking big about thinking small...and to the emerging inventors and investors who seek to profit from the unexpected and the unseen...

Nano in the News

Biomimicry targets energy and biofuels

The Australian Institute for Bioengineering and Nanotechnology (AIBN) at Queensland University in Australia partnered with **Dow Chemical** [DOW] to conduct joint research and development work on biofuels and energy derived through biomimicry.

Next Generation Vaccines

Once upon a time, vaccines were a losing business. They were slow to develop, were often based on primitive scientific techniques, and yielded low profit margins. But all that is changing—and fast. The vaccine space is exploding, with big pharma producing blockbuster vaccines like Prevnar and Gardasil at one end and smaller biotech companies leading the way in discovery and development for next generation vaccines at the other. The rise of antibiotic-resistant microbes, the fear of biowarfare, and the threat of emerging infectious diseases like avian flu are inspiring a renewed interest in vaccines in government, non-profits and the corporate world. At the same time, advances in cellular immunology and ever-more sophisticated biotech tools have opened up the field—which has been relatively stagnant for decades—to exciting new breakthroughs. Of course the pharma giants are going to be the major players in the vaccine game-especially **Wyeth** [WYE], **Sanofi** [SNY], **GlaxoSmith Kline** [GSK] and **Merck** [MRK]—but that isn't where the real action is. I prefer to focus on the cutting edge smaller biotechs driving innovation.

Cell-culture derived vaccines—where viruses are grown in mammalian cells rather than the usual chicken eggs—represent a new advance in vaccine technology. Last May, the government awarded more than $1 billion in contracts for the development of cell-based vaccines to Solvay ($299 million), GlaxoSmithKline ($275 million), **Novartis** [NVS] Vaccines and Diagnostics ($221 million), MedImmune ($170 million) and DynPort Vaccine ($41 million). Cell-based vaccines are believed to be more effective than traditional egg-based ones, and can be produced much more rapidly and easily scaled up for large-scale manufacturing.

But a key path to next generation vaccines will be antigen discovery. Traditional vaccines are made with entire organisms, but next generation vaccines are looking to use only portions of the organism—that is, specific antigens. Makers of these next generation vaccines need tools to rapidly identify the necessary antigens out of thousands of possibilities for any given pathogen.

That's exactly what start-up Genocea Biosciences is offering. Based in Cambridge, Massachusetts, Genocea is developing a game-changing technology that will help open up entirely new markets for vaccine commercialization [*Full disclosure: my venture firm Lux Capital is an equity investor in Genocea*]. Its technology, first developed at U.C. Berkeley and Harvard Medical School, is a high-throughput screening system that replicates the human immune system in vitro to sort through thousands of antigens from an individual pathogen, finding which will best stimulate the immune system upon vaccination.

The vaccine space is exploding, with big pharma producing blockbuster vaccines and smaller biotech companies leading the way in discovery and development for next generation vaccines.

Genocea's screening system promises to make it possible to develop vaccines for previously formidable complex pathogens—like intracellular pathogens, which grow inside of human cells, effectively hiding from the immune system. Malaria, tuberculosis and Chlamydia are all caused by pathogens that are capable of growing within cells.

Genocea has done studies in mouse models for Chlamydia trachomatis, identifying and patenting novel t-cell antigens that were shown to provide protection from the pathogen. The technology has the potential to be used for the development of prophylactic and therapeutic vaccines as well as antigen discovery for cancer, autoimmune disorders and clinical diagnostic applications, providing a way to rapidly make vaccines for complex and aggressive viruses and bacteria while saving significant amounts of time and dollars in research and development.

In addition to antigens, next generation vaccines will require powerful adjuvants—immunological agents that amplify the body's immune response. A biotech company leading the way is California-based Juvaris BioTherapeutics with adjuvants that are showing impressive results in pre-clinical studies.

Founded in 2003, Juvaris is developing both prophylactic and therapeutic vaccines for infectious diseases and cancer based on its adjuvant technology: proprietary lipid and (non-gene containing) DNA complexes that can be used on their own as powerful immune stimulants or together with antigens to enhance the efficacy of a vaccine. Its JuvImmune adjuvant has been shown to stimulate the immune system at least 10 times more than known immune stimulants in pre-clinical trials, which has exciting potential for cancer therapeutics as well as infectious diseases. Its JuvaVax vaccine, which combines its adjuvant with an antigen, has shown to be a potent therapeutic cancer vaccine in tests on mice and dogs, working well even in diseased mouse models. This suggests JuvaVax could provide powerful immune stimulation even in immuno-suppressed patients, such as those with cancer.

"These lipid-DNA complexes are showing profound efficacy in not only preventing disease but also in a therapeutic application in models where an animal has already been infected by a virus or has an established tumor," says John Warner, Juvaris's Chief Scientific Officer and Vice President of Research and Development. "If you can robustly activate the immune response, you can enable it to provide a protective environment against future infections." Both JuvImmune and JuvaVax take advantage of the body's own immune system, which is bound to be more sophisticated and effective than an artificial substitute. "We're activating the immune system from inside the patient and not with some pre-made molecule designed in a factory," says Warner.

Juvaris plans to initiate phase 1 clinical trials of its adjuvant combined with a commercially available flu vaccine in Q2 2008. The company, which recently completed a $12 million Series A financing led by Kleiner Perkins, is working on a therapeutic application for chronic hepatitis, which will likely take off in the second half of 2008. The company is also expecting to start on a cancer program targeting leukemia in late 2008. Completing the vaccine revolution's triad of antigens and adjuvants are delivery systems to get the vaccines to the right places in the body, activating the necessary immune-related cells. North Carolina-based AlphaVax has sparked

wide-ranging interest for its potential to develop an HIV vaccine using its proprietary vaccine delivery technology. Its technology, the alphavaccine platform system, uses genetic engineering to efficiently deliver a wide variety of vaccines, from HIV to cancer. The company uses a disabled virus and replaces its genes with genes from an infectious disease or cancerous cell. The resulting particle expresses the substitute genes rather than the original genes; the disabled virus attaches to important immunity cells in the body, activating a powerful immune response, while delivering the vaccine.

Results announced last month from a phase 1 clinical trial for an influenza vaccine administered with this delivery system were encouraging, showing that antibody and t-cell responses were efficiently stimulated. AlphaVax is also in phase 1 trials for a CMV vaccine and for a therapeutic vaccine for colon cancer in collaboration with Duke University. The company has raised more than $129 million, with 70% coming from grant funding and corporate partners, including a partnership with Wyeth. Wyeth has an equity stake in the company and licenses its delivery technology for selected infectious diseases. AlphaVax's own pipeline is targeting pandemic flu and CMV, while it is working on HIV, prostate and breast cancer, and various biodefense vaccines in collaboration with partners. In July, AlphaVax received $3.6 million from the National Institute of Allergy and Infectious Diseases (NIAID).

The successes of vaccines like Wyeth's Prevnar and Merck's Gardasil have proven that vaccines have impressive revenue potential. Prevnar—a vaccine to protect infants and toddlers from the pathogen that causes pneumonia and meningitis, among other diseases—is the first vaccine to reach $2 billion in annual sales, making it the best-selling vaccine of all time. Gardasil—a vaccine against human papilloma virus (HPV), which can cause cervical cancer, brought Merck $235 million in sales in 2006 and is projected to reach $1.6 billion by 2009. Sanofi's meningitis vaccine is expected to reach approximately $580 million in sales this year. Currently at approximately $13 billion, the global vaccine business is predicted to reach $30 billion by 2011 according to Lehman Brothers, a figure that explains big pharma's reinvigorated efforts in the vaccine space. Novartis, for instance, paid $5.4 billion last year to gain full control over Chiron in order to build its vaccine business, and broke ground in August on their $600 million North Carolina influenza vaccine manufacturing facility, the first vaccine production plant in the US to use cell-culture technology, with actual production (barring FDA approval) expected in 2011. Sanofi is building a $148 million flu vaccine manufacturing facility in China. GlaxoSmithKline is expecting to introduce seven new vaccines over the next five years, including Cervarix, Glaxo's answer to Gardasil, which is still awaiting market approval from the FDA.

But the glass is not always half-full. Merck's recent failed HIV vaccine has put a damper on the recent vaccine optimism. Although it had been hailed as one of the most promising HIV vaccines, it was reported last month that the vaccine may have actually increased HIV risk in recipients of the vaccine in a clinical trial. This may discourage companies from developing HIV vaccines and make it more difficult to get candidate vaccines into human trials. This has ramifications for all adenoviruses, which cause common respiratory illnesses like pneumonia and the common cold as well as gastroenteritis and conjunctivitis. Last month the CDC reported that a new, virulent form of adenovirus Ad14 has caused 10 deaths in the last 18 months in the US, as well as 140 illnesses in New York, Oregon, Texas and Washington.

The tackling of other viruses, however, is looking more promising—like influenza. Just look at New Jersey-based biotech Vaxinnate. Founded by immunologists from Yale University and Howard Hughes Medical Institute, Vaxinnate is developing novel proprietary vaccines for pandemic and seasonal influenzas. Unlike traditional vaccines, in these vaccines the genes for the relevant antigens are inserted into a delivery system, a process that can improve cost-effectiveness, manufacturing capability and vaccine potency. The company has a leading candidate for a vaccine against hemagglutinn (HA) influenza, which has been shown to demonstrate full protection in mouse models. In September, Vaxinnate initiated its first clinical trial, a phase 1 study to test its M2e universal influenza vaccine for safety and immunogenecity. The trial, which is supported by a $9.5 million grant from the Bill and Melinda Gates Foundation, will provide a key test of the company's core technology. So far Vaxinnate has raised more than $64 million and is backed by a handful of VC firms.

Big advances are also coming in the form of potential malaria vaccines. Maryland-based Sanaria is working to develop a vaccine against the notoriously drug-resistant parasite responsible for more than 95% of malaria-associated severe illness and death worldwide. Led by tropical disease expert Stephen Hoffman, who formerly worked as an executive with Craig Venter at Celera, Sanaria expects to enter into clinical trials next year. They recently opened a new manufacturing facility, thanks to a $29.3 million grant from the Bill and Melinda Gates Foundation, in collaboration with the PATH Malaria Vaccine Initiative. Sanaria's vaccine uses the whole parasite (made harmless with a bit of radiation) rather than recombinant DNA, which means its technology is based on clinically-proven methods that should inspire confidence in investors.

There's no doubt the vaccine market is undergoing rapid growth, thanks in large part to increased support from the government, NGO and non-profit foundations (especially the Bill and Melinda Gates Foundation), and the corporate sector. While large pharmaceutical companies demonstrate the revenue potential of vaccines, smaller biotechs in its shadow are the "engine for development of innovative vaccine technologies," says Kleiner Perkins partner TomMonath. According to Monath, the gaps in the current vaccine market that biotechs are most hoping to fill include "cancer vaccines, therapeutic vaccines against chronic infectious diseases, vaccines against major tropical diseases like malaria and dengue, differentiated flu vaccines, better adjuvants, and improved TB vaccines." It's an exciting time, and I'll be keeping track of it in future issues.

Nano in the News

DuPont Engineering Polymers invests in Morph

Morph Technologies, a developer of nanostructured ceramic automotive components, received an equity investment from **DuPont** [DD] Engineering Polymers, the giant chemical company's high-performance polymers unit. Deal terms were not disclosed.

Thinking Small: Janine Benyus

From spider silk, to synthetic gecko feet made of nanowires, to solar cells that mimic photosynthesis in plant leaves—engineers find inspiration in nature. Indeed, many entrepreneurs have been inspired by Janine Benyus. Janine authored the highly recommended book "Biomimicry: Innovation Inspired by Nature". Through her consulting firm, she helps businesses learn from and imitate Mother Nature's models. A graduate of Rutgers University, she currently lives in Montana.

What initially inspired you to explore the concept of biomimicry?

I'm a natural history writer, and I completed five books with the common theme of natural adaptations in plants and animals. For 15 years, I was reading about organisms that are uniquely adapted to their habitats using all sorts of amazing technologies, and in 1990, while working on another book, I started to ask: "is anyone consciously trying to emulate these adaptations?" Once I asked that question, I started finding countless articles in primary literature. I was seeing innovations in materials science, energy, agriculture, and medicine: scientists were trying to copy spider silk to create new high-tech materials, and people were looking towards photosynthesis to derive new kinds of solar cells. I saw an opportunity to give a name to this unique approach to innovation, and hence the now-popular concepts of bio-inspired design and biomimicry were born. I started collecting examples since then and I've never stopped!

Can you tell us about some of the more interesting examples you've come across during your research?

Right now there's an Australian company called BioSignal that has found a new method of controlling bacteria. Bacteria normally like to work in groups to form surface layers called biofilms. Biofilms are what actually make us sick—when bacteria sense that there are enough of them congregated together in a biofilm, they release chemical signals to simultaneously "turn on" their toxicity. BioSignal is mimicking a red algae that naturally prevents biofilms from forming. Scientists discovered that this algae releases tiny molecules called furanones which jam the communications of bacterial colonies, preventing them from activating their toxic payloads. By "confusing" the bacteria instead of killing it, this approach will not result in antibiotic resistance. The trials are amazing—they've found that these molecules work in vanishingly small quantities against the bacteria that cause cystic fibrosis, legionnaire's disease, gingivitis, and even microbes that cause corrosion (which were responsible for a recent **BP**[BP] oil pipeline leak).

Speaking of oil, what's happening in the energy space?

There is a lot happening with solar energy. Dye-sensitized solar cells are based on some of the principles of natural photosynthesis, and there are companies like Konarka which are very close to commercializing these technologies. Many other improvements to solar cells are also biomimetic. For instance, people are putting photonic crystals inside of solar cells in order to capture more light.

In fuel cells, a U.K. company named Morgan Fuel Cell is working with a part of the fuel cell called the bi-polar plate, which distributes gasses throughout the cell. In essence, a fuel cell is a breathing apparatus, which requires gas and oxygen to produce electricity. To improve the bi-polar plate, they looked at breathing structures in nature—lungs! By mimicking the branching structures in lungs and applying this to fuel cells, they were able to increase peak power output by 16%!

Also, the platinum catalyst found in fuel cells is prohibitively expensive, and we're running out of this precious metal. We need to find a simpler catalyst in order to make a cheaper fuel cell, and nature uses iron as its catalyst. I find it almost poetic that some of the most ancient bacteria, blue-green cyano bacteria, can bubble off hydrogen all day long using an enzyme called hydrogenase. A group at the John Innes Center in the U.K. has mimicked this enzyme, and they're working to coat membranes with a double-iron hydrogenase to make fuel cells more efficient.

I'm also really interested in CO2 sequestration. Not pumping it underground, but actually using it as a building block. Plants don't see CO2 as a poison, but rather as a building block for making long chain polymers. We build our polymers (plastics) using carbon atoms from petroleum, but why not mimic plants and try to get the carbon from CO2? A startup called Novomer based on the work of Geoff Coates at Cornell University is pursuing this strategy.

Carbon is also a building block for every single seashell and coral reef in our ocean, and that carbon also comes from CO2. Our most prevalent hard building material is concrete, and making it causes roughly 8% of worldwide CO2 emissions. We make concrete by mining limestone, which is basically the compacted results of millions of years of seashell creation. By looking at how mollusks turn CO2 into a shell, scientists discovered an enzyme that can turn CO2 into a fine-powdered calcium carbonate (limestone) feedstock using only flu gasses and seawater.

What other areas do you think could benefit from biomimicry?

You'd think fan blades and propellers have been optimized over time, but they haven't reached the efficiency of some of the flow shapes found in the natural world. I serve on the board of a company called

Pax IT, which is making computer fans that are quieter and far more efficient. This type of work makes me wonder: what other natural shapes in the world are we missing?

Interesting. And which natural organisms inspire you the most?

You can't ask a biologist that question! Insects in general—in terms of everything from physical structures, to sensors, to locomotion—are amazing sources of inspiration. Plants are also interesting as models for how to collect energy more efficiently. But if I had to pick one organism to learn more from, it would be the live oak. You know those big, beautiful Southern trees that make you think of Scarlet in gone with the wind? There are about 400 of them on St. Charles Street in New Orleans, and only four of them died during hurricane Katrina. Only four! There are scientists who know exactly what makes this organism so well adapted to its habitat, and we should be looking to these natural creations when building our own structures.

Why does it seem so many of our approaches are counter-intuitive to natural systems?

We used to be much better at learning from our environment, but somewhere around the Industrial Revolution, we got really entranced with technologies as the machine model began to take over. Back in the 1800s, a really well educated person—the "renaissance" person—would know all about biology. Then, we fell in love with machines and synthesis through chemistry, followed by genetic engineering and computing. I believe that nature IS a technologist, and that's what we don't realize. If you really want to geek out on great chemistry, beautiful physics, and elegant design, it's all right there in the natural world.

What companies have reached out to you?

In 1998, Dayna Baumeister and I got together to form the Biomimicry Guild the first consultancy for bio-inspired design. Our clients, including **GE** [GE], **Kraft** [KFT], **General Mills** [GIS], **Nike** [NKE], and **Herman Miller** [MLHR] hire us to help solve problems and assist with sustainability issues.

Follow the Money

A monthly look at who is getting funded and who's giving it.

Venture Capital Funding

Unidym

Location: Menlo Park, CA
CEO: Art Swift
Funding Announced: 12/7/2007
Investors: Arrowhead Research, Tokyo Electron Ventures, Batelle Memorial Institute
Funding Amount: $10.4 million (Series C)
Notes: **Arrowhead Research** [ARWR] subsidiary Unidym raised $10.4 million in a Series C round with investment from entities such as Tokyo Electron's corporate venture capital arm and Columbus, OH-based Batelle Memorial Institute.
Outlook: Unidym acquired Carbon Nanotechnologies earlier to form the carbon nanotube company. With the growth capital in the bank and strategic investors on board, Unidym can pursue the commercialization of carbon nanotube-based electrodes and electronic components for the display, touch panel and solar markets.

Altair Nanotechnologies

Location: Reno, NV
CEO: Alan J. Gotcher
Funding Announced: 11/30/2007
Investors: Al Yousuf LLC
Funding Amount: $40 million (private placement)
Notes: Altair Nanotechnologies sold a 15% stake to Dubai-based Al Yousuf LLC for $40 million, at $3.50 per share. Altair plans to deploy the funds for expanding manufacturing capacities for its power and energy storage products.
Outlook: Al Yousuf is a Dubai-based industrial conglomerate that brings to the table relationships with leading auto and consumer manufacturers Altairnano can leverage this network as it continues to develop its advanced battery and power products for the automotive and consumer electronics sectors.

NanoTune Technologies

Location: Mountain View, CA
CEO: Unknown
Funding Announced: 12/14/2007
Investors: Draper Fisher Jurvetson (lead)
Funding Amount: $3.12 million
Notes: Company says it has developed technology to precisely control the properties of silica-derived nanostructured materials. NanoTune is targeting applications in drug delivery, biomolecular separation and sensors.
Outlook: NanoTune is in stealth mode, and information about it is scarce.

Nano in the News

New: The California NanoSystems Institute

UCLA inaugurated the California NanoSystems Institute, the second such institute after the one at the University of California at Santa-Barbara, in the presence of Former California governor Gray Davis and special economic advisor to current governor, Arnold Schwarzenegger. The Institute draws faculty from various departments, and aims to bridge academic research and industry at UCLA.

Companies to Watch

Treadstone Technologies

Private

www.treadstone-technologies.com **609-734-2368**

Princeton, NJ

Chief Executive: Gerald DeCuollo

What it does: Developing a corrosion-resistant metal plate technology designed to cut the weight, volume and cost of fuel cells.

The comparatively low weight of polymer electrolyte membrane (PEM) fuel cells has generated interest among automakers developing hybrid vehicles. But in addition to being large and heavy, current fuel cell designs are prone to corrosion.

Treadstone is hoping to change that by developing anti-corrosive technology that would greatly expand the viability of fuel cells for automotive and other applications.

A typical PEM cell design forms a stack from several individual cells to produce a usable voltage. Within the stack, the largest components are the separator plates, which provide electrical connections between cells and physically separate the oxidant flow of one cell from the fuel flow of another.

These plates are generally made from a graphite composite. But metal plates enable stacks with lower volume, weight and cost, and they provide better heat and water management, which improves long-term reliability. The problem is that metal plates tend to corrode long before they meet the automotive industry's targeted lifetime of 5,000 hours.

Treadstone's surface treatment coats off-the-shelf metal separator plates with a non-corrosive inorganic layer. In addition to potentially reducing fuel cell stack weight by 40 percent less, this enables metal plates to meet the automotive industry's reliability standards.

"So we've achieved the first hurdle," said CEO Gerry DeCuollo. "Now everyone's asking, 'What's the cost?'"

Other metal plate technologies have surpassed the 5,000-hour mark. But the expensive alloys and coatings on which these technologies rely raise the cost of fuel cells to between $15 and $20 per kW—well above the U.S. Department of Energy's target of $6/kw.

Through the use of off-the-shelf metals like titanium and stainless steel, Treadstone can enable cells that run between $4 and $7 per kW. The use of steel drops those estimates further to $2 or $3 per kW."

Treadstone provides only the metal separator plates. They don't manufacture fuel cells. But their technology is applicable to direct methanol fuel cells as well as PEMs, so the company is positioned to tap cell makers in the three biggest markets: automotive/transportation, stationary and portable.

The next step, said DeCuollo, is to establish relationships with fuel cell OEMs in all three markets. The company currently has samples under evaluation at an undisclosed automaker, and it's finalizing projects with two other customers, including an OEM that targets stationary applications.

Last January, the company received $400,000 in seed funding from Virginia-based Commerce International, and another $50,000 in July from the New Jersey Commission on Science and Technology. Next year, the company may start looking for additional financing from a strategic partner, like a client or a VC firm, said DeCuollo.

Companies to Watch

BG Medicine

Private

www.bg-medicine.com **781-890-1199**

Waltham, MA

Chief Executive: Uwe Maschek

What it does: Focusing on the discovery, development and commercialization of molecular diagnostic tests based on biomarkers

As health care moves toward personalized medicine, biomarkers have increasingly become important molecular signposts signaling the progression of a disease in a patient, the effectiveness of a therapeutic treatment, and/or a patient's ability to metabolize certain drugs.

BG Medicine has developed a proprietary technology platform designed to maximize the efficiency of biomarker discovery, and generate a steady flow of molecular diagnostic tests. The company's scalable, automated approach enables integrated and precise analysis of thousands of potential biomarkers, such as proteins, metabolites and nucleic acids. Currently, the company has the capacity to field 16 to 20 new discovery projects per year.

Founded in 2000 as Beyond Genomics, the company changed to its current name three years ago. Since its inception, it has raised $52.1 million in financing from investors, such as Flagship Ventures and Gilde Investment Management.

In August, it filed plans with the SEC to list stock on Euronext Amsterdam under the symbol BGMDX. At the time, the company sought to raise up to $80 million, based on a share price between $14 and $16. Cowen & Co. was named as the IPO's lead underwriter, supported by Leerink Swann.

Then, earlier this month, it amended its filing, shifting its IPO to the Nasdaq under the ticker BGMD, and slashing its targeted proceeds. The company now plans to issue 4.5 million common shares, priced from $8 to $10 per share. That puts its market capitalization between $152.4 million and $190.5 million, and its expected gains at just over $35 million, after fees and expenses, assuming its stock reaps $9 per share.

The company plans to use its equity to develop new diagnostic products, enhance its R&D infrastructure, build a marketing and distribution force, repay debt and pay for administrative costs.

Like any early stage company, BG Medicine's IPO poses risks, among them a history of quarterly net losses—with more expected. It currently lacks a commercial product. But it has generated steady revenues from collaborative partnerships, including one with Philips to discover biomarkers for use in conjunction with Philips' medical technologies for disease diagnosis and patient monitoring.

The company also claims to have a broad pipeline of product candidates focusing on cardiovascular disease, cancer and central nervous system, or CNS, disorders. Most notable among them is a molecular diagnostic biomarker for testing the severity and prognosis of patients with congestive heart failure. The test could be commercially available as early as 2009.

The Emerging Tech Portfolio

Company [symbol]	Coverage Initiated	Current Price	52-week range	Mkt Cap ($mil)	Buy/Sell/Hold
Intellectual Property Incumbents *Leading researchers in the physical sciences, with big potential for spin-offs and revolutionary breakthroughs*					
GE [GE]	8/07	$36.48	3 3.90-42.15	368,580.00	Buy
Hewlett-Packard [HPQ]	3/02	50.93	38.15-53.48	131,240.00	Buy
IBM [IBM]	3/02	104.53	88.77-121.46	144,630.00	Buy
Materials *Companies producing materials with novel properties that have applications for a wide range of industries*					
Symyx [SMMX]	3/02	7.09	6.95-21.90	238.10	Buy
Life Sciences *Companies that are working at the cutting edge of medical technology*					
Invitrogen [IVGN]	11/05	92.63	55.73-99.15	4,330.00	Buy
Nanosphere [NSPH]	11/07	11.97	11.50-22.04	266.10	Buy
Electronics *Companies that have corralled the key intellectual property that will be the foundation for next generation electronics*					
Nanosys [private]	3/02	n/a	n/a	n/a	n/a
NVE Corporation [NVEC]	7/03	25.35	20.75-41.95	117.90	Hold
Energy *Companies that are developing high-efficiency, low-cost alternative energy technologies*					
First Solar [FSLR]	8/07	231.97	26.54-256.45	17,900.00	Hold
Enabling Technologies *Tools and instrumentation that enable critical science and technology discoveries*					
Veeco [VECO]	3/02	16.05	15.47-22.28	508.60	Buy
FEI Company [FEIC]	1/03	24.88	24.01-39.25	898.20	Buy
Accelrys [ACCL]	3/02	7.49	5.51-8.24	196.30	Buy
Investment Vehicles *Funds that have investments in promising emerging technology companies*					
Harris & Harris Group [TINY]	5/02	8.02	8.00-14.32	188.20	Buy
PowerShares Lux Nanotech Portfolio [PXN]	8/07	15.28	15.21-18.75	139.40	Buy
PowerShares WilderHill Clean Energy [PBW]	8/07	25.05	16.61-26.53	1,010.00	Buy

Word on the Street

GE: GE remained flat for the month, taking a breather from last month's downward slide. The conglomerate's Wind unit won orders for over 500 wind turbines, worth about $1 billion. Chairman Jeff Immelt said profits would rise at least 10%, with EPS at $2.42 and revenues rising to $195 billion. GE will also buy back $15 billion worth of stock over the next three years.

HPQ: HP rose by 5.6% for the month after issuing fiscal 2009 guidance in line with analyst estimates. The company projects EPS ranging from $3.74-$3.84 on revenues of $117.1-$118.2 billion. The company also continued to increase its PC market share, which rose to 19.1% for the quarter.

IBM: Big Blue shares were lifted by 2.4%. Toshiba joined an IBM-led R&D group, including **AMD** [AMD], Freescale Semiconductor and **Infineon Technologies** [IFX], focusing on designing and developing 32 nanometer circuitry. The company will also buy back $1 billion worth of stock by February 2008, in addition to the $12.5 billion buyback plan announced in May.

SMMX: Symyx Technologies gained 3.1% for the month, despite a lack of news flow.

IVGN: Invitrogen drifted lower by 2.3%. The company licensed a catalyst-based biological labeling and detection technology from Harvard University. CFO David Hoffmeister sold over 27,000 shares in the open market, and doesn't own any more IVGN shares.

NSPH: Nanosphere was down 4.9% for the month after it reported a $9.9 million operating loss for Q3. The company's net loss stood at $28.6 million, but included a number of one-time charges. Investment bank Piper Jaffray initiated coverage of the stock with a Buy rating, whereas Credit Suisse rated the stock Outperform with a price target of $22.

NVEC: NVE Corporation bounced back from November's precipitous fall to move 13.7% higher. Company founder James Daughton won an award from the IEEE for his contribution to the development of MRAM.

FSLR: First Solar rose another 9.4%. A slew of senior executives, including the president, exercised options or sold stock to cash in the richly valued holdings. First Solar also acquired Turner Renewable Energy, a solar power-plant deve oper, for $34.3 million in cash and stock. CNBC's Jim Cramer spoke favorably about the company, noting that even at a price of $200, the company trades at 24x projected earnings for 2010.

VECO: Veeco Instruments was marginally higher but lost a patent suit claim to Asylum Research, with a court in California throwing out six of 13 claims that Veeco had brought against Asylum. Veeco also introduced a new 3D atomic force microscopy (AFM) system, the only one of its kind for non-destructive 3D imaging of 32-nm and 45-nm semiconductors.

FEIC: FEI Company rose 3.4%, as it entered into a joint development partnership with the Netherlands-based Foundation for Fundamental Research on Matter. The project will focus developing advanced electron microscopy and focused ion-beam systems for materials characterization at the single-atom scale, with funding to the tune of EUR 2.7 million over five years.

ACCL: Accelrys ended the month down by 2.4% despite lack of any new information.

TINY: Harris & Harris Group fell sharply by 10.1%, making a new 52-week low of $8.00. Harris & Harris had reported net asset value per share at $5.69 as of September 30. We believe TINY's stated Net Asset Value does not reflect the true market value of many of its private equity holdings.

PXN: The PowerShares Lux Nanotech Portfolio was flat for the month. Key holding **Altair Nanotechnologies** [ALTI] raised $40 million in private placement to Dubai-based Al Yousuf, while **Arrowhead Research** [ARWR] subsidiary Unidym also raised $10.4 million in a Series C round.

PBW: The PowerShares WilderHill Clean Energy Portfolio rallied by 13.5%. **American Superconductor** [AMSC] rebounded by 20% and **EMCORE** [EMKR] also surged sharply by over 50%, and the other solar stocks continued trending upward to round off a strong month for the fund.

Stock prices as of December 17, 2007

Forbes/Wolfe Emerging Tech Report
is published monthly by Forbes Inc. and Angstrom Publishing LLC, 60 Fifth Avenue, New York, NY 10011
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