# NanoBiotech News

*The global nanobiotechnology intelligence source*

**Volume 3 • Number 29 • August 3, 2005**


## 'Photonic pill' uses light scattering for real-time diagnostics optical imaging

*By Marie Powers*

With inspiration from Isaac Asimov's Fantastic Voyage, scientists at the City College of City University of New York (CCNY) are leading a collaboration of regional universities to develop an ingestible diagnostic device that will send images to physicians in real time as it travels through the gastrointestinal (GI) system.

Robert R. Alfano, PhD, distinguished professor of science and engineering and director of the Institute for Ultrafast Spectroscopy and Lasers and the Center for Advanced Technology (CAT) at CCNY, and colleagues have already constructed a prototype of the spectroscopic-based device, called the Compact Photonics Explorer (CPE). Their "photonic pill" is capable of using multiple wavelengths of light to survey tissues for abnormalities and to report its findings using wireless technology.

Reporting in *Biomedical Microdevices*,[1] the CCNY

*continued on page 4*

*Accelerating molecular diagnostics R&D*

## Nanogen takes equity position in European gene marker company

*By Russell A. Jackson*

Nanogen, Inc., (NASDAQ:NGEN) has made a $1.5 million equity investment in Jurilab Ltd., of Kuopio, Finland, a company that focuses on the discovery and identification of new genes and gene markers associated with the root causes of common diseases and drug responses.

San Diego, CA-based Nanogen also reports a five-year, $2.5 million government grant for a research project to develop a prototype fully integrated diagnostic system for clinical labs to identify infectious agents that cause sepsis and community-acquired pneumonia.

The Jurilab investment is the first of two identical moves, Nanogen notes. The second is due within six months and, when it's all said and done, the California company will own about 25% of the Finnish firm at a cost of about $3 million. In fact, Nanogen may own Jurilab outright, reports Robert

*continued on page 5*

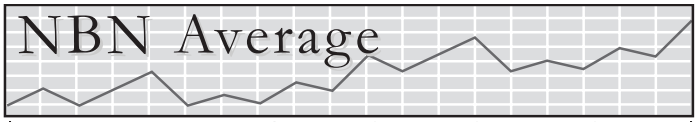
## Customized nanoparticles deliver gene therapy to mice with no toxic effect

*By Steve Lewis*

Using customized nanoparticles, University at Buffalo (NY) scientists have for the first time delivered genes into the brains of living mice with an efficiency that is similar to, or better than, viral vectors -- and with no observable toxic effect, according to a paper published in *Proceedings of the National Academy of Sciences*.[1]

The paper describes how the UB scientists used gene-nanoparticle complexes to activate adult brain stem/progenitor cells in vivo, demonstrating that it may be possible to "turn on" these otherwise idle cells as effective replacements for those destroyed by neurodegenerative diseases, such as Parkinson's.

*continued on page 7*




| Company | Symbol | Close 07/26 | Close 08/02 | % Change |
|---|---|---|---|---|
| Acacia Research Corporation | ACTG | $ 4.75 | $ 4.74 | -0.21% |
| Accelr8 Technology | AXK | $ 3.01 | $ 3.19 | 5.98% |
| Advanced Magnetics | AVM | $ 10.90 | $ 11.82 | 8.44% |
| Advectus Life Sciences | AVXSF.PK | $ 0.03 | $ 0.03 | 0.00% |
| Affymetrix | AFFX | $ 45.19 | $ 46.70 | 3.34% |
| Agilent Technologies | A | $ 25.98 | $ 26.63 | 2.50% |
| Altair Nanotechnologies | ALTI | $ 2.98 | $ 3.13 | 5.03% |
| American Pharmaceutical Partner | APPX | $ 42.04 | $ 46.18 | 9.85% |
| Biophan Technologies | BIPH.OB | $ 3.01 | $ 2.84 | -5.65% |
| Biosante Pharmaceuticals | BPA | $ 3.90 | $ 4.12 | 5.64% |
| Caliper Life Sciences | CALP | $ 7.05 | $ 6.95 | -1.42% |
| CombiMatrix | CBMX | $ 2.56 | $ 2.24 | -12.50% |
| Flamel Technologies | FLML | $ 19.50 | $ 20.15 | 3.33% |
| Nanobac Pharmaceuticals | NNBP.OB | $ 0.10 | $ 0.09 | -5.26% |
| Nanogen | NGEN | $ 4.53 | $ 4.33 | -4.41% |
| Novavax | NVAX | $ 0.98 | $ 0.97 | -1.02% |
| pSivida | PSDV | $ 6.11 | $ 7.00 | 14.57% |
| SkyePharma | SKYE | $ 10.05 | $ 10.46 | 4.08% |
| Starpharma Holdings Limited | SPHRY.PK | $ 3.95 | $ 4.40 | 11.39% |
| TOTAL | | 196.62 | 205.97 | ▲ 4.76% |




Copyright © 2005 National Health Information, LLC. Reproduction is strictly prohibited.
To subscribe call (800) 597-6300 or (404) 607-9500 or visit http://www.nanobiotechnews.com.

# Researchers attach nanograins to superparamagnetic iron oxide particles for drug delivery

*By Russell A. Jackson*

Researchers at the University of New Orleans' Advanced Materials Research Institute have attached gold nanograins to superparamagnetic iron oxide particles, making it easier to attach a payload to the nanocrystals, thus facilitating drug delivery.

The procedure "takes advantage of the very high quality of our team's magnetic nanoparticles," says Charles J. O'Connor, PhD, a UNO distinguished professor of chemistry and AMRI director. "The synthetic method we have developed is a green chemistry approach that combines our precise control of the nanoparticles' size and agglomeration degree with their very high solubility in water or other polar solvents."

But one company already operating in the iron oxide nanocrystal space says the development may be a case of much ado about very little.

In their research,[1] the Crescent City scientists successfully attached 2- to 3-nm gold particles to ~10 nm Fe3O4 nanocrystals "through a simple, two-step, chemically controlled procedure," they report. "The surfaces of individual, relatively monodisperse Fe3O4 nanospheres forming a stable colloidal methanolic solution are coated with an amino-terminated silane," they explain in the journal article, "peptized to induce positive charges on the particles' surfaces and then treated with a colloidal solution of negatively charged Au nanoparticles."

Then, the researchers report, "a detailed investigation by transmission electron microscopy, X-ray diffraction, UV-vis, inductively coupled plasma and superconducting quantum interference device magnetometry was performed to elucidate the morphology and properties of the nanocomposites." The key finding: "The colloidal Fe3O4-Au nanocomposites are highly stable against separation and exhibit magnetic properties similar to those of the parent Fe3O4 nanocrystals." The "novel nanoarchitectures" that result, the scientists continue, "open up new opportunities for the use of magnetite nanoparticles for in vivo biomedical applications through chemical bonding of bioactive molecules to the attached Au nanoparticles."

O'Connor says "a lot of groups are trying to attach gold to magnetic nanoparticles because their chemistry otherwise makes it difficult to functionalize them. You need to have something to attach things to, and it's easy to attach things to gold." Many of the resulting applications will be in the biomedical space -- including site labeling for diseases or bacterial agents and drug delivery. "One way to accomplish both," he tells *NanoBiotech News*, "is to have a magnetic particle you can functionalize and then attach a biomolecule to a chemical agent or an antibody." Then, he explains, "you can use a magnetic field to direct the resulting molecule where it should go."

## More effective HIV/AIDS therapy

One possible application, he continues, is treating HIV/AIDS. "Patients treated with drug cocktails may see their viral load drop to undetectable," he comments. "But the virus is still hiding. One of the things we think we can do with the composite nanoparticle is attach AIDS antibodies to them that can find where the virus is hiding and attach to it there. That could lead to an additional drug treatment that could completely eradicate the virus -- an actual cure, rather than just treatment for the symptoms."

"There's been a lot of emphasis on gold," he explains. "We've been trying to attach it pretty much all along." His team had some success with pure iron, he adds, noting, "magnetic iron nanocrystals have been shown to enhance MRI images." Attaching gold to them, though, "could potentially open new avenues in drug delivery because it has been recognized by the scientific community that the surface of the gold nanoparticles can be repeatedly functionalized with organic molecules -- which is not the case with bare magnetic nanoparticles. Recent reports have claimed the successful attachment of co-enzymes and DNA to gold particles, which is much more likely to occur successfully in the case of our nanocomposites than in that of bare magnetic particles."

But Jerome Goldstein, CEO and president at Advanced Magnetics Inc., Cambridge, MA,

*continued on page 3*

**NanoBiotech News**™ is published 48 times per year by National Health Information, LLC, 1123 Zonolite Rd., Suite 17, Atlanta, GA 30306-2016.
Telephone: (800) 597-6300 or (404) 607-9500. **E-mail:** info@nanobiotechnews.com **Website:** www.nanobiotechnews.com
POSTMASTER: Send address changes to **NanoBiotech News**, P.O. 15429, Atlanta, GA 30333-0429.
Associate Publisher: **Lynn Yoffee** President: **David Schwartz**
**Subscription rates:** USA, one year (48 issues): $1295. **Back issues**: $25 each.
Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other forms of professional advice are offered for general guidance only; competent counsel should be sought for specific situations. Copyright © 2005 by National Health Information, LLC. All rights reserved. Any reproduction, distribution, or translation without express written permission is strictly prohibited. **NanoBiotech News**™ is a trademark of National Health Information.

Copyright © 2005 National Health Information, LLC. Reproduction is strictly prohibited.
To subscribe call (800) 597-6300 or (404) 607-9500 or visit http://www.nanobiotechnews.com.

## Nanograins *from Page 2*

respectfully disagrees. His company develops superparamagnetic iron oxide nanoparticles for use in pharmaceutical products to treat anemia, as well as imaging agents to aid in the diagnosis of cardiovascular disease and cancer. "As best I can tell," he says, "I don't believe [the finding from UNO] affects us in any way. We are fully capable, without the addition of gold nanoparticles, to attach bioactive ligands to our particles."

Indeed, he adds, "I would characterize this as a solution in search of a problem."

O'Connor says that "the functionalization of bare magnetic particles with organic molecules is possible, but the attachment of gold nanograins helps create multifunctional and highly reactive magnetic nanoparticles, thus offering a viable, highly reproducible alternative route to the problem of functionalization, especially with molecules possessing multiple functional groups. We're not necessarily competing with any private companies. Our system is capable of different things and we're looking for different types of things. I do think our system is more versatile, though."

The idea behind the discovery, he continues, is "most biomolecules have sulfur atoms available and those attach easily to gold. Anything with sulfur in it will form a covalent bond with the gold nanoparticle." The chemical process his team uses to link the nanoparticles is simple and inexpensive -- and should work for any number of metal nanoparticles.

There are obstacles, of course. "We're looking at ways to attach drug molecules or antibodies to the gold without denaturing them or destroying their efficacy," he reports. The key is using just enough -- but not too much -- gold. "When you're doing magnet-assisted drug delivery you get a tremendous amount of dead weight with gold because it's very heavy. You expend a lot of effort trying to push around the gold -- whose only purpose is a platform for deliverables. So, you attach smaller grains of gold so that you don't have the whole nanocrystal coated, but you do have a gold surface present for attaching -- with just a fraction of the dead weight."

His team is moving toward commercialization of the intellectual property. A spin-off of AMRI called NanoPrism Technologies, Inc., has already been formed by the researchers. The scientists have also "discovered a reaction that allows us to [attach gold nanoparticles to iron oxide nanocrystals] on a large scale. We'll patent everything that isn't already patented, then license the IP to NanoPrism," O'Connor says.

When it does hit the market, it could well be in many distinct applications. "It's hard to say what is going to happen," he comments. "There may be some direct applications that are very quick -- such as treating tumors or even migraine headaches."

There are also microelectronic applications, he points out, which is why the federal Defense Advanced Research Project Agency is interested. Indeed, DARPA funded a great deal of O'Connor's preliminary research and is a significant source of funds moving forward as the O'Connor team examines biomagnetic interfacing concepts.

*Editor's Note: Contact Charles O'Connor at (504) 280-6846 and Jerome Goldstein at (617) 497-2070.*

### *Reference*

1. Caruntu D, Cushing BL, Caruntu G, O'Connor CJ. Attachment of gold nanograins onto colloidal magnetite nanocrystals. *Chem Mater* 2005. 17(13):3398 -3402. ⊙

*New Datamonitor Market Research Report available*

**Emerging Drug Discovery Technologies: Building competitive advantage through lab-on-a-chip, nanotechnology and RNAi**

Emerging Drug Discovery Technologies: Building competitive advantage through lab-on-a-chip, nanotechnology and RNAi, is a new report which provides an in-depth analysis of three technological innovations that are being heralded to revolutionize the drug discovery process by rapidly expediting drug discovery research.

This report focuses on lab-on-a-chip (LOC) devices, nanotechnology and RNA interference drug discovery technologies that are increasingly being used to identify novel drug targets and to successfully reduce R&D timelines. This report also provides: in-depth analysis of the market forces, current and future technological advances, detailed company profiles, eight year forecasts of market size for LOC devices, nanotechnology in, drug discovery and RNA interference technologies and therapeutics.

Incorporate the most innovative technologies into your drug discovery process, significantly reduce R&D timelines and build a unique competitive edge with the help of this latest report.

This must-have resource is available for $1,900 plus shipping and handling. To order, go to www.nhionline.net, send your order to NHI, PO Box 15429, Atlanta, GA 30333-0429, or call 800-597-6300. All orders must be prepaid and are protected by NHI's 100% money back guarantee. ⊙

Copyright © 2005 National Health Information, LLC. Reproduction is strictly prohibited.
To subscribe call (800) 597-6300 or (404) 607-9500 or visit http://www.nanobiotechnews.com.

## Photonic pill *from Page 1*

team describe their novel miniature spectroscopic, which uses fluorescence, Raman, and elastic light scattering properties to provide diagnostic information on a molecular scale. Unlike technologies developed by Israel's Given Imaging, Ltd., (NASDAQ:GIVN) or proposed by scientists at Carnegie Mellon University in Pittsburgh (see *NanoBiotech News*, Aug. 27, 2005, p. 1), the CPE device is capable of producing traditional optical images at various wavelengths of light, revealing abnormalities in the density and structure of tissue.

"Unlike white light scattering-based imaging units, the multi-wavelength spectral imaging technique equipped in the CPE device can provide much richer information, produced in the interaction between light at a particular wavelength with the tissue molecules," the scientists write.

The CPE prototype consists of a sensitive CMOS detector array, LED light sources with wavelengths from blue to near-infrared (NIR), video transmitter, control electronics, and battery power source. The "upscale" version is equipped with a UV light source to provide spectroscopic detection in the shorter wavelength at 340 nm. Images are transferred to a remote computer and receiving station, enabling the CPE to provide real-time spectroscopic images of biomedical specimens to provide the absorption, reflection, and fluorescence properties of a specimen.

### *Evaluating skin cancer*

One application of the CPE would allow clinicians to evaluate subsurface skin lesions and assist in detecting and monitoring skin cancer. Due to the stronger absorption of tissue at shorter wavelengths, longer wavelength light penetrates deeper under the surface, Alfano explains. Images acquired with NIR light provide more subsurface features than those using blue light illumination. Thus, analysis of images acquired with different wavelength illumination can be used to determine the depth of a skin lesion -- an important factor in the treatment of melanoma and cancer. In fact, the investigators demonstrated that this capability enabled them to distinguish common moles from skin cancer better than existing technology.

Other images acquired with the CPE were used to find blood vessels below the surface under blue and NIR illumination. The blue illuminated image showed the upper surface of the skin while the NIR illuminated image revealed greater detail under the surface.

In addition, the device can acquire spectral images, which can detect a target image in a cluttered background by comparing the differences in reflection and absorption properties between the target and the host background under different illumination wavelengths. When fully developed, this capability could be used to detect cancer and bacterial infections by identifying molecular signatures unique to malignant or infected tissue, the researchers suggest.

Additional microfluidics components could be added to the device to dispense a drug in response to the optical and spectroscopic analysis obtained by the device, Alfano points out.

Currently, the device operates at the millimeter scale -- 17 mm wide by 35 mm long, or a little larger than a penny -- so additional work is needed to shrink the components to nanometer scale and the device to pill-size, Alfano says. Nevertheless, the researchers already hold a U.S. patent on the technology[2] and have generated proof of principle for the device.

"We still have some problems to solve, but we have the know-how to develop the next generation of microcapsules," Alfano tells *NanoBiotech News*.

During the past two years, New York State's Infotonics Technology Center, the National Aeronautics and Space Administration (NASA), and the New York Office of Science, Technology, and Academic Research have supported the CPE development by a consortium of universities that includes CCNY, The State University of New York (SUNY) at Albany, Rensselaer Polytechnic Institute in Troy, NY, Rochester (NY) Institute of Technology, and Boston University. With that grant funding drawing to a close, Alfano and colleagues hope to partner with a company that already has some interest in endoscopic diagnostic devices.

"The CPE has the potential ability to scan the entire digestive tract, from the esophagus to the small intestine," Alfano says, noting that, eventually, the device could be introduced into the urinary tract and even into the arterial system.

"We could be faster to market by partnering with a company that is developing these types of devices and wants to incorporate the wireless spectroscopic technology," he adds, estimating that a new product developed by this route could be ready for market in as little as one to two years.

*Editor's Note: Contact Robert R. Alfano at (212) 650-5533.*

### *References*

1. Wang L, Zhang G, Luo JC, et al. Wireless spectroscopic compact photonic explorer for diagnostic optical imaging. *Biom Microdevices* 2005;7(2):111-1.

2. U.S. Patent No. 6,240,312: Remote-controllable, micro-scale device for use in in vivo medical diagnosis and/or treatment. ⊙

Copyright © 2005 National Health Information, LLC. Reproduction is strictly prohibited.
To subscribe call (800) 597-6300 or (404) 607-9500 or visit http://www.nanobiotechnews.com.

**Nanogen** *from Page 1*

Saltmarsh, Nanogen's CFO. "Nanogen has initially invested EUR 1.25 million for a less-than-20% equity interest, and will invest an equal amount within six months. The investment agreement includes provisions for the full acquisition of Jurilab at Nanogen's election."

While additional terms of the agreement were not disclosed, Saltmarsh did tell *NanoBiotech News* that other investors are expected to line up. "There are no guarantees, of course, but we're pretty sure." For its part, he notes, Nanogen is "getting its feet wet." "I'm not going to speculate at this point on whether we'll acquire the company. It's a bit early for that. I'd say it's 50-50 right now. We like the people and the company has great technology, so we'll see how things work when we get a closer look at each other."

## Access to molecular targets

Through its investment, Nanogen will acquire "certain rights to develop diagnostic products based on genes and gene markers discovered by Jurilab." The Finnish company's initial efforts focus on cardiovascular and metabolic diseases, including adult onset diabetes. Nanogen will also become a distributor of Jurilab's pharmacogenomic products and services and offer business development infrastructure and other resources.

"The investment in Jurilab is an important part of our strategic operating plan to secure access to important molecular targets for advancing the use of diagnostics and personalizing healthcare," says Howard C. Birndorf, Nanogen's chair and CEO. "Its programs in cardiovascular diseases and diabetes and related pharmacogenomics match our own commercial product programs. Working together, we can accelerate development of products for the growing molecular diagnostic market."

"Jurilab has a variety of technologies that move statistical observation to the specific area of a gene causing a problem. That's the reason we're doing this. It really gives us access to novel markers." Birndorf adds: "Does it pair Jurilab's research capabilities with our distribution capabilities? That's a nice benefit of the deal. Does it give us easier access to European markets? It helps us build relationships there. Would acquiring the company eliminate a competitor? We don't really see it that way. It's really about the unique content."

Part of that content, he explains, is a catalog of the gene pool of a regional population that hasn't had much exposure to outsiders for hundreds of years. Jurilab -- which has an office in Stamford, CT -- is a privately owned company founded in 1999 by members of the Research Institute of Public Health at the University of Kuopio. Its research and development projects use comprehensive data derived from almost 20 years of scientific research carried out at the university on that group of people, called the East Finland founder population.

The relationship with the university has allowed Jurilab, and will now allow Nanogen, "rights and access to the unique collection of DNA samples and phenotypic data from the East Finland founder population," Saltmarsh points out. "Founder populations are excellent resources for genetic studies because their high degree of homogeneity makes them ideal for the discovery of disease-linked gene mutations. Based on the extent of data collected, and the prospective nature of the collection over 20 years, Jurilab's genetic discovery and validation not only address the underlying causes of common diseases, but also those factors that contribute to disease progression or disease complications."

Jurilab researchers, he continues, "have studied 3,000 people to see how diseases have progressed, so they can now map those findings against the genetic map. This is a pretty exciting opportunity to translate that huge database into something more identifiable and useable."

Jurilab's BlockMap genetic discovery platform uses -- and can support -- programs in more than 30 disease indications, the company says. It applies proprietary technologies -- including Hierarchical Phenotype-Targeted Sequencing (HPTS) -- to mine that database and identify disease-relevant genetic variants. The biomarkers can then be used in Jurilab's testing services or licensed to diagnostic or pharmaceutical customers that may be interested in the markers as targets for the development of diagnostic tests or new drugs.

HPTS, the firm adds, is a "fast and economic means of finding new functionally important mutations in humans and other species." When used with the founder population, it "offers a much faster and more cost-efficient means of identifying disease-relevant genetic variants because unlike typical genetic studies, which only investigate a single disease at a time, the HPTS method allows Jurilab to study dozens of diseases simultaneously, with no additional cost."

The technology, the company continues, has already been used to identify novel variants associated with prostate cancer and Type II diabetes, which have potential to be used in both predictive tests and as therapeutic targets. Candidate genes would be selected on the basis of their patho-physiological role. Specific phenotypic measurements that reflect the expression of the genes -- such as enzyme activity -- would be measured in carefully selected population samples. DNA samples would be taken from subjects with extreme phenotypes --

*continued on page 6*

Copyright © 2005 National Health Information, LLC. Reproduction is strictly prohibited.
To subscribe call (800) 597-6300 or (404) 607-9500 or visit http://www.nanobiotechnews.com.

**Nanogen** *from Page 5*

say, a complete lack of enzyme activity -- and would be sequenced to find new variations, most of which would likely be single nucleotide polymorphisms. Any new SNPs discovered would then be typed in the entire population sample and their association with the incidence of multiple diseases and drug effects would be analyzed.

Finally, family studies would be conducted to confirm any SNP-disease associations. Genetic variants could be identified in a matter of weeks. Thus, the companies state, "the Jurilab partnership will provide Nanogen with a source of proprietary diagnostic markers for use in identifying the predisposition to disease and pharmacogenetic testing for related drug responses."

Jurilab, not surprisingly, likes the arrangement as well. "Nanogen is an ideal investment partner for us," says CEO Kari Paukkeri. "While we provide research and testing services based on our extensive scientific resources, Nanogen provides a ready commercial outlet for markers we identify -- as well as access to diagnostic development expertise. The union of our intellectual property portfolios will create the opportunity to make a significant impact on healthcare."

### *Miniaturizing biological methods*

So might the grant from the National Institute of Allergy and Infectious Diseases, a division of the U.S. National Institutes of Health. It will "enable Nanogen to develop improved molecular biological methods," the company reports, "miniaturize those methods and demonstrate the performance of the new approach to diagnose sepsis and CAP in a hospital laboratory setting."

Full lab work-ups to determine the cause of sepsis or pneumonia from the large number of possible disease-causing bacterial and viral agents is time-consuming and expensive, a statement points out. And broad spectrum antibiotics, it adds, "which may not effectively treat patients," are often administered while awaiting test results. To ameliorate that situation, Nanogen will be using its chemistry and multiplex detection technologies and employing the Medical College of Wisconsin's technologies and clinical and microbiological expertise. The goal of the partnership is to develop an automated diagnostic system that would be able to rapidly detect a number of bacteria and viruses that cause sepsis and pneumonia in patients."

In previous government grant programs, Nanogen has "greatly reduced the size of its instrument and integrated essential biological sample preparation, amplification and detection technologies to design a sample-to-answer diagnostic system," Birndorf says. "This NIAID research program will further the design of a sophisticated prototype assay and instrument system and sepsis and pneumonia detection panels to help physicians expedite test results in the hospital lab and make better treatment decisions."

Mortality from sepsis can range from 28 to 50%, and pneumonia remains the seventh-leading cause of death in the country. Estimates of the incidence of CAP range from 4 million to 5 million cases a year.

Nanogen's diagnostics include real-time PCR reagents, the NanoChip Molecular Biology Workstation platform for molecular diagnostic applications and a line of rapid point-of-care diagnostic tests.

*Editor's Note: Contact Robert Saltmarsh at (858) 410-4600.* ⊙


## *NanoBiotech News* releases 2005 Nanomedicine, Device & Diagnostic Report

A new executive briefing has for the first time compiled a comprehensive status report of all nano-based drugs and medical devices, providing a remarkable look at the market's quickening pulse. According to data compiled in the just-released *NanoBiotech News 2005 Nanomedicine, Device & Diagnostic Report*, 61 nanotech-based drugs and delivery systems and 91 devices or diagnostic tests have entered preclinical, clinical, or commercial development.

Each of the 152 listings in the *2005 Nanomedicine, Device & Diagnostic Report* includes the associated company or academic research center name, product name, type, indication and status. Additionally, senior *NanoBiotech News* reporters have interviewed key experts for an in-depth analysis of the state of the industry and the products currently under development.

The *2005 Nanomedicine, Device & Diagnostic Report* provides the hard data you need to spot important trends and seize opportunities for collaborations and competitive developments in 2005.

- Price: $199
- New subscribers will receive the report for free as a bonus!
- Report buyers who subscribe to ***NanoBiotech News*** within 30 days will have the price of the report deducted from the already discounted $995 annual subscription rate for 48 weekly issues.

Call (800) 597-6300 or (404) 607-9500 to order your copy! Or, visit our website at www.nanobiotechnews.com. ⊙


Copyright © 2005 National Health Information, LLC. Reproduction is strictly prohibited.
To subscribe call (800) 597-6300 or (404) 607-9500 or visit http://www.nanobiotechnews.com.

## Nanoparticles *from Page 1*

In addition to delivering therapeutic genes to repair malfunctioning brain cells, the nanoparticles also provide promising models for studying the genetic mechanisms of brain disease.

The UB researchers make their nanoparticles (<30 nm) from hybrid, organically modified silica (ORMOSIL), the structure and composition of which allow for the development of an extensive library of tailored nanoparticles to target gene therapies for different tissues and cell types. In their experiments, targeted dopamine neurons -- which degenerate in Parkinson's disease, for example -- took up and expressed a fluorescent marker gene, demonstrating the ability of the nanoparticle technology to deliver effectively genes to specific types of cells in the brain.

Using a new optical fiber in vivo imaging technique (CellviZio, developed by Mauna Kea Technologies, of Paris), the researchers were able to observe the brain cells expressing genes without having to sacrifice the animal. They then decided to go one step further, to see if they could not only observe, but also manipulate the behavior of brain cells. Their finding that the nanoparticles successfully altered the development path of neural stem cells is especially intriguing because of scientific concerns that embryonic stem cells may not be able to function correctly, since they have bypassed some of the developmental stages cells normally go through.

### *Replacing viral vectors?*

In the ongoing effort to effectively deliver genes to a target cell, viral vectors became attractive in terms of the scientific strategy of exploiting natural mechanisms; however, serious limitations due to their health risks have prevented the extensive development of the viral delivery systems, notes Paras N. Prasad, PhD, executive director of the UB Institute for Lasers, Photonics and Biophotonics, State University of New York Distinguished Professor in UB's Department of Chemistry and principal investigator of the institute's nanomedicine program. "On the other hand, non-viral vectors are attractive in terms of low cost, non-infectivity, absence of host response, good patient compliance, well-defined characteristics and the possibility of repeated clinical administration. But low transfection efficiency of other non-viral vectors restricted their therapeutic application."

That's what makes this approach unique, he continues. "In vitro techniques have been used for decades and yet until now, no non-viral technique has proven to be as effective in vivo," Prasad asserts. "Our hybrid ORMOSIL approach provides the opportunity to systematically optimize each step and achieve efficient transfection. We utilize nanochemistry that allows for the optimization of the surface charge and nanoparticle size for efficient binding of DNA at multiple sites; environmental degradation; surface linkage sites for targeting groups; and incorporation of multiple probes [enhanced contrast MRI, fluorescence and PET] for monitoring efficiency of each step."

### *A major leap forward*

Prasad's team believes that successful in vivo ORMOSIL-mediated transfections represent "a major leap forward" in the development of new experimental techniques to study brain biology, as well as the development of new therapies. "For example, in the present study we have shown that ORMOSIL nanoparticles can be effectively used to introduce genes into the dopaminergic cells of the SNc (substantia nigra pars compacta)," Prasad observes.

"This should allow for the modeling of Parkinson's disease, which appears to have a diverse genetic/molecular background, by transfecting with mutant alpha-synuclein gene, by blocking fibroblast growth factor and Glia-derived growth factor signaling with dominant negative receptor mutants, or by knocking down the parkin gene activity using antisense or small interfering-RNA technology. The ORMOSIL-mediated transfections of the midbrain dopamine neurons would also allow the testing of diverse gene therapeutic strategies for the Parkinson's disease as well as for other disorders involving dopamine neurons."

### *Exploring future vectors*

Prasad says his team's immediate goals are to explore future modified vectors that may deliver small inhibitory RNA for therapeutic approaches. "We have already started the work to explore the fate of the nanoparticles inside the body," he notes. "As we mentioned in our PNAS paper, these nanoparticles are biocompatible and can be possibly bio-degraded through biochemical decomposition of the Si-C bond. The expression of a specific gene for a limited time, the ability to introduce multiple genes and to repeat transfections with different genes, will likely have benefit in therapies where immediate and transient therapeutic intervention is required, i.e., the treatment of stroke or brain cancer."

The key challenges they face, he adds, include delivering these RNAi to specific cells and verifying lack of or low toxicity in longer term experiments. Looking down the road, he says, "Highly efficient gene transfer into the brain using a non-

*continued on page 8*

Copyright © 2005 National Health Information, LLC. Reproduction is strictly prohibited.
To subscribe call (800) 597-6300 or (404) 607-9500 or visit http://www.nanobiotechnews.com.

**Nanoparticles** *from Page 7*

viral technique brings closer gene transfers as a viable therapeutic approach, and may revolutionize how we learn about functions of genes and their products in the brain."

As with any therapeutic approach, he continues, getting to clinical trials and subsequent U.S. FDA approval is a long process. "We have already been approached by several investment groups who are interested in this technology," he notes.

*Editor's Note: Contact Paras N. Prasad, (716) 645-6800, ext. 2099.*

### Reference

1. Bharali DJ, Klejbor I, Stachowiak EK, Dutta P, Roy I, Kaur N, Bergey EJ, Prasad PN, Stachowiak MK. Organically modified silica nanoparticles: A nonviral vector for in vivo gene delivery and expression in the brain. *Proc Natl Acad Sci U.S.A.* 2005 July 28 [Epub ahead of print.] ⊙

## New oncological center at Purdue will have major nano component

*By Steve Lewis*

Nanotechnology will play a major role in the new Oncological Sciences Center planned at Purdue University in West Lafayette, IN. The Oncological Sciences Center is one of four new centers in Purdue's Discovery Park, some of which have yet to be announced. Together, the four centers will receive a combined $10 million over the next three years from Lilly Endowment to establish themselves as interdisciplinary research facilities.

The existing Purdue Cancer Center will function as a cornerstone of the new Oncological Sciences Center, allowing continued research in three areas:

- Experimental therapeutics: the discovery of new cancer drugs and diagnostic tools;
- Cell growth and differentiation: the discovery of new ways for these drugs to attack cancer cells; and
- Structural biology: the close examination and visualization of cancer cell proteins to help these drugs target them more effectively.

The center will integrate broad areas of the research communities in the life sciences, liberal arts, engineering and chemical sciences to focus on wider aspects of the cancer problem. It will also build on the existing research areas, permitting expansion into fields that include:

- Nanotechnology: Cancer prevention via naturally occurring substances, such as compounds extracted from plants and microorganisms.
- Early detection of cancer through imaging and blood protein analysis.
- Drug delivery.

"We're very excited and pleased that Purdue supports this center," says Rashid Bashir, PhD, a professor in the School of Electrical and Computer Engineering and the Weldon School of Biomedical Engineering. "One of the key things we want to do is make an effort to engage engineers and applied scientists along with life scientists."

This, he notes, will include the Schools of Engineering, Chemistry, and Physics. "We will get them to come together to work on this very important problem of cancer diagnostics and therapeutics," says Bashir. "The National Institutes of Health has set a goal that by 2015 we will eliminate death and suffering from cancer; this will not happen if we continue to look at problems in the same manner. We need a new set of eyes, combined with the guidance of people who came before."

### Two nano-related 'trusts'

The new center will be divided into multiple 'trusts,' two of which will be nano-related according to Bashir. "One will be Nanotechnology in Cancer," he shares. "The other is Diagnostics and Therapeutic Devices, which would combine nano and non-nano technology."

In terms of nanotechnology and, cancer, he says, "Clearly there is a huge opportunity to apply recent advances in disease detection. Most people believe we could do a lot more if we could detect cancer earlier. Here, you're talking about the ability to detect very small, early on cases of cancer where very few cells are involved. That's' where nanoscale diagnostics and imaging modalities would be very important, as well as nanoscale therapeutics -- the ability to design multi-functional, intelligent nanoparticles to sense, image and release therapeutics on-site."

There is existing research at Purdue on which the new center may build, says Bashir. "In the last five years we opened an entirely new research complex, Discovery Park; the first two centers were the Birck Nanotechnology Center, which soon will have some facilities that will be unique in the world; and the Bindley Bioscience Center, where advanced proteomics and genomics work is being done."

Examples of ongoing projects at Purdue, says Bashir, include: Detection of cancer proteins; sorting of cancer cells; using nanosensors and microfluidic devices for sorting and detection of cancer cells; biological nanomotors for drug delivery and gene therapy; and nanoscale particles for imaging of cancer cells.

*Editor's Note: Contact Rashid Bashir at (765) 496-6229.* ⊙

Copyright © 2005 National Health Information, LLC. Reproduction is strictly prohibited.
To subscribe call (800) 597-6300 or (404) 607-9500 or visit http://www.nanobiotechnews.com.

## Protein Drug Delivery: Penetrating a Growth Market

The protein therapeutic market is forecast to grow rapidly at a CAGR of 10.5% from 2003 to 2010, to almost double in value. The increased use, development and discovery of protein therapeutics will lead to increasing opportunities for drug delivery companies.

Find out how you can utilize these technologies to gain a competitive edge in an increasingly crowded therapeutic protein market with Datamonitor's in-depth analysis: *Protein Drug Delivery: Penetrating a Growth Market*. Through this special e-mail offer, you can purchase this business solution for just $7,600 by clicking on this link: http://www.nhionline.net/products/datamonitormr110.htm. A full table of contents is also available for viewing online.

This study evaluates the protein drug delivery market, including analysis of:

- Market size
- Key drivers and resistors to growth
- Technology types
- Therapeutic applications

The report also provides 20 mini profiles of technologies being developed by key players.

Use this information to:

- Identify the opportunities provided by current and future protein drug delivery technologies to effectively plan your clients' product development
- Help your clients understand the trends across technological and therapeutic fields to target resources effectively and recognize pipeline opportunities
- Optimize your clients market penetration through improved knowledge of the growth drivers and corporate dynamics of the protein drug delivery market

To purchase the *Protein Drug Delivery: Penetrating a Growth Market* report, call 1-800-597-6300 with your credit card information, fax your order to 404-607-0095 or mail payment to NHI, PO Box 15429, Atlanta, GA 30333. You may also order online at http://www.nhionline.net/products/datamonitormr110.htm. All orders are protected by NHI's 100% money back guarantee. ⊙

## DNA/RNA Therapies: Opportunities for Future Success

DNA/RNA products represent some of the most innovative and direct technologies aimed at commercializing the human genome. The market is in its infancy with no significant products launched across the seven major markets. Despite the unproven nature of the sector in terms of market potential, it is commanding considerable interest across the biotechnology industry. Datamonitor has identified 99 companies developing DNA/RNA therapies, with 229 products in development. Of these programs, 19 are set to be on the market by 2010.

Published by Datamonitor, *DNA/RNA Therapies: Translating the Genome into a $1.2bn Market by 2010* analysis provides a comprehensive evaluation of the global DNA/RNA market, encompassing market dynamics, company strategy and comparative benchmarking of the development programs of 99 players by technology and therapy area. Through this special e-mail offer, you can purchase this business solution for just $7,600 by clicking on this link: http://www.nhionline.net/products/datamonitormr104.htm. A full table of contents is also available for viewing online.

Content overview:

- Analysis of market trends and future opportunities for both biotech and pharmaceutical players
- Full profiles of 19 DNA/RNA programs set to launch by 2010, encompassing product development and company strategy
- Benchmarking of the current and future DNA/RNA market, by technology and therapeutic focus, in terms of number of projects and dollar value
- Investigation of the steps that the industry's emerging players are taking to increase innovation in their businesses and improve their strategic position

To purchase the *DNA/RNA Therapies: Translating the Genome into a $1.2bn Market by 2010* report, call 1-800-597-6300 with your credit card information, fax your order to 404-607-0095 or mail payment to NHI, PO Box 15429, Atlanta, GA 30333. You may also order online at http://www.nhionline.net/products/datamonitormr104.htm. All orders are protected by NHI's 100% money back guarantee. ⊙

**Subscribe to *NanoBiotech News* and Save $300**

**Please Complete:**

Name _____

Title _____

Company _____

Address _____

_____

City _____ State _____

Zip Code/Postal Code_____ Country _____

Telephone ( _____ ) _____

Fax ( _____ ) _____

E-Mail **(Required)** _____

Georgia residents please add applicable sales tax

**One Year Subscription (48 weekly e-mailed issues)**

**Two Payment Options:**

❑ Check enclosed for $995 (regularly $1,295) payable to: NHI Publications

❑ Charge my: ❑ VISA ❑ Mastercard ❑ AMEX

Account # _____

Expiration Date _____ / _____

Signature (please type name) _____

*NBN8305*

**100% Money Back Guarantee**

If you become dissatisfied at any time during your subscription, just let us know and we'll send you a 100% refund -- no questions asked.

**There's no risk to you.**

**NHI Publications • P.O. Box 15429 • Atlanta, GA 30333 • (800) 597-6300 • Fax (404) 607-0095 • http://www.nanobiotechnews.com**

Copyright © 2005 National Health Information, LLC. Reproduction is strictly prohibited.
To subscribe call (800) 597-6300 or (404) 607-9500 or visit http://www.nanobiotechnews.com.