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NCI nanotechnology platform partnerships span cutting-edge, near-term projects

By Marie Powers

The \$35 million award by the National Cancer Institute (NCI) Alliance for Nanotechnology in Cancer for 12 cancer nanotechnology platform partnerships (see *NanoBiotech News*, Oct. 19, 2005, p. 1) is designed to develop technologies that will serve as the foundation for new products in six key program areas: molecular imaging and early detection, in vivo imaging, real-time monitoring of treatment, multifunctional therapeutics, prevention and control, and research enablers.

"The future of oncology -- and the opportunity to eliminate the suffering and death due to cancer -- will hinge upon our ability to confront cancer at its molecular level," according to Andrew von Eschenbach, MD, NCI director. "Nanodevices will enable researchers to probe genetic defects inside cells, detect the earliest aberrations of cellular function that lead to cancer, and correct those errant pro-

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Arrowhead's anti-cancer drug IT-101 entering human trials, funding accelerated

By Steve Lewis

Encouraged by the faster-than-expected progress of Insert Therapeutics' lead anti-cancer drug, IT-101, Arrowhead Research Corp. (NASDAQ:ARWR) has accelerated the investment of an additional \$3 million to its majority-owned subsidiary. Insert has just revealed that it is preparing to enter IT-101 into human clinical trials at the City of Hope Comprehensive Cancer Center in Duarte, CA.

"We've gotten outstanding results in small and large animals, though the large animal studies aren't totally complete," notes R. Bruce Stewart, president of Pasadena, CA-based Arrowhead. "There had been milestones [set up] to put in \$1 million, then another, and then another, but we felt we had achieved the necessary milestones to go with the entire \$3 million." He adds that the large animal studies should be completed "in the

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UCSD researchers developing tumor-targeting 'mothership' to carry targeted anti-cancer agents

By Russell A. Jackson

Editor's Note: This is the second in a series of articles featuring seven university-based Centers of Cancer Nanotechnology Excellence (CCNE) recently funded with a \$26.3 million investment from the U.S. National Cancer Institute.

Researchers at the University of California at San Diego's Center for Nanotechnology for Treatment, Understanding, and Monitoring of Cancer and Moore's Cancer Center will use new money from the National Cancer Institute to develop a "mothership" cell capable of carrying targeting agents and tumor toxins in a variety of shapes and sizes. The just-designated Center of Cancer Nan-

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Company	Symbol	Close 10/18	Close 10/25	% Change
Acacia Research Corporation	ACTG	\$ 6.34	\$ 6.14	-3.15%
Accelr8 Technology	AXK	\$ 3.16	\$ 3.15	-0.32%
Advanced Magnetics	AVM	\$ 8.87	\$ 8.75	-1.35%
Advectus Life Sciences	AVXSF.PK	\$ 0.03	\$ 0.03	0.00%
Affymetrix	AFFX	\$ 43.41	\$ 45.12	3.94%
Agilent Technologies	A	\$ 30.65	\$ 31.18	1.73%
Altair Nanotechnologies	ALTI	\$ 2.22	\$ 2.26	1.80%
American Pharmaceutical Partners	APPX	\$ 43.06	\$ 43.08	0.05%
Biophan Technologies	BIPH.OB	\$ 2.06	\$ 1.97	-4.37%
Biosante Pharmaceuticals	BPA	\$ 3.03	\$ 3.00	-0.99%
Caliper Life Sciences	CALP	\$ 6.69	\$ 6.86	2.54%
CombiMatrix	CBMX	\$ 1.43	\$ 1.38	-3.50%
Flamel Technologies	FLML	\$ 17.92	\$ 19.52	8.93%
Nanobac Pharmaceuticals	NNBP.OB	\$ 0.06	\$ 0.06	-9.84%
Nanogen	NGEN	\$ 2.75	\$ 2.81	2.18%
Novavax	NVAX	\$ 2.93	\$ 5.53	88.74%
pSivida	PSDV	\$ 6.12	\$ 6.40	4.58%
SkyePharma	SKYE	\$ 6.45	\$ 6.88	6.67%
Starpharma Holdings Limited	SPHRY.PK	\$ 5.00	\$ 4.70	-6.00%
TOTAL		192.18	198.82	▲ 3.45%

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\$1.6M grant enables research on nanomaterials to mimic living cells

By Marie Powers

The National Science Foundation (NSF) has awarded a \$1.6 million Nanoscale Integrated Research Team (NIRT) grant to researchers at the University of California (UC) at Davis who are combining artificial membranes and nanomaterials to mimic the functions of a living cell.

The four-year NIRT grant will allow a multi-disciplinary, international team to study the synthesis and functions of nanobiostructures assembled on aerogels -- solid materials riddled with nanometer-size pores, making them lighter than styrofoam, explains Subhash H. Risbud, PhD, professor of chemical engineering and materials science at UC Davis and principal investigator on the project.

All living cells are wrapped in a double-layered membrane of oily lipid molecules, Risbud explains. Cell membranes are studded with proteins and other molecules, which govern how food and wastes move into and out of a cell, how cells signal to and react to their environment, and how they divide and grow.

Currently, researchers studying artificial membranes to examine and mimic cell behavior mount them on solid substrates such as gold, glass, or polymers. "But once you have solid support, you close off one side of the membrane," Risbud points out.

The aerogels developed by Risbud and colleagues on the Nanoscale Research Team at UC Davis provide a wet cushion for the membranes, enabling them to behave more like the lipid bilayers that form actual cell membranes.

The aerogels are fabricated using a solution gelatin (Sol-Gel) process that Risbud and colleagues described in two scientific papers published last year.¹ The process -- "similar to making Jell-O," Risbud says -- mixes silicon dioxide powder with a solution of water, methanol, and ammonium hydroxide to form soft gels, which are transferred into a mold. The gels are placed into a supercritical point drier in which the methanol solvent in the pores of the wet gel is exchanged for liquid carbon dioxide. The use of supercritical

extraction removes the liquid from the pores and replaces it with gas, leaving a sponge-like silica substance that is 98% air and 2% interconnected silica beads measuring 10 nm to 25 nm in diameter that are strung together in random fashion, Risbud explains.

The silica substance appears no different than any other typical gel -- semi-transparent and lightweight -- but molecularly, it behaves like a living cell membrane, permeable on both sides. Water can soak into the material, but in the confined space the water molecules arrange themselves in unusual ways, enabling a lipid membrane to spread across a wet aerogel just as it does around a living cell.

Like a real human cell

"The idea behind the technology is that you can access and treat an aerogel like a real human cell," Risbud says, allowing researchers to conduct countless experiments that were once impossible.

Risbud began studying aerogel technology more than a decade ago -- initially using the pores to study the growth of Quantum dots in a confined space. In early 2000, Risbud and colleagues demonstrated the formation of gallium nitride nanoparticles embedded in a silicate matrix.² About three years ago, working with researchers at Stanford (CA) University who were growing lipid bilayers on slides, he began exploring the biological applications of the technology.

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Using the NSF grant, the research team will assemble lipid bilayers and biomolecules on aerogel supports to form various types of biomembranes.

"We want to develop gels that are more chemically versatile and also more mechanically robust," Risbud says, including the use of nontoxic materials that could eventually be used in clinical trials.

The studies could lead to new insights into how real cell membranes behave. Each type of aerogel can be tailored to study an individual protein, Risbud says, from its thickness to chemical composition.

The scientists also plan to examine a number of applications during the life of the NIRT grant. For example, they hope to develop a process for preserving blood platelets at or above room temperature, enabling transport and storage for months at a time in locations without refrigeration.

Risbud and colleagues also plan to examine the diffusion and transportation properties of aerogels in moving molecules across skin membrane for dermatology and potential drug delivery applications. In fact, more than \$30,000 of the grant was used to purchase a camera capable of imaging individual molecules as they enter and exit a membrane.

Another potential application is the detection of diseases, such as multiple sclerosis, that are focused around the func-

tion of a specific protein. Proteins carry a variety of functions within a cell, and many reside on cell membranes or interact with them in some way, Risbud points out.

Editor's Note: Contact Subhash H. Risbud at 530-752-0474.

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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.

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cesses long before they give rise to cancers large enough to be diagnosed by today's methods."

The NCI Alliance, launched in September 2004, encompasses four major program components. Earlier this month, the NCI Alliance established seven multi-institutional Centers of Cancer Nanotechnology Excellence (CCNE) designed to integrate nanotechnology across the cancer research continuum and provide new solutions for cancer diagnosis and treatment. (See *NanoBiotech News*, Oct. 5, 2005.) The institute also has begun characterizing nanoparticles of interest in its Nanotechnology Characterization Lab (NCL), which is designed to facilitate a quicker transition of nanomaterials from the lab to the clinic. (See *NanoBiotech News*, Oct. 19, 2005.)

The NCI Alliance also is supporting multidisciplinary research training and team development through mechanisms such as the National Institutes of Health (NIH) National Research Service Awards for Senior Fellows and NIH National Research Service Awards for Postdoctoral Fellows, both of which are accepting applications.

The nanotechnology platform partnerships, modeled after the NIH bioengineering research partnerships, reflect a cross-section of technologies, disciplines, cancer types, geographies, and risk/reward profiles, linking universities to NCI-designated Cancer Centers. The five-year awards offer a breathtaking scope of nanobiotech expertise and clinical oncology potential, ranging from near-term projects to cutting-edge technology. They include:

1. Nanotherapeutic strategy for multidrug resistant tumors, Northeastern University, Boston, MA. Principal investigator (PI): Mansoor M. Amiji, PhD, associate professor of pharmaceutical sciences, School of Pharmacy, Bouve College of Health Sciences. This partnership also encompasses researchers from the Roger Williams Medical Center, Massachusetts General Hospital, and Massachusetts Institute of Technology (MIT) with the goal of developing multifunctional, targeted nanoscale devices to deliver therapeutic agents and tumor resistance modulators directly to cancer cells -- initially, breast and ovarian cancers. With preliminary work by the team already producing biodegradable, tumor-targeted drug nanocarriers, they will prepare to scale-up for development to the clinic.

2. DNA-linked dendrimer nanoparticle systems for cancer diagnosis and treatment, University of Michigan, Ann Arbor. PI: James Baker, Jr., MD, Ruth Dow Doan professor, Internal Medicine, and director, Michigan Nanotechnology Institute for Medicine and Biological Sciences. An offshoot

of work initiated under NCI's Unconventional Innovations Program, this partnership is expected to develop multi-component, dendrimer nanoparticles that will target, image, and treat cancer. In a paper published this summer in *Cancer Research*,¹ Baker and colleagues demonstrated they could smuggle a chemotherapeutic drug inside tumor cells using single modified dendritic polymers measuring less than 5 nm in diameter as carriers. (See *NanoBiotech News*, June 29, 2005, p. 1.) Earlier this year, the researchers described studies developing a combination therapeutic using dendrimer arrays connected by oligonucleotide bridges² -- the focus of the new NCI partnership.

3. Metallofullerene nanoplatform for imaging and treating infiltrative tumor, Virginia Commonwealth University, Richmond. PI: Panos Fatouros, PhD, FACR, professor of radiology and chair, Division of Radiation Physics and Biology, Department of Radiology. Researchers will develop metal-based fullerenes, also known as buckyballs, to deliver imaging and anticancer therapeutic agents simultaneously -- initially to brain gliomas.

4. Detecting cancer early with targeted nanoprobe for vascular signatures, University of California, San Francisco (UCSF). PI: Douglas Hanahan, PhD professor of biochemistry and program leader, Mouse Models of Cancer Program, UCSF Comprehensive Cancer Center. UCSF researchers with expertise in angiogenesis and mouse models of cancer and in clinical and experimental molecular imaging will collaborate with Erkki Ruoslahti, MD, PhD, distinguished professor in the Cancer Research Center at Burnham Institute in La Jolla, CA, an expert in vascular profiling, to develop molecular imaging probes for noninvasive early detection of incipient cancer. The team plans to use peptides that seek "zip codes" on the angiogenic blood or lymphatic neovasculature of high-grade neoplasias and/or invasive carcinomas.

5. Photodestruction of ovarian cancer: ErbB3 targeted aptamer-nanoparticle conjugate, Massachusetts General Hospital, Boston. PI: Tayyaba Hasan, PhD, professor of dermatology, Wellman Center for Photomedicine. This partnership is focused on developing multifunctional nanoparticles to deliver light-activated anticancer compounds to ovarian cancer cells. Once bound to the target cells, the nanoparticles are activated using a miniature endoscopic laser to illuminate only the tumors, providing a secondary method to ensure that healthy tissue is spared during therapy.

6. Hybrid nanoparticles in imaging and therapy of prostate cancer, University of Missouri, Columbia (UMC). PI: Kattesh Katti, PhD, FRSC, professor of radiology and physics and senior research scientist, MU Research Reactor. Katti

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already has demonstrated the ability to produce biocompatible gold and silver nanoparticles in five to 10 minutes. (See *NanoBiotech News*, Dec. 8, 2004, p. 1.) By incorporating gold nanoparticles on cancer-specific peptides, this partnership aims to create agents that can image and treat prostate tumors simultaneously.

7. Near-infrared fluorescence nanoparticles for targeted optical imaging, The University of Texas M.D. Anderson Cancer Center, Houston. PI: Chun Li, PhD, associate professor, Experimental Diagnostic Imaging. Collaborators aim to use fluorescent nanoparticles developed at Eastman Kodak for targeted molecular optical imaging of early-stage tumors in a wide variety of cancers, including brain, breast, and skin.

8. Integrated system for cancer biomarker detection, MIT, Cambridge. PI: Scott Manalis, PhD, associate professor of biological and mechanical engineering. This partnership will develop low-cost microfluidic devices with nanochannels capable of concentrating rare proteins from biospecimens. The devices will be integrated with another chip-based device to detect and quantify panels of proteins that may serve as early signs of cancer. Manalis is co-inventor of more than a dozen patents, including several that could be incorporated into this partnership.³

9. Novel cancer nanotechnology platforms for photodynamic therapy and imaging, Roswell Park Cancer Institute, Buffalo, NY. PI: Allan Oseroff, MD, PhD, chair, Department of Dermatology. This partnership, which includes members from the University of Buffalo and the University of Michigan, plans to develop targeted nanoparticle platforms for detecting and imaging cancers and selectively delivering light-activated anti-cancer compounds for guided photodynamic therapy (PDT). Previous work by team members was funded by NCI's Unconventional Innovations Program.

10. Multifunctional nanoparticles in diagnosis and therapy of pancreatic cancer, State University of New York (SUNY), Buffalo. PI: Paras N. Prasad, PhD, distinguished professor of chemistry, physics, electrical engineering, and medicine and executive director, Institute for Lasers, Photonics and Biophotonics. This collaboration is designed to link multifunctional, hybrid ceramic-polymeric nanoparticles for delivering imaging and therapeutic agents to pancreatic tumors developed at SUNY Buffalo with prostate cancer markers and animal models developed by researchers at Johns Hopkins School of Medicine in Baltimore, MD. The SUNY Buffalo group has a strong history of developing biocompatible nanoparticles and has demonstrated

the ability to deliver gene therapy to mice with no toxic effect.⁴ (See *NanoBiotech News*, Aug. 3, 2005, p. 1, and Jan. 12, 2005, p. 8.)

11. Nanotechnology platform for targeting solid tumors, The Sidney Kimmel Cancer Center, San Diego, CA. PI: Jan Schnitzer, MD, scientific director and director of Vascular Biology and Angiogenesis Program, Cellular and Molecular Biology Program. Building on the center's experience in nanoparticle development and blood vessel biology, researchers intend to create nanodevices to target specific cells lining blood vessels to improve transit out of the bloodstream and into tumors. The miniaturized probes will be injected into the bloodstream to seek out and treat cancer and report back the state of each organ. The technology is applicable across a wide range of solid tumors -- both primary and metastatic -- including breast, prostate, kidney, colon, and lung.

12. Nanotechnology platform for pediatric brain cancer imaging and therapy, University of Washington, Seattle. PI: Raymond Sze, MD, associate professor of radiology. This effort, which involves researchers from the Fred Hutchinson Cancer Research Center, Children's Hospital and Regional Medical Center, and Philips Medical Systems, aims to develop imaging agents and multifunctional nanoscale drug delivery vehicles for medulloblastoma -- the most common brain tumor in children.

A good mix of projects

Together, the platform partnerships represent "an excellent mix of projects that include advanced technologies as well as technologies in earlier stages of development that have significant potential to exponentially increase progress in all aspects of cancer treatment and diagnosis," according to NCI deputy director Anna Barker, PhD. The partnerships include collaborations across scientific disciplines and seek to balance "well-established researchers with those newly entering the field," she adds.

UMC's in-house process for producing biocompatible gold nanoparticles, for instance, was a key to its selection as a platform partnership, Katti maintains.

"If we did not have that capability, we would not be where we are today," he tells *NanoBiotech News*. The partnership will allow his team to take the next steps: tagging the gold nanoparticles with prostate-specific peptides and delivering them to prostate cancer cells in mice, then demonstrating their imaging and therapeutic properties.

Katti is optimistic the group will demonstrate sufficient safety and efficacy to proceed to phase I
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human trials by the end of the five-year NCI Alliance partnership.

The SUNY Buffalo-Johns Hopkins linkage also "will enable us to move more quickly from the lab to the bedside," Prasad says. The partnership initially aims to conduct in vitro tumor targeting and in vivo PET imaging studies before moving to stability studies and live animal PET imaging studies. SUNY Buffalo already has partnerships with several commercial organizations -- including Buffalo-based NanoDynamics, Inc. -- and also has been approached by venture groups about the prospect of commercializing its nanoparticle technologies, according to Prasad.

Baker, who is among the most prolific U.S. researchers in nanomedicine, with two spinoff companies -- NanoBio Corporation and Avidimer Therapeutics, Inc. -- under his belt, is more cautious. Despite the complexity of his dendrimer nanoparticle platform, he expects to develop a dendrimer conjugate for cancer cell-specific targeting, in vivo testing, and animal model results. And he says Avidimer last week received seed money from Cambridge, MA-based Flagship Ventures, helping the start-up to ramp up for commercialization efforts.

Will there be enough funding

But Baker worries that the NCI Alliance funded both the CCNEs and the platform partnerships well below requested funding amounts -- a concern shared by other researchers -- and he says NCI hasn't clearly stated how it will handle either of these initiatives after their first year.

Moreover, the toxicity and biocompatibility of many of the materials under study are not well

defined, says Baker, an allergist by training.

"We need to look at animal testing very early on -- before we get too invested in the technology," he says. "We need to think long and hard about this stuff before putting it into compounds that go into the body."

At their size, nanoparticles will penetrate pores and hair shafts, perhaps unintentionally, and even if they're not poisonous, they could cause a wide range of reactions in people, Baker says.

"If we don't address this issue up front, we'll find nanomaterials handled just like genetically engineered food," he predicts. "We'll have standards defined and imposed from outside the industry."

Editor's Note: Contact James R. Baker, Jr., at (734) 647-2777, Kattesh Katti at (573) 882-5656, and Paras N. Prasad at (716) 645-6800 ext. 2098.

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next week or so."

In late spring, Insert released data demonstrating effective anti-cancer results in animal studies of IT-101 against various cancers, including pancreatic cancer, colon cancer, breast cancer, lung cancer, and Ewing's sarcoma, a cancer primarily affecting children and young adults. In the case of two of the cancers, total tumor remission was achieved and the animals remained tumor free throughout the length of the 90-day study. The data were presented at the American Association of Cancer Research Annual Meeting in Anaheim, CA. (See *NanoBiotech News*, May 4, 2004, p. 9.)

IT-101 is a conjugate of Insert's nano-engineered drug delivery vehicle, Cycloset, and the anti-cancer drug camptothecin. Analogues of camptothecin, specifically irinotecan and topotecan, have nearly \$1 billion in annual reported worldwide sales, despite the serious side effects of these medications. In the study, anti-tumor activity in IT-101 treated animals was superior to irinotecan treated animals in all tumor models tested.

"Insert's drug has achieved complete remission of non-small cell lung cancer and Ewing's sarcoma, and significant knockdown of other tumor types in preclinical results in mouse xenografts,

showing promise across a wide range of cancers," Stewart says. "Obviously, if the [human trial] results are anywhere near as good, this will be a significant event for us."

A January start?

Stewart was not certain when the human trials would start, but estimated it would be in January. He says it is not yet possible to identify specific cancers that will be targeted.

It is difficult to accurately project the financial potential of IT-101, Stewart continues, but it is clearly significant. "Camptothecin and its derivatives are just short of a \$1 billion a year," he notes. "As for the entire area of chemotherapy, I've read numbers anywhere from \$35 billion to \$45 billion a year. This delivery system could be used with any number of chemotherapy drugs and offer hopefully significant improvement; it certainly does with camptothecin."

Insert Therapeutics controls a portfolio of U.S. and foreign issued patents and pending applications covering therapeutics based on linear cyclodextrin-containing polymers, which comprises Insert's Cycloset family of drug delivery polymers.

Editor's Note: Contact R. Bruce Stewart at (626) 792-5549. ©

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otechnology Excellence -- dubbed a "CCNE" -- will also work to develop instruments to better measure and monitor the activity of that very versatile cell and its payload.

The university received \$3.9 million for the first year of a five-year grant from the NCI, or approximately \$20 million overall, says Sadik Esener PhD, professor of electrical and computer engineering and materials sciences at the UCSD Jacobs School of Engineering, director of the new CCNE and principle investigator for the research the grant money will fund.

"The CCNE is a consortium of scientists, with 35 investigators participating from five institutions," he tells *NanoBiotech News*. "Approximately 60% of the grant will fund research at UCSD. The remaining 40% will fund research at the other participating institutions -- the University of California at Santa Barbara, the University of California at Irvine, the University of California at Riverside and the Burnham Institute." NanoBioNexus, he adds, will receive funds to organize the CCNE's educational component.

That's a powerful group of partners with a dense web of their own additional affiliations,

research agendas and corporate partnerships. What happens to any discoveries they make together with the federal grant money? "The university has the right of first refusal to patent any discoveries that are made by investigators involved with the nanotechnology center," Esener reports. "If the university exercises that right, it, the investigator and the investigator's department will share in any royalties resulting from the discovery."

If the university does not choose to patent the discovery, the investigator can file for a patent and will receive any royalties associated with the invention. But the big beneficiaries, of course, have no ties to the CCNE at all. "The cancer patients will be the recipients of the benefits of the discoveries," Esener says, "including the best benefit of all -- improved outcomes."

Mothership evades immune system

The ultimate goal of the research is to develop a multi-functional "mothership" and its associated payload of nanosensors and nanotherapeutic and imaging agents that will specifically target a tumor and the blood vessels that feed it, Esener continues.

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"The mothership will deliver therapeutics, imaging agents and other sensors to the tumor or tumor blood vessels," he says. "It will also contain elements that will evade the immune system and liver, increasing the level of therapeutic or imaging agent that reaches the tumor."

The mothership may also contain elements that can be activated by the tumor or by outside sources -- such as ultrasound or magnetic fields -- that will also improve specificity. In addition, the researchers hope to develop instruments to purify and characterize tumor cells and DNA from human blood samples. "Identification and characterization of tumor cells may be useful to predict the most effective treatment regimen," Esener notes, "measure the effects of a therapeutic regi-

men on the tumor and identify tumor cells that survive therapeutic treatment. Characterization of therapy-resistant tumor cells may lead to effective treatments for residual disease."

If all goes well, Esener says, his team should be able to commercialize instruments to purify and characterize tumor cells and nanoparticles specifically targeted to tumors or tumor blood supplies with therapeutics and imaging agents. "Many of the participating investigators have founded companies and therefore have the knowledge and experience to move discoveries to the marketplace," he emphasizes. "Toward that goal, we have established interactions with GE, Nanogen, Irvine Sensors, Honeywell and Enterprise Partners, a venture capital firm."

Editor's Note: Contact Sadik Esener at (858) 534-2732. ☉

Nanogen begins shipping NanoChip 400 systems

By Steve Lewis

Nanogen, Inc. (NASDAQ:NGEN) has begun shipping its second-generation instrument, the NanoChip 400, both domestically and to Europe. The general laboratory system for molecular biology applications uses the company's improved NanoChip 400-site electronic microarray, upon which home brew molecular assays can be developed in clinical and research laboratories.

Building on features of the first-generation NanoChip Molecular Biology Workstation and 100-site chip, the new multi-purpose system combines sample and reagent handling robotics with detection in an instrument half the size of its predecessor. The open platform creates the opportunity for labs to use one system for multiple molecular applications, including the detection of single nucleotide polymorphisms (SNPs) and multi-gene targets like those tested for pharmacogenetics.

"This system is second-generation, with some improved features and capabilities, and we fully intend to take [it through] the next stages of the regulatory process," says Graham Lidgard, senior vice president of R&D at San Diego, CA-based Nanogen. "It already is fully designed under QSI regulations, and will be available in Europe." (The NanoChip 400 is manufactured by Nanogen's long-standing collaborator Hitachi Instruments Group, under the U.S. Food and Drug Administration's Quality System Regulation.)

The NanoChip 400 cartridge used with the system is a blank microarray template that constructs the user-defined panel of genetic markers

on one chip at the time of sample testing. The cartridge has 400 test sites that can be used for any combination of multiple genes and multiple samples, and can be used multiple times until the 400 test sites are used. This cartridge reusability, says Nanogen, makes the NanoChip 400 system easier and more cost-effective to use than research-grade thousand-gene chip arrays, and more suitable than polymerase chain reaction (PCR) when multi-allele or multi-gene assays are of interest.

"From an operational point of view it is more automated; the current system requires a fair amount of user intervention between the two parts of the system," explains Lidgard. In terms of loading and reading for arrays, he notes, the reader had to perform a number of manual operations.

"This is a smaller unit, and from time you place PCR, for example, on the system, it is programmed to automatically go through to data analysis," Lidgard continues. "And, since it is an open platform, people can develop their own arrays. The system comes without any content on the chip, so the user loads up their own arrays, and/or determines how they will organize them."

Lidgard says Nanogen's competition for the NanoChip 400 will be "everybody's home-brew arrays." However, he adds, "We've pitched this into an area that is not well-served by the market -- high-multiple systems. The classic model is one chip per sample. Productivity for a well-defined panel of analysis is highly suited to our system, and in fact, there's nothing quite like this on the market at all."

Nanogen recently completed a stock sale, raising \$18.9 million. (See NanoBiotech News, Oct. 5, 2005, p. 2.)

Editor's Note: Contact Graham Lidgard at 858-410-4794. ☉

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