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PAGE 1 OF 7

Domantis Raises US$33M For Program In Domain Antibodies

By Karen Pihl-Carey
Staff Writer

Domantis Ltd. raised US$33 million in a Series B financing that could take the company into clinical trials with its lead domain antibody (dAb) therapeutics.

The first antibody is expected to enter the clinic in the second half of 2005, following continued preclinical work this year. The $33 million (£17.5 million) funding is the largest financing round for the three-year-old company, which has research and development operations in Cambridge, England, and administrative operations in Cambridge, Mass.

"This funding, along with revenue that should come in from our existing partners, should get the company to the real significant milestone of having human efficacy data," said Bob Connelly, CEO of Domantis. "If you take this with

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FDA Accepts Celgene's sNDA To Broaden Thalomid's Label

By Aaron Lorenzo
Staff Writer

Celgene Corp. moved one step closer to expanding Thalomid's label.

The Warren, N.J.-based company said the FDA accepted for review its supplemental new drug application seeking approval to market the drug for multiple myeloma, an indication for which the product is getting increased use off-label. Thalomid (thalidomide) generated about $224 million in sales during 2003, more than $100 million more than the previous year, and this year Celgene expects it to produce revenue ranging from $280 million to $290 million.

Such sales growth stems from the compound's use for multiple myeloma, which is the second most common blood cancer in the U.S., affecting about 50,000 people.

See Celgene, Page 5

Science Scan

Scripps Scientists Level Synthetic Chemical, Cardiogenol C By Name, From Mouse Stem Cells Into Heart

By David N. Leff
Science Editor

Editor's Note: Science Scan is a roundup of recently published biotechnology-relevant research.

Stem cells have a huge potential in medical therapy because it's in their nature to differentiate into many different cell types. They potentially provide replacements for cells that have been permanently lost by a patient (or a mouse).

An example would be a neurodegenerative malady such as Parkinson's disease, in which neurons that secrete dopamine are lost from the brain. Stem cells may ameliorate that condition by regenerating the missing neurons.

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Antares Intends To Raise Profile After $14.6M Private Placement

By Karen Pihl-Carey
Staff Writer

In hopes of relisting its stock on a national exchange and to beef up its capital reserves, Antares Pharma Inc. completed a $14.6 million private placement.

The company said Monday that it raised $5.1 million, adding to the $9.55 million it raised earlier this month. Shares were sold at $1 each. All purchasers also received five-year warrants to purchase common stock equal to 33 percent of the total number of shares sold. They can use the warrants to purchase stock for $1.25 per share.

"We did the financing for basically two reasons," said Lawrence Christian, vice president of finance and chief financial officer at Antares. One, it needed money to remain attractive to its pharmaceutical partners that fund its development programs. And two, it needed to gain enough net

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OTHER NEWS TO NOTE

• **4SC AG**, of Martinsried, Germany, said it spun off of an independent company, Quattro Research GmbH, which develops software solutions for the integration of chemical and biological data in drug discovery and development. Quattro draws on know-how and software developments within 4SC. Its 4Scan technology for the virtual screening of large data sets does not constitute part of the spin-off.

• **Acacia Research Corp.**, of Newport Beach, Calif., said its CombiMatrix group signed a research agreement with Case Western Research University in Cleveland for work in developing a diagnostic for Alzheimer's disease using the CustomArray platform. The university work is directed by Alzheimer's researcher Mark Smith, professor in the department of pathology.

• **Acambis plc**, of Cambridge, UK, named Gordon Cameron CEO. He served as the president of the company's U.S. division in Cambridge, Mass., since March 2001. He came to Acambis in 1996 as chief financial officer. Separately, Acambis changed the ratio of its American depositary receipts (ADRs), which are traded on the Nasdaq exchange, from one ADR for 10 ordinary shares to one ADR for two ordinary shares. ADR holders on record as of Feb. 20 will be issued four additional ADRs for every ADR held. There is no change to the company's ordinary shares, whose primary listing continues to be on the London Stock Exchange.

• **Alteon Inc.**, of Parsippany, N.J., said efficacy and safety findings from a post hoc analysis of ambulatory blood pressure measurements in the Phase IIb Sapphire/Silver trial of ALT-711 support the potential for using the A.G.E. crosslink breaker as an antihypertensive agent with unique characteristics for the treatment of uncontrolled systolic hypertension. Data showed that ALT-711 treatment resulted in highly significant lowering of systolic blood pressures in patients with a baseline systolic ABPM of 140 mm Hg or greater, with little concurrent effect on diastolic blood pressure readings.

• **Atrix Laboratories Inc.**, of Fort Collins, Colo., submitted a new drug application to the FDA for Eligard 45mg (leuprolide acetate for injectable suspension), a six-month, sustained-release product for hormone-sensitive, advanced prostate cancer. Already reported interim Phase III data suggested Eligard 45mg suppresses testosterone to low levels with minimal breakthroughs, a situation in which testosterone levels rise above the castrate threshold of 50 ng/dL. Sanofi-Synthelabo Inc., a unit of **Sanofi-Synthelabo SA**, of Paris, is marketing one-, three- and four-month extended-release Eligard products (7.5mg, 22.5mg and 30mg) in the U.S., and would market the six-month product should it receive approval.

• **BioMarin Pharmaceutical Inc.**, of Novato, Calif., began its clinical program for the treatment of phenylketonuria (PKU), an enzyme deficiency disorder that can cause mental retardation and brain damage and affects at least 50,000 diagnosed people in the developed world. Originally projected to start at the end of next month, the first pilot trial will evaluate PKU patient responsiveness to the enzyme co-factor 6R-BH4. Expected to be completed in the second quarter, the study's goal is to define the 6R-Bh4 screening method that will be used to identify the population of PKU patients who most likely would respond to Phenoptin, BioMarin's form of 6R-Bh4.

• **Cengent Therapeutics Inc.**, of San Diego, and the Center for Biophysical Sciences and Engineering of the University of Alabama at Birmingham, said they created the first integrated computational and physical structure determination service offering for in-house drug discovery efforts of the pharmaceutical and biotechnology industries. Cengent and the center provide a solution for 3-D, structure-based drug lead discovery and structure-based optimization. The service also may provide structurally validated initial drug leads in support of existing in-house screening efforts by providing compound pre-selection and overflow capacity.

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OTHER NEWS TO NOTE

• **Cytopia Pty. Ltd.**, of Melbourne, Australia, and **Myomatrix Therapeutics LLC**, of Rensselaer, N.Y., said they achieved a milestone in their collaboration to develop treatments for cardiovascular disorders, including heart failure. Kinase inhibitors developed by Cytopia have been shown to block signaling pathways in cardiac myocytes that are associated with heart failure. The new data showed that in the in vitro cardiac myocyte model, Cytopia's specific molecules are more effective than the molecules tested in previous work at the State University of New York.

• **Diversa Corp.**, of San Diego, entered a long-term contract with **Fermic SA de CV**, of Mexico City, to provide manufacturing capacity for the production of Diversa's enzyme products. Diversa will increase its available manufacturing capacity to a level sufficient for the production of enzyme products representing more than $100 million in potential future annual product sales by Diversa and its partners. Fermic will provide manufacturing capacity for enzymes exclusively to Diversa, which will co-invest in certain mutually agreed-upon capital equipment in exchange for credits for manufacturing services to be provided by Fermic.

• **Exelixis Inc.**, of South San Francisco, said its scientists published two articles in the online edition of *Nature Genetics* describing the most complete functional genetic toolkit for studying a multicellular organism. The Exelixis collection includes specific disruptions in a majority of genes in the fruit fly, *Drosiphila melanogaster*, and the company called the toolkit an example of its ability to industrialize the use of model system genetics to identify modifiers of important disease pathways.

• **Generex Biotechnology Corp.**, of Toronto, entered a collaboration with the Chinese Academy of Science in Shanghai to develop a vaccine for severe acute respiratory syndrome. Antigen Express, Generex's subsidiary, developed technologies to enhance the potency of DNA vaccines. Together they seek to create an effective DNA vaccine for protection against SARS infections. Antigen Express's technology focuses on modulating immune responses mediated by T helper cells.

• **Genetronics BioMedical Corp.**, of San Diego, completed the special protocol assessment review process with the FDA for two pivotal Phase III studies to evaluate its MedPulser Electroporation Therapy System as a treatment for recurrent and second primary squamous cell carcinomas of the head and neck. Both protocols will compare the investigational system to surgery, with a primary endpoint designed to demonstrate that patients treated with electroporation therapy have superior preservation of function (e.g., eating, swallowing and talking) when compared to surgery.

• **GPC Biotech AG**, of Martinsried, Germany, said data published in this month's issue of *Chemistry and Biology* described its drug-target interaction technology, LeadCode. Human protein kinases represent a family of more than 500 enzymes that are drug targets for various therapeutic areas, including cancer. In the published study, LeadCode was applied to several cyclin-dependent kinase (Cdk) inhibitors. GPC Biotech has a program to develop Cdk inhibitors as anticancer drugs.

• **Guilford Pharmaceuticals Inc.**, of Baltimore, said the National Institutes of Health in Bethesda, Md., began a Phase II trial to test the company's neuroimmunophilin ligand, GPI 1485, as part of a program investigating neuroprotective therapies for Parkinson's disease. The study is being funded by the National Institute of Neurological Disorders and Stroke, part of the NIH also located in Bethesda. Guilford said the institute selected GPI 1485 based on preclinical animal data. GPI 1484 also is in a Phase II trial for post-prostatectomy erectile dysfunction.

• **Lorus Therapeutics Inc.**, of Toronto, said its common stock began trading on the American Stock Exchange under the ticker symbol "LRP." Lorus is developing products and technologies for the management of cancer.

• **Marshall Edwards Inc.**, of Washington, began a clinical trial of the investigational anticancer drug phenoxodiol in patients with cancer of the cervix. In the study of patients with squamous cell carcinoma and adenocarcinoma of the cervix, vagina and vulva, subjects will have a primary diagnosis of cancer. It will evaluate the safety and ability of phenoxodiol when it is given as a monotherapy in early-stage cancer. Marshall Edwards licensed phenoxodiol from **Novogen Ltd.**, of Sydney, Australia.

• **MedImmune Inc.**, of Gaithersburg, Md., said preclinical findings published in the Feb.15, 2004, issue of *Clinical Cancer Research* showed that elevated levels of PC cell-derived growth factor (PCDGF) may be an early signal of prostate cancer progression. Along with collaborators at **A&G Pharmaceutical Inc.**, of Columbia, Md., and Indiana University, the researchers documented significantly higher levels of PCDGF expression in clinical samples of invasive prostate cancer tissue than in adjacent benign or normal tissue.

• **Nabi Biopharmaceuticals Inc.**, of Boca Raton, Fla., called preliminary results of its Phase I/II trial of Civacir encouraging, noting that the product was well tolerated in both high- and low-dose treatment arms. The findings also revealed a trend toward a reduction in levels of ALT (serum alanine aminotransferase, a liver enzyme that measures liver function). The study was designed to evaluate the safety and pharmacokinetics of two dose levels of Civacir (hepatitis C immune globulin [human]), an antibody-based therapy being developed to prevent hepatitis C virus re-infection of transplanted livers in patients with chronic hepatitis C, vs. a control in a total of 18 patients who underwent liver transplantation due to hepatitis C-induced end-stage liver failure.

Domantis

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money we have in the bank, and other money coming in, it should give us three years of run time, and hopefully more depending on how many deals we do."

Before completing the latest round, the company had about US$9 million in cash. It has raised a total of $54 million since its inception in December 2000, including $20 million through its partnership with Peptech Ltd.

Domantis will use the funds raised to fast-track its lead dAb programs into the clinic, as well as to build a preclinical and clinical pipeline.

"It's for R&D, with the 'D' part of it eating up a lot more cash than what it has to date," Connelly said.

The company's dAb programs show broad therapeutic potential in respiratory disease, inflammation, cancer and cardiac disorders. The technology can be used in a variety of formulation and delivery options, including oral and pulmonary administration. Domantis has eight therapeutic programs and three partner programs, with Sydney, Australia-based Peptech Ltd., New York-based ImClone Systems Inc., and Abbott Laboratories, of Abbott Park, Ill.

Connelly told *BioWorld Today* that Domantis will have a number of programs at the preclinical stage this year. He also expects the company to enter into more research and development or technology partnerships, and to expand its existing partnerships. It also could enter into some co-development partnerships in the near term.

"I don't think we'll license out any leads this year, but that's likely to start in 2005," he said.

Domantis formed its US$17 million collaboration with Peptech in April 2001, shortly after the company came into existence. As part of the Peptech collaboration, London-based MVM Ltd. invested US$3 million in Domantis. Domantis agreed to develop single-domain antibody drug candidates against four Peptech targets using technology developed at the UK Medical Research Council's Laboratory of Molecular Biology.

In November, Domantis received the final payment in the $20 million investment from Peptech and MVM as an anti-tumor necrosis factor-alpha dAb entered preclinical testing. The compound is expected to enter clinical testing in the second half of 2005.

Domantis completed the lead generation and optimization for the compound in less than 11 months. It reached preclinical efficacy at 14 months, when the dAb completely prevented the onset of rheumatoid arthritis in a clinically predictive model of human disease.

Connelly said its efficiency is one of the things that attracts investors. Domantis is able to conduct 10 to 12 programs a year, pushing them through from discovery to animal studies, all with only a 40-person organization.

"The chance of creating a really deep pipeline with fairly low capital needs is really a unique part of the story," he said.

Domantis would receive royalties on any product sales resulting from its collaboration with Peptech. And Peptech has the option to negotiate the co-development of dAbs against three additional targets.

Aside from its deal with Peptech, Domantis formed a research and license agreement with Abbott in November 2002 to discover therapeutics based on the dAb technology. And in March 2003, Domantis entered a nonexclusive licensing agreement with ImClone, allowing ImClone to select dAbs for therapeutic and research use.

Domantis also signed agreements with the Medical Research Council last April giving the company an exclusive commercial license to use a polymerase technology to search therapeutic polypeptides, including dAbs.

Domain antibodies, or dAbs, are the smallest functional binding units of antibodies, consisting of the variable regions of the human heavy or light chain.

Investors in the latest financing round were led by 3i Group plc, of the UK. Other new investors that participated included Gray Ghost LLC, of Baltimore; Albany Ventures, of the UK; and an undisclosed institutional investor in the U.S. Existing shareholders that participated were MVM and Peptech.

In connection with the financing, Nigel Pitchford, an associate director at 3i, joined Domantis' board.

The company changed its name in May 2002 from Diversys to Domantis, in order to reflect its core domain antibody technology. ■

OTHER NEWS TO NOTE

• **NeoRx Corp.**, of Seattle, raised gross proceeds of about $9.7 million after entering a securities purchase agreement with certain institutional investors in a private placement. The company sold about 1.85 million common shares at $5.25 apiece, a 2 percent premium to the 10-day volume-weighted average of the stock. The investors also received five-year warrants to purchase 922,500 shares at an exercise price of $7 apiece. Reedland Capital Partners, a Division of Financial West Group, served as the placement agent in the financing.

• **Pharmion Corp.**, of Boulder, Colo., said the FDA accepted its Vidaza new drug application for filing and granted priority review status for the NDA, reducing the standard agency response time to six months and targeting an agency response on or before June 29. The submission was based upon a National Cancer Institute-sponsored Phase III study of Vidaza (azacitidine for injectable suspension) for myelodysplastic syndromes, conducted by Cancer and Leukemia Group B, and two supportive Phase II studies conducted and sponsored by the same groups. Pharmion filed the NDA about two months ago. (See *BioWorld Today*, Dec. 30, 2003.)

Celgene

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"For Celgene, to have a label indication for multiple myeloma is certainly a milestone achievement," Brian Gill, Celgene's director of investor and public relations, told *BioWorld Today*. "We believe that in 2005, there will be some upside opportunity from the commercial side."

The company submitted its application at the end of December, and expects to receive a response from the agency in October.

"Going forward, assuming that there is an approval for Thalomid in multiple myeloma, it certainly gives the immunology [sales] specialists an opportunity to really help oncologists better understand treatment regimens and results," Gill added, noting the use of Celgene's program for prescribers and patients, STEPS (Systems for Thalomid Education and Prescription Safety).

About 14,600 new cases of multiple myeloma are diagnosed each year and about 11,000 Americans are expected to die each year of multiple myeloma. Clearly the chance to further market Thalomid to such patients adds to the drug's positive profile.

The compound, long associated with severe birth defects, has a checkered history as a result. First used in the 1950s in Europe for morning sickness, its harmful side effects became apparent through shortened or absent limbs in children born to mothers who began taking the drug when pregnant.

But Thalomid first received an FDA approval more than five years ago for a condition related to leprosy. More specifically, the product is approved for the acute treatment of cutaneous manifestations of moderate to severe erythema nodosum leprosum and as maintenance therapy for prevention and suppression of cutaneous manifestations of the disease's recurrence.

Though Gill said sales associated with those indications remains nominal, interest in using the drug for multiple myeloma and other cancers remains high. Thalomid has been evaluated in hundreds of investigator-sponsored clinical trials around the world, he added, with various supporting data published in a variety of peer-reviewed publications.

"These are the things that promote the use and uptake of Thalomid in the marketplace," Gill said. "When we go to medical meetings, our people can't believe the feedback we get from investigators who are doing work on thalidomide in some shape or form."

It seems to directly affect multiple myeloma cells by inhibiting their growth and survival, according to findings published in the Nov. 1, 2000, issue of *Blood*.

He said that for cancer, the drug is used about 77 percent of the time for blood-borne malignancies. About 70 percent of that wedge represents use in treating multiple myeloma, another 5 percent for myelodysplastic syndromes and the remainder in other hematologic cancers. The other 23 percent of Thalomid's use is in treating solid tumors, such as prostate, renal cell, brain, bladder and liver cancers, as well as melanoma and others.

One in five users receives the drug at no cost as part of Celgene's compassionate use program.

"It's a wonderful thing to have Thalomid continuing to do so well, particularly in the oncology community, because its success fuels a very broad and deep pipeline here at Celgene that has a lot of high-potential cancer-fighting drugs," Gill said. "More than 45 percent of our revenues go right back into our R&D programs."

Celgene has a late-stage investigational compound for multiple myeloma in development as well. Called Revimid (CC-5013), the Thalomid analogue is in pivotal trials in multiple myeloma, for which it has been granted fast-track status, and metastatic melanoma.

The company paid about $27 million to gain access to the thalidomide analogue program from Rockville, Md.-based EntreMed Inc. Previously, both parties had begun legal scraps over patent issues surrounding thalidomide, but settled all disagreements through the license agreement. Celgene first licensed thalidomide in 1998, but only for angiogenesis-related uses. (See *BioWorld Today*, Jan. 3, 2003.)

Celgene's stock (NASDAQ:CELG) gained 21 cents Monday to close at $39.89. ■

OTHER NEWS TO NOTE

• **SuperGen Inc.**, of Dublin, Calif., told the SEC it plans to withdraw its proposed offering of 9.5 million common shares, which also included 250,000 shares to be offered by a selling stockholder. The company said its management would provide additional business updates during a financial results conference call later this week.

• **Tissera Inc.**, of Tel Aviv, Israel, raised net proceeds of $1.6 million after completing a private equity placement with a group of individual and institutional investors. Tissera is developing tissue precursor regeneration technologies to address a variety of illnesses in which organ transplantation is necessary.

• **Transkaryotic Therapies Inc.**, of Cambridge, Mass., said it will extend enrollment in its pivotal trial evaluating iduronate-2-sulfatase (I2S) enzyme replacement therapy for Hunter's syndrome (MPS II). The company intended to close enrollment this month, but with 84 patients currently enrolled and commitments to additional patients, it believes the study will reach its 90-patient target early next month. The extension allows TKT to fulfill commitments to four families from Japan who are relocating to the U.S. to participate in the trial, referred to as the AIM study (Assessment of I2S in MPS II). This effort, conducted with the help of TKT's partner for Japan, Genzyme Corp., also of Cambridge, may result in a slight over-enrollment.

Antares

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equity in order to apply for listing on a national exchange.

"So now we can say we have capital reserves to show the large pharma companies that we will be around," Christian told *BioWorld Today*. "We have no immediate plans of spending that money."

Antares Pharma lost its Nasdaq SmallCap Market listing last year when its net equity fell below the market's requirements. The company's stock has since been listed on the Over-the-Counter Bulletin Board under the symbol "ANTR." It closed Monday at $1.16.

Christian said he is unsure whether Antares will attempt a listing on the Nasdaq or American stock exchanges.

The company develops specialty pharmaceutical products, such as needle-free and mini-needle injector systems, transdermal gel technologies and fast-melt oral tablet technology. Antares distributes its needle-free injector systems in more than 20 countries. It also conducts research and development with transdermal gel products and has several products in the clinic with U.S. and European partners.

Antares was formed in 2001 with the merger of Basel, Switzerland-based Permatec Holding AG and Minneapolis-based Medi-Ject Corp. Medi-Ject brought to Antares its device technologies, including needle-free injector systems, while Permatec brought the drug formulation capabilities, the liquids and gels.

"Both of them combine to be drug delivery across the skin," Christian said.

Permatec also brought two contracts to Antares for the development of hormone replacement therapy gels. The contracts were with Solvay Pharmaceuticals Inc., a division of Brussels, Belgium-based Solvay SA, and BioSante Pharmaceuticals Inc., of Lincolnshire, Ill.

"Both Solvay and BioSante are in the clinical trial stages on several of our products in female hormone replacement therapy," Christian said.

All of the products are in Phase II or further along, he said. In October 2002, BioSante initiated a Phase II trial with a transdermal testosterone gel. And in May 2003, it completed a Phase II/III trial for its estradiol topical gel product, Bio-E-Gel.

Antares has several hormone therapy products, including estradiol, an estradiol-progestin combination, testosterone for male hypogonadism and testosterone for the treatment of female sexual dysfunction.

Solvay holds European rights to some of Antares' products being developed, while BioSante holds North American rights. In September 2001, Solvay sublicensed from BioSante the U.S. and Canadian rights to an estrogen and progestogen combination transdermal hormone replacement gel product. The product incorporates Antares' advanced Combi Gel transdermal gel technology that enables multiple drugs to be delivered across the skin.

Antares recently formed a development agreement with ProSkelia SAS, of Paris, and a license agreement with privately held NPMG, both for the development of products that use Antares' ATD gel technology.

In December, Antares received a milestone payment from Eli Lilly and Co., of Indianapolis, as part of its license agreement for its needle-free injection technology in the fields of diabetes and obesity. Lilly initiated a clinical trial of the needle-free delivery system in April of last year. Financial terms of the agreement, which was formed in February 2002, were not disclosed.

Antares is based in Exton, Pa., but has manufacturing and research facilities in Minneapolis and research facilities in Basel, Switzerland.

SCO Securities LLC acted as the placement agent for the financing. ■

OTHER NEWS TO NOTE

• **Varian Inc.**, of Palo Alto, Calif., added the Pursuit Diphenyl column to its line of laboratory consumable products for liquid chromatography. The company said the column contains bonded-phase chemistry that is more sensitive to analytes with double bonds or aromatic rings, both of which it called challenging for pharmaceutical and environmental scientists.

• **Vertex Pharmaceuticals Inc.**, of Cambridge, Mass., said findings published in *Nature Medicine* showed that VX-680 blocked cancer cell proliferation and also triggered cell death in a range of tumor cell types. A selective small-molecule inhibitor of the Aurora kinases, which are known to be overexpressed in many tumor types, VX-680 was shown to reduce tumor growth in cancer models. Data from in vivo xenograft models indicated that VX-680 achieved complete inhibition of tumor growth at well-tolerated doses. Vertex's stock (NASDAQ:VRTX) gained 76 cents Monday, or 7.4 percent, to close at $10.97.

• **Y's Therapeutics Co. Ltd.**, of Tokyo, raised 2.4 billion yen (US$22 million) through a Series B financing that included new and existing investors. The privately held company said it would use the proceeds to advance its product development pipeline, which includes antibody therapeutics and small-molecule products for oncology and autoimmune diseases. The financing was led by Softbank Investment Corp., with additional investments from Zenkoku Hosho Co. Ltd., Biovision Capital Corp. and unnamed venture capitalists.

Stem Cells

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Another example is Type I diabetes mellitus in which beta cells are lost from the pancreas. They might be treated by generating new beta cells.

As a rule, gestational cells develop along a pathway of increasing specialization. In humans and other mammals, those developmental events are controlled by mechanisms and signaling pathways that researchers are only beginning to comprehend. One of science's great challenges is to find ways of selectively differentiating embryonic stem cells (ESCs) into specific cell types of interest. "It's hard to control which specific lineage the stem cells differentiate into," observes Xu Wu, a doctoral candidate in the Kellogg School of Science and Technology at the Scripps Research Institute in La Jolla, Calif.

He and his colleagues have identified a small synthetic molecule that can control the fate of embryonic stem cells. "This compound," Wu volunteered, "is called Cardiogenol C. It causes mouse embryonic stem cells to selectively differentiate into 'cardiomyocytes,' or heart muscle cells. This is an important step on the road to developing new therapies for repairing damaged heart tissue. Likewise," he went on, "a damaged heart, which is composed mainly of cardiac muscle cells that the body may be unable to replace, could potentially be repaired with new muscle cells derived from stem cells."

Wu is first author of the study to be published in an upcoming issue of the *Journal of the American Chemical Society*. Its senior author is chemical biologist Peter Schultz, a professor at Scripps. The paper is titled "Small molecules that induce cardiomyogenesis in embryonic stem cells." It was released online Jan. 3, 2004, by the journal.

The Scripps scientists reasoned that if stem cells were exposed to certain synthetic chemicals, they might selectively differentiate into particular types of cells in the body. To test that hypothesis, they screened some 100,000 small molecules from a combinatorial library that they synthesized. From the assortment they designed a method to identify molecules able to differentiate mouse embryonic stem cells into heart muscle cells. Cardiogenol C proved to be effective at directing more than half of their tests to thus differentiate. Existing methods reportedly result in merely a 5 percent success rate of their tested stem cells – namely ESCs – turning into cardiomyocytes.

The Genomics Institute of Novartis Research Foundation collaborated in the embryonic stem cell research project.

'Metabolic Syndrome' – Obesity, Low HDL-Cholesterol, Impaired Glucose Tolerance – Hits Hispanic Youth

Large numbers of Hispanic youth already have complications of obesity. They include impaired glucose tolerance, which can lead to diabetes and metabolic syndrome. The findings are published in the January 2004 issue of *The Journal of Clinical Endocrinlogy and Metabolism*. They caution that Hispanic youth may have underlying risk factors that make them more susceptible to diabetes, cardiovascular risks and the so-called metabolic syndrome. That is a collection of health risks that, besides obesity, include dyslipidemia (high blood triglycerides and low HDL-cholesterol and high blood pressure). Those symptoms include the chance of developing heart disease, stroke and diabetes. They affect more than 20 percent of adults in the U.S. Hispanics experience the highest rates of metabolic syndrome, with rates near 32 percent.

During the past 10 years, the obesity rate, which increases risk of developing metabolic syndrome, has doubled among Hispanic youth. The rates of Type II diabetes and impaired glucose tolerance also have increased in that group. Researchers at the University of California at Los Angeles (UCLA) conducted two separate surveys on data collected in overweight Hispanic children to determine some of the risk factors they incur.

Obesity and the complications associated with the problem are growing among minority children in the U.S., explained Martha Cruz, the primary author on the study and an assistant professor at UCLA. "We hope that our research will help the medical community better understand how to determine which children are at risk for developing diabetes, metabolic syndrome and cardiovascular disease," she observed.

Studies From Holland, Canada Report Widespread Environmental Presence of *Enterobacter sakazaki*

A bacterium called *Enterobacter sakazakii* might be dangerous to premature babies and young infants. It could be more widespread in the environment than previously thought. An issue of *The Lancet*, dated Jan. 4, 2004, is titled "Occurrence of *Enterobacter sakazakii* in food production environments and households." It is accompanied by a commentary headed, "*Enterobacter sakazakii* – new food for thought?" In previously described outbreaks, infant formulas contaminated during factory production or bottle preparation were recognized as a harmful source for bacterial colonization.

Chantal Kandhai, from Wageningen University in the Netherlands, and her co-authors used a refined isolation and detection method to investigate the presence of *E. sakazakii* samples from eight of nine food factories and five of 16 households that contained the bacterium. In the accompanying commentary, Jeffrey Farber from Health Canada concludes: "Current industry efforts to reduce the occurrence of *E. sakazakii* have focused on improving hygiene practices, coupled with environmental monitoring and end-product testing for the organism. Since powdered infant formula is not sterile and there is the potential risk of contamination during preparation, there is a need for care when preparing and handling reconstituted powdered infant formulas. Health care professionals should follow recommendations provided by public health officials and organizations such as the American Dietetic Association," the editorial concluded, "and be alert to possible modifications." ■