

STEM CELL lab world

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Volume 2, No. 11

The Latest News For Researchers & Laboratory Staff

October 10, 2008

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Top of the News...

New Products

Minerva Biotech's Growth Factor Supports "Massive Growth" Of hESCs

Boston, Mass.-based Minerva Biotechnologies said on October 2 that collaborators at the University of California, Santa Barbara, have discovered that a single, new growth factor not only supports massive growth of human embryonic stem cells (hESCs) in vitro, but also maintains them in a nearly 100 percent undifferentiated state without the need for fibroblast "feeder cells."

"This represents a major step forward for potential stem cell therapies as well as in the basic understanding of the mechanisms that regulate stem cell growth and differentiation," the company said in a statement.

The research team, led by Minerva chief scientific officer Dr. Cynthia Bamdad, discovered that a cell surface protein, MUC1, is in an altered form, MUC1*, on pluripotent embryonic stem cells but returns to its normal form when the stem cells begin to differentiate.

This suggests that this receptor may be a pivotal switch in the process of differentiation.

The investigators showed that by adding the growth factor that binds to MUC1* they could expand the hESCs and maintain pluripotency essentially indefinitely, yet commence differentiation

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upon removal of the factor.

“Given the extreme difficulty of isolating pure primitive human stem cells and amplifying them, these studies represent a big step forward for human stem cell research and the future of stem cell transplantation,” said Kenneth S. Kosik, M.D., a professor of neuroscience at UC Santa Barbara and a co-author on the paper.

In a research article published earlier this year (“A Minimal Fragment of MUC1 Mediates Growth of Cancer Cells”, *PLoS ONE* 3(4): e2054 doi:10.1371/journal.pone.0002054), the company reported that MUC1 exists in the same altered form, MUC1*, on over 75 percent of human cancers.

An emerging theory in cancer research is that cancer may be caused by a stem cell mechanism that has gone awry.

Until now, parallels between stem cell

growth and cancer growth have largely been speculative.

The present study provides evidence of a fundamental growth mechanism that mediates the growth of both cancer cells and embryonic stem cells.

The hunt for a stem cell mechanism that is “hijacked by cancer cells” was a challenge because it involved a molecular change that was only apparent when “viewed” using Minerva’s proprietary nanoparticles.

The new study, “MUC1* Mediates the Growth of Human Pluripotent Stem Cells” (<http://dx.plos.org/10.1371/journal.pone.0003312>), was published October 3 in the journal *PLoS ONE*.

Minerva is focused on a next generation novel nanoparticle platform. Minerva has more than 100 nanotechnology patents or patent applications filed with U.S. and worldwide rights reserved.

The company’s intellectual property covers a wide range of uses for its nanoparticle systems in fields as diverse as drug discovery, proteomics, opto-electronics and nano-scale biosensors.

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Reversible 3-D Cell Culture Gel Invented

Singapore’s Institute of Bioengineering and Nanotechnology (IBN) said on September 28 that its scientists have invented a unique user-friendly gel that can liquefy on demand, with the potential to revolutionize three-dimensional (3D) cell culture for medical research.

As reported in *Nature Nanotechnology* (Y.S. Pek, A. C. A. Wan, A. Shekaran, L. Zhuo and J. Y. Ying, “A Thixotropic Nanocomposite Gel for Three-Dimensional Cell Culture”), IBN’s novel gel media has the unique ability to liquefy when it is subjected to a moderate shear force and rapidly resolidifies into a gel within one minute

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Stem Cell Lab World

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Published 24 times a year
 DataTrends Publications, Inc., P.O. Box 4460
 Leesburg VA 20177-8541 USA
 Phone: 703-779-0574
 Fax: 703-779-2267
 Subscription: US\$195.00
 Advertiser subscription: US\$395.00
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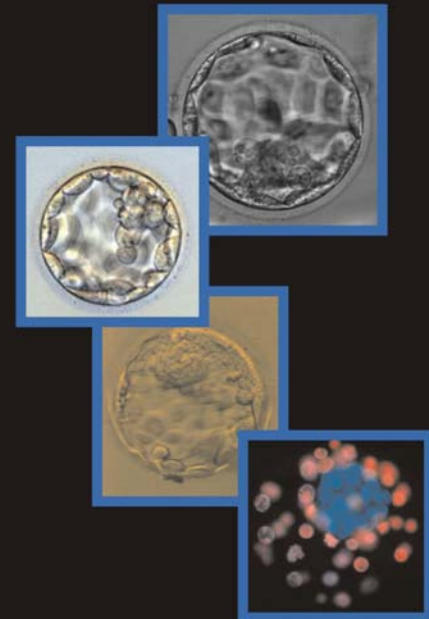
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upon removal of the force.

This phenomenon of reverting between a gel and a liquid state is known as thixotropy.

IBN's thixotropic gel is synthesized from a nanocomposite of silica and polyethylene glycol (PEG) under room temperature, without special storage conditions.

This novel material facilitates the safe and convenient culture of cells in 3D since cells can be easily added to the gel matrix without any chemical processes.

"Cell culture is conventionally performed on a flat surface such as glass slides," said IBN Executive Director Jackie Y. Ying, Ph.D. "It is an essential process in biological and medical research, and is widely used to process cells, synthesize biologics and develop treatments for a large variety of diseases.

"Cell culture within a 3D matrix would better mimic the actual conditions in the body as compared to the conventional 2D cell culture on flat surfaces. 3D cell culture also promises the development of better cell assays for drug screening."

Another key feature of IBN's gel is the ease with which researchers can transfer the cultured cells from the matrix by pipetting the required amount from the liquefied gel.

Unlike conventional cell culture, trypsin is not required to detach the cultured cells from the solid media.

As trypsin is an enzyme that is known to damage cells, especially in stem cell cultures, the long-term quality and viability of cells cultured using IBN's thixotropic gel would improve substantially without the exposure to this enzyme.

Researchers are also able to control the gel's stiffness, thus facilitating the differentiation of stem cells into specific cell types.

"Ways to control stem cell differentiation are important as stem cells can be differentiated into various cell types. Our gel can provide a novel method of studying stem cell differentiation, as well as an effective new means of introducing biological signals to cells to investigate their effect in 3D cultures," said Shona Pek, IBN Research Officer.

"Another interesting property of the gel is its ability to support the extracellular matrix (ECM) secretions of cells. Gel stiffness is modulated by ECM secretions, and can be used to study ECM production by cells responding to drug treatments or disease conditions," said Andrew Wan, Ph.D., principal research scientist said. "The thixotropic gel may then provide new insights for basic research and drug development."

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Student Designs Chromosomal Analysis Tool

A college student has invented a tool to ease challenges of chromosomal analysis, which involves research using genes, embryo, clone and stem cells to help diagnose medical conditions.

"It's hard to be consistent, efficient, and produce quality results when dropping chromosomes on a slide by hand," said Yunyan Qu, a physician assistant student at Central Michigan University (Mount Pleasant, Mich.) and inventor of the tool. "My professors at CMU taught me the importance of accuracy and have pushed me to think more innovatively."

And that is what led Qu to invent this much-needed tool, which enables a technician to drop chromosomes exactly where they need to be on a slide. It also produces more efficient results because the angle is always accurate, and it's flexible to allow a change of degree, spot location or height.

Lab technicians can easily be trained to use the tool, which creates even more efficiency



Yunyan Qu

(Continued on page 5)

in the lab as a whole.

Once a scientific supply company purchases rights to the tool, it will be widely distributed.

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Basic Research

Japanese Researcher Eliminates Viral Vector In Stem Cell Reprogramming



Shinya Yamanaka

Japanese stem cell researcher Shinya Yamanaka, M.D., Ph.D., has taken another step forward in improving the possibilities for the practical application of induced pluripotent stem (iPS) cell technology.

Previously, Dr. Yamanaka of Kyoto University and the Gladstone Institute of Cardiovascular Disease (GICD) showed

that adult cells can be reprogrammed to become embryonic stem cell–like using a cancer-causing oncogene as one of the four genes required to reprogram the cells, and a virus to transfer the genes into the cells.

In the last year, Yamanaka and other labs showed that the oncogene, *c-Myc*, is not needed.

However the use of viruses that integrate into the genome prohibit use of iPS cells for regenerative medicine because of safety concerns: its integration into the cell's genome might activate or inactivate critical host genes.

Yamanaka's laboratory has now eliminated the need for the virus.

In a report published in *Science*, he and colleagues showed that the critical genes can be effectively introduced without using a virus.

The ability to reprogram adult cells into

iPS cells without viral integration into the genome also lays to rest concerns that the reprogramming event might be dependent upon viral integration into specific genomic loci that could mediate the genetic switch.

“The iPS field and stem cell research in general is progressing rapidly,” said GICD Director Deepak Srivastava, M.D.. “But, as Shinya has shown, each step forward reveals a new set of challenges.”

Yamanaka's team began this series of experiments by replacing the retrovirus with an adenoviral vector.

While transfections with the genes on separate vectors didn't work, they did work when the genes were arranged in a specific order on a single vector.

The same arrangement worked when the genes were incorporated into a plasmid.

To determine if the plasmid-mediated reprogrammed cells were pluripotent, the scientists transplanted the cells under the skin of immunocompromised mice.

The resulting tumors contained a wide variety of cell types from all three germ layers. iPS cells injected into embryos resulted in chimeric mice with the injected cells contributing to almost all cell types.

Still, other problems remain to be solved.

The efficiency of the gene transfer with the plasmid was lower than with the retrovirus.

Nevertheless, this significant step moves us closer to realizing the promise of stem cells in the understanding and eventual cure of diseases.

Citation: Okita K, Nakagawa M, Hyenjong H, Ichisada T, Yamanaka S. “Generation of mouse induces pluripotent stem cells with viral vectors.” *Science*, in press.

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Study Unlocks Stem Cell, DNA Secrets



David M. Gilbert

Florida researchers have discovered that as embryonic stem cells turn into different cell types, there are dramatic corresponding changes to the order in which DNA is replicated and reorganized.

The groundbreaking study, led by a molecular biologist at Florida State University (Tallahassee), bridges a critical knowledge gap for stem cell biologists, enabling them to better understand the enormously complex process by which DNA is repackaged during differentiation: when embryonic stem cells, jacks of all cellular trades, lose their anything-goes attitude and become masters of specialized functions.

As a result, scientists now are one significant step closer to the central goal of stem cell therapy, which is to successfully convert adult tissue back to an embryo-like state so that it can be used to regenerate or replace damaged tissue.

Such therapies hold out hope of treatments or cures for cancer, Parkinson's disease, multiple sclerosis, spinal cord injuries and a host of other devastating disorders.

Using mouse and human embryonic stem cells, FSU researchers employed advanced imaging techniques and state-of-the-art genomics technology to demonstrate, with unprecedented resolution along long stretches of chromosomes, which sequences are replicated first, and which occur later in the process of differentiation.

"Understanding how replication works during embryonic stem cell differentiation gives us a molecular handle on how information is packaged in different types of cells in manners characteristic to each cell type," said David M. Gilbert, the study's principal investigator. "That handle will help us reverse the process in order to engineer different types of cells for use in disease thera-

pies."

Results from the FSU study, which includes contributions from researchers at three other institutions, are described in a paper published in the October 7 edition of *PLoS Biology*, a peer-reviewed journal that showcases biological science research of exceptional significance.

The current paper ("Global Reorganization of Replication Domains During Embryonic Stem Cell Differentiation") is focused solely on results observed in the mouse embryonic stems cells.

Data on the human cells will be detailed in a future report.

"We know that all the information (DNA) required to take on the identity of any tissue type is present in every cell, because we already can, albeit very inefficiently, create whole animals from adult tissue through cloning," Gilbert said. "We also can make a kind of artificial embryonic stem cells, called induced pluripotent stem cells, out of many adult cell types, but there are two major hurdles remaining. First, the methods currently used rely on the unnatural retroviral insertion of genes into patients' cells, and these genes are capable of forming tumors. Second, this method is very inefficient as well because only one in 1,000 cells into which the genes are inserted becomes pluripotent. We must learn how cells lose pluripotency in the first place so we can do a better job of reversing the process without risks to patients.

"The challenge is, adult cells are highly specialized and over the course of their family history over many generations they've made decisions to be certain cell types rather than others. In doing so, they have tucked away the information they no longer need on how to become other cell types. Hence, all cells contain the same genetic information in their DNA, but during differentiation they package it with proteins into 'chromatin' in characteristic ways that define each cell type. The rules that determine how cells package DNA are complicated and have been difficult for scientists to decipher."

But, Gilbert noted, one time that the cell

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“shows its cards” is during DNA replication.

“During this process, which was the focus of our FSU research, it’s not just the DNA that replicates,” he said. “All the packaging must be replicated as well in each cell division cycle.”

Embryonic stem cells have many more, smaller “domains” of organization than differentiated cells, and it is during differentiation that they consolidate information.

“In fact, ‘domain consolidation’ is what we call the novel concept we discovered,” he said.

Gilbert likened the concept of domain consolidation to the undeclared or “undifferentiated” college student who then consolidates her literature resources during the course of declaring a major and specialization.

“From a student with books on all subjects on all of her bookshelves comes a student who has placed all texts pertaining to her major on the eye-level shelf and moved the distantly-related, potentially distracting texts to the hard-to-reach bottom or top shelves,” he said.

“Now, our challenge as scientists,” said Gilbert, “is to build on what we’ve learned about domain consolidation so that we can efficiently and safely create patient-specific induced pluripotent stem cells or even coax the body’s cells to change their specialization in response to medications.”

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Time Of Day Influences Yield For Stem Cell Mobilization

A new study uncovers a previously unrecognized, species-specific impact of circadian rhythms on the production of mobilized stem cells.

The research suggests that when it comes to collecting human stem cells for clinical transplantation, picking the right time of day to harvest cells may result in a greater yield.

A variety of organisms have evolved an endogenous timing system, called a circadian clock, to regulate metabolic activities in a day/night cycle.

In mice, the cells that give rise to mature blood cells, called hematopoietic stem cells (HSC), are regulated under the influence of rhythmic circadian signals that influence expression of *Cxcl12*, a gene involved in white blood cell migration.

“Previous research has shown that the “sympathetic” branch of the nervous system, which is involved in stress responses, tightly regulates the amount of *Cxcl12* expressed in the bone marrow by circadian oscillation of noradrenaline release. Blood stem cell patterns are basically the mirror image of *Cxcl12* expression in bone marrow,” said lead study author, Dr. Paul S. Frenette from the Mount Sinai School of Medicine.

Frenette and colleagues were interested in examining whether circadian time continues to influence mobilization of HSCs when mice are treated with granulocyte-colony-stimulating factor (G-CSF), the most common stem cell mobilizer used in the clinic.

The researchers found that after stimulations with G-CSF, synchronization of blood collection with the peak circadian time produced greater HSC recovery.

Therefore, even when pharmacological manipulation is used to stimulate HSC mobilization, circadian clock genes continue to influence yield.

The researchers also demonstrated the existence of significant oscillations in the number of human HSCs and found that the circadian rhythm in humans is inverted when compared to that of the mouse.

An examination of healthy donors who were contributing HSCs for bone marrow transplantation at Mount Sinai Medical Center between the years of 2000 and 2006 revealed that the average yield was greater for those who underwent the procedure in the afternoon compared with those who were harvested in the morning.

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“Our results suggest that the human HSC yield for clinical transplantation might be greater if patients were harvested during the evening compared to the morning,” Frenette said. “Although prospective clinical studies are needed to ascertain the optimal time for HSC collection, it is possible that a simple adjustment in the collection time may have a significant clinical impact. Further, the maximum release of HSCs at the beginning of the rest period for both species (early night for humans, early morning for mice), supports the intriguing possibility that this phenomenon may contribute to regeneration.”

The study was published in the October 9 issue of the journal *Cell Stem Cell*.

Citation: Lucas et al.; “Correspondence: Mobilized Hematopoietic Stem Cell Yield Depends on Species-Specific Circadian Timing;” *Cell Stem Cell* 3, October 9, 2008. DOI 10.1016/j.stem.2008.09.004

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Researchers Uncover Key Mechanism Regulating Neural Stem Cell Development

A Canadian research team has discovered a novel mechanism that regulates how neural stem cells of the retina generate the appropriate cell type at the right time during normal development.

These findings, published by scientists at the Institut de recherches cliniques de Montreal (IRCM, Montréal in *Neuron*, could influence the development of future cell replacement therapies for genetic eye diseases that cause blindness.

In their report, the scientists show that a gene called *Ikaros* is expressed in the most immature retinal stem cells in the mouse, which are “competent” to generate all seven different cell types that compose the retina.

But this gene is not expressed in the “older” stem cells, which are more restricted in their differentiation potential and produce only the late-born neurons.

“By studying the retina of a mouse in which the *Ikaros* gene was inactivated, we found that the generation of early-born retinal cell types was impaired, whereas the generation of the late-born retinal cell types was not affected,” said Dr. Michel Cayouette who led the study.

In contrast, forcing the expression of *Ikaros* in older retinal stem cells, which have normally turned off its expression, was sufficient to give back the competence to these cells to generate early-born neurons.

Overall, these results indicate that the expression of *Ikaros* in retinal stem cells is both necessary and sufficient to confer the competence to generate early-born retinal neurons.

The identification of adult retinal stem cells in recent years has opened up the possibility that such cells could one day be used to replace damaged or lost cells in various retinal diseases such as glaucoma, macular degeneration or retinitis pigmentosa.

For such approaches to be effective, however, it is crucial that stem cells generate only the appropriate cell type for a particular condition.

This study suggests that it may be possible to manipulate the competence of retinal stem cells so that they only generate retinal cells associated to a particular temporal stage.

“For example,” Cayouette said, “inactivating *Ikaros* could favor the production of later-born neurons such as photoreceptors, which are lost progressively in retinal degenerative diseases.”

Future studies will be required to assess the usefulness of this approach for potential cell replacement therapies.

Cayouette is director of the cellular neurobiology research unit at the IRCM and associate researcher at the Université de Montréal.

The research was funded by the Foundation Fighting Blindness – Canada and the Canadian Institutes of Health Research (CIHR),

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Citation: Jimmy Elliott, Christine Jolicoeur, Vasanth Ramamurthy, and Michel Cayouette. (2008), "Ikaros confers early temporal competence to mouse retinal progenitor cells," *Neuron* Volume 60 October 9, 2008, 26-39.

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Scientists Shed Light On The Puzzle Of Stem Cell Division

New research by Austrian scientists sheds fresh light on the central question of developmental biology: how a single fertilized egg can divide repeatedly to produce multiple different cell types.

Publishing in this week's issue of the journal *Cell*, Jürgen Knoblich's group at the Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA) in Vienna say their findings are likely to be highly relevant to the development of cancer in humans.

It had previously been established that asymmetric cell division is extremely important in determining cell fates.

Asymmetric cell division occurs when a molecule is inherited by only one of the two cells that arise following cell division (mitosis).

The process can be compared to a children's puzzle in which a sphere containing a number of differently colored balls on either side of a divide is shaken until all the balls of one color are together on one side, with all the balls of the other color on the other side.

With a little patience most schoolchildren can manage this.

But cells have a much more difficult task: they must ensure that all the "balls" (in reality proteins that control or affect various intracellular processes) are segregated at the appropriate time, so that the cells divide to produce offspring that differ substantially from each other.

Only in this way can a single cell divide repeatedly to give rise to the complicated organism that is man – or the fruit fly *Drosophila melanogaster*.

The principle of asymmetric cell division may be simple but how it occurs has been taxing the minds of biologists for generations.

About fifteen years ago there was a major advance, when a system to investigate the process was discovered.

In particular cells (sensory organ precursor cells or SOP cells) of the fly the so-called "Numb" protein is segregated into only one of the two daughter cells that result from cell division.

This groundbreaking discovery was made in the lab of Lily and Yuh Nung Jan at the University of California at San Francisco (UCSF) and Knoblich was one of the scientists involved.

When he left UCSF he was determined to understand the underlying mechanism and he took up a position at the Research Institute of Molecular Pathology (IMP) in Vienna with this goal clearly in mind.

The infrastructure at the IMP and its partner-institute IMBA, to which Knoblich moved in 2004, enabled a wide range of methods to be brought to bear on the problem.

Knoblich has been studying Numb localization by means of a uniquely multidisciplinary approach, combining genetics and biochemistry with a recently developed method for visualizing live flies.

He is enthusiastic about the facilities at the two institutes in Vienna.

"There's a whole range of techniques set up here and all of them are freely available to everyone," he said. "The live imaging method was especially important - without it our experiments would simply not have been possible."

Some time ago, Knoblich and others showed that the protein "Lethal giant larvae" (Lgl) was involved, as were two protein kinases, named aPKC and Aurora-A (AurA).

Protein kinases are proteins that chemically modify (phosphorylate) other proteins and are known to have key roles in the control and

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coordination of a large number of cellular processes.

aPKC was known to phosphorylate Lgl, while Aur-A was known to be switched on at the start of cell division and to be required for Numb activity, which gave a clue that it might be involved in Numb's asymmetric segregation.

Knoblich has now shown that AurA phosphorylates a further protein known as Par-6, which causes activation of the kinase aPKC and thus phosphorylation of Lgl. When Lgl is phosphorylated it no longer binds to a multiprotein complex known as "Par" and Par is free to bind a further protein, fascinatingly termed "Bazooka."

In other words, when AurA is activated, the entire Par complex is remodeled.

Knoblich went on to prove that, unlike the initial, Lgl-bound form, the remodeled Par complex is able to phosphorylate the Numb protein.

When Numb is phosphorylated it no longer binds to the complex but is released and because it only moves slowly through the cell cortex it is localized in a very precise way.

Taken together, Knoblich's results have identified a chain of interactions among the various proteins required for restricting Numb's localization.

The activation of the AurA kinase at the start of cell division leads inexorably to the segregation of Numb to only one of the two daughter cells that result from mitosis. Our schoolchildren now only have to press a button to cause all the balls of one color to go automatically to one side of the divide in the cell.

These results on the fruit fly are likely to turn out to have important ramifications in human medicine.

Many of the components involved in asymmetric cell division in fly cells have homologues (counterparts) in humans and the segregation of molecules during mitosis in cultured human cells seems to be controlled in a highly similar manner.

The molecular mechanism responsible for regulating asymmetric cell division in *Drosophila* may thus control self-renewal and prevent tumor formation in other types of stem cell.

Mutations in the fly numb gene have been

shown to lead to the formation of brain tumours, and a permanently active form of aPKC has a similar effect.

The human Numb homologue is known to act as a suppressor of breast cancer, whereas the Lgl homologue has been linked to metastasis of colon carcinomas.

The potential implications of Knoblich's latest results for human therapy are thus enormous, although Knoblich stresses that they lie well in the future.

"The idea that we might be able to develop drugs to prevent cell division from getting out of control is extremely appealing but we all now how long it takes for drugs to come on the market even when the idea seems so good," Knoblich said.

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Licensing

Hamilton Thorne Granted Exclusive Rights To Intelligent Monitoring System

Beverly, Mass.-based Hamilton Thorne, Inc. said on October 7 that it has finalized an OEM partnership agreement with KD Secure, Inc., (Cambridge, Mass.) giving Hamilton Thorne exclusive rights to manufacture, market and distribute the intelligent monitoring technology developed by KD Secure within the fields of regenerative medicine and transgenic research.

To be marketed under the trade name HAWK-i, the intelligent monitoring system provides researchers with a Control and Command Center to oversee all aspects of the laboratory, including the ability to remotely check experiments or facility security from the included iPhone or any Web-enabled device.

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In addition, automatic alerts are sent when specific conditions are identified so staff may intervene as needed to maintain the integrity of the experiment or ensure laboratory and animal security.

“The ability to view remotely the status of tissue engineering growths and stem cell cultures and to be proactively alerted to unwanted cellular changes gives researchers unprecedented control over experimental outcomes,” said Meg Spencer, CEO of Hamilton Thorne. “With the HAWK-i, researchers now have a ‘safety net’ that can catch early-stage changes in cells and allow preventive measures to be taken immediately.”

Contact: <http://www.hamiltonthorne.com>

Contact: <http://www.kdsecure.com>

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Moraga Announces Licensing Agreement With Pharmacells

Los Angeles, Calif.-based Moraga Biotechnology Corporation, an adult stem cell company, said on October 8 that it has licensed its blood-derived Blastomere-Like Stem Cells (BLSCs) with Pharmacells, Ltd. (Glasgow, Scotland).

The licensing agreement provides Pharmacells access to Moraga’s proprietary adult stem cell technology for banking its BLSCs that have been isolated, processed, and cryopreserved from the blood of individuals.

Moraga’s scientists have found that its BLSCs are able to differentiate into most tissues and organs of the body.

“The potential for their proprietary technology is immense, and together with Moraga we are certain that we will be able to make significant progress and introduce BLSCs as a new and better way to research and use adult stem cells,” Pharmacells’ managing partner Neil R. Fell said.

Fell also said Moraga’s BLSCs, which will be banked in their facility, can be used in the clinic for treating a plethora of human diseases such as heart attacks, chronic obstruction pulmonary dis-

ease, Parkinson’s disease and stroke in the near future.

Contact: <http://www.moragabiotech.com>

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Grants & Contracts

ZenBio Awarded NIH Grant For Skeletal Muscle Program

Research Triangle Park, N.C.-based ZenBio, Inc. said on September 28 that it has been awarded a Phase II SBIR grant to commercialize their primary human skeletal myocyte and adipocyte co-culture system.

The \$1.38 million award from the National Institutes of Health will fund the continued optimization and commercial development of this unique tool for type 2 diabetes and obesity research.

Skeletal muscle and adipose tissue are the body’s major doorways for insulin-stimulated glucose disposal and are the sites of insulin resistance in obese individuals.

“We still do not know much about the interplay between these two tissues as insulin resistance progresses to diabetes and its related complications”, said Renee Lea-Currie, Ph.D., ZenBio’s director of cell biology.. “We have seen profound effects on skeletal muscle cell metabolism when muscle cells are cultured along with adipocytes from obese donors. This grant will allow us to continue investigating these interactions and the complex mechanisms involved in the development of type 2 diabetes.”

“We are excited to move forward into the commercial development phase for this program”, said ZenBio’s Ben Buehrer. “Investigating the interactions between different cell types involved in obesity related diseases is extremely difficult. We hope to reduce some of the difficulty by providing a customizable co-culture system for researchers to use. This grant will allow us to opti-

(Continued on page 13)

mize and validate the cell system in much greater detail.”

The company said that frees up time and money for researchers to focus on using the system to discover novel treatments and therapeutics for type 2 diabetes and metabolic disease.

ZenBio provides research tools for the study of human metabolic disease.

The company performs contract research for major pharmaceutical and biotechnology companies around the world.

Contact: <http://www.zenbio.com>

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Briefly Noted

High-Performance Bio-Coatings Available For Co-Development, Licensing

Denver, Colo.-based Accelr8 Technology Corporation (AXK) said last month that two teams of university research collaborators reported new methods for scalable production with the company’s patented OptiChem bio-coatings.

Advanced cell culturing methods for cancer and stem cell research could use patterned surfaces in microfluidic devices to enhance analysis of specific biological properties.

Accelr8 hopes to attract commercial partners for markets that would benefit from such selective patterning innovations.

Led by Dr. David Grainger at the University of Utah, researchers from the University of Utah, the University of Washington, and Accelr8 developed production-scalable methods to make OptiChem surface micro-patterns for live-cell and biomolecular attachment.

The new study overcame the technical obstacles that have limited previous high-performance, patterned bio-coatings to laboratory-scale fabrication.

Examples of potential applications include cell patterning for candidate molecule screening in drug development, and tissue generation for regenerative medicine.

Patterned coatings also offer new opportunities

for innovative bio-sensor designs that can use live cells as sensing elements for multiplexed diagnostic devices.

Implanted medical devices can benefit from coatings that have selective properties to spatially select or promote tissue ingrowth, or prevent tissue adhesion, or to inhibit bacterial seeding that can develop into an infection.

To demonstrate the coating’s success, the scientists allowed live mammalian cells to self-select and attach to activated capture zones that alternated with inert zones in target micro-patterns.

Adherent cells grew and behaved normally for many days, and remained selectively confined to the capture zones. The inert regions blocked encroachment by growing cells, and prevented bio-fouling by cellular byproducts and serum-based culture media.

Contact: <http://www.accelr8.com>

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European Mark for Bone Marrow Collection System

Menlo Park, Calif.-based StemCor Systems, Inc., said last month that it has received the CE (Conformite European) Mark for its MarrowMiner System, a minimally invasive device used to harvest adult stem cells from the ilium (pelvis).

According to the company, the device represents next-generation technology for use in bone marrow transplants, for accelerating bone healing in spinal fusions and other orthopedic procedures, and an expanding array of clinical applications utilizing bone marrow-derived cells.

The CE Mark indicates that the product complies with the appropriate quality and safety standards to be commercialized in the EU, and furthers StemCor’s goal of becoming a global company.

The MarrowMiner System is designed to rapidly and easily harvest bone marrow in a minimally invasive manner, in the outpatient setting, and without general anesthesia.

The System consists of an access guide, a powered handle that drives a flexible atraumatic shaft through which marrow is aspirated, and an integrated marrow collection container.

The MarrowMiner shaft gains access to the

(Continued on page 14)

bone marrow cavity through the access guide to allow the removal of bone marrow through a single entry site.

This is in contrast to the current practice of bone marrow aspiration through the insertion of a needle into multiple sites in the iliac crest of the hip, which usually requires general anesthesia, an operating room, and multiple clinical personnel.

Preclinical and recent clinical studies demonstrated the ability of the MarrowMiner to safely harvest marrow with significantly higher stem cell activity than is contained in standard needle aspirates.

Contact: <http://www.stemcoursystems.com>

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InVitria's Cellastim Mentioned In Journal Article

Fort Collins, Colo.-based InVitria said on October 7 that a study published in the scientific journal *Nature* examining embryonic stem (ES) cell self-renewal reported that the company's Cellastim (recombinant human serum albumin) was an effective replacement to bovine serum albumin in ES cell culture.

The article entitled, "The ground state of embryonic stem cell self-renewal," said that researchers used Cellastim as a recombinant albumin in place of animal-derived serum to eliminate contaminants in the cell culture.

The Cellastim was a contributing factor in the enhancement of bulk passaging and clonal propagation.

"This study further supports the use of InVitria's Cellastim as an enhancement to cell culture media," said InVitria President Scott Deeter. "Cellastim is the only supplement available that not only improves cell culture performance, but does so while maintaining a defined and animal free media."

InVitria has developed cell culture ingredients that enhance productivity, safety and time to market for companies in the biopharmaceutical, cell culture, regenerative medicine, life science research and diagnostics industry.

Cellastim is used to enhance cell growth and productivity.

It is animal component free and has been used as a cell culture ingredient in regenerative medicine, mammalian cell culture media, stem cell media and primary cell media.

Citation: Ying, Q.L., et al. "The ground state of embryonic stem cell self-renewal." *Nature* 453, 519-524 (May 2008).

Contact: <http://www.InVitria.com>

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Genome Institute Of Singapore Purchases Genome Analyzers For Stem Cell Research

San Diego, Calif.-based Illumina, Inc. (ILMN) said on October 9 that the Genome Institute of Singapore (GIS), a flagship institution of Singapore and one of the top research centers in the world, has purchased four additional Genome Analyzers taking its installed base to six.

Among researchers at GIS, the Genome Analyzer continues to be the preferred platform for conducting sequencing studies, the company said.

The Genome Analyzers will be used in a variety of projects, including the construction of transcriptional networks linked to cancer and stem cells.

"We will use it across a broad array of applications including construction of transcriptional networks through identifying transcription factor interactions and chromatin modifications in stem cells and cancer cells, characterization of genome and transcriptome variations in healthy and patient samples, and discovery of new pathogens through metagenomic sequencing," said Dr. Ruan Yijun, associate director of genome technology at GIS said. "This expansion of our sequencing capacity is necessary for us to deliver high impact discoveries through our innovative PET sequencing platform."

PET, or the Pair-End-diTag technology, is a new approach developed by researchers at GIS to study genome structures and functions.

In October 2007, the National Human Genome Research Institute (NHGRI) and the National Cancer Institute (NCI) awarded GIS US\$3M grants to further advance the PET technology for human genome annotation and to identify complete fusion genes that function as oncogenes, or cancer-causing genes.

Illumina markets next-generation life-science tools and integrated systems for the analysis of genetic variation and biological function.

Contact: <http://www.illumina.com>

(Continued on page 15)

Invitrogen Redesigns GIBCO Media Bottles

Carlsbad, Calif.-based Invitrogen Corporation (IVGN) said on October 8 it has redesigned its GIBCO cell culture media bottles.

The new bottle design has an angled neck for easier pipetting and pouring; compact form for improved handling and storage; and a wider mouth to reduce the chance of contact with the pipette.

Contact: <http://www.invitrogen.com/gibcobottle>

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510(k) Clearance for Cell-Freeze Cryogenic Storage Containers

Manchester, Ct.-based Lydall, Inc.'s (LDL) Charter Medical, Ltd. said on October 7 that it has received 510(k) clearance for its Cell-Freeze cryogenic storage containers designed for peripherally derived stem cell applications.

The U.S. Food and Drug Administration (FDA) issuance of 510(k) clearance allows the company to begin selling the product.

Cell-Freeze is used for cryogenic temperature applications as low as -196 degreesC for storage, preservation and transfer.

Contact: <http://www.chartermedical.com>

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