



- Advanced lab & stem cell technologies
- New products: Culture media, reagents, etc.
- New research equipment & devices
- Research services
- National stem cell policy
- Law & litigation

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Editor's Note: This is the last issue of *Stem Cell Lab World* for 2011. Our next issue, Vol. 6, No. 1, will be published January 16, 2012. Happy Holidays!

hESC Supply & Demand

Forty Percent Of Scientists Report Delays In Obtaining Human Embryonic Stem Cells

A survey conducted in 2010 of more than 200 human embryonic stem cell researchers in the United States found that nearly four in ten researchers have faced excessive delay in acquiring a human embryonic stem cell line and that more than one-quarter were unable to acquire a line they wanted to study.

“The survey results provide empirical data to support previously anecdotal concerns that delays in acquiring or an inability to acquire certain human embryonic stem cell lines may be hindering stem cell science in the United States,” said Aaron Levine, an assistant professor in the School of Public Policy in the Ivan Allen College of Liberal Arts at the Georgia Institute of Technology.

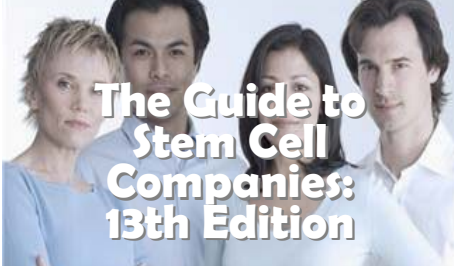
Levine administered the Web-based survey in November 2010 to more than 1,400 stem cell scientists working at U.S. academic and nonprofit medical research institutions.

Almost 400 respondents from 32 states completed the survey. Of those, 205 respondents reported using human embryonic stem cells in their research, and their responses were used in this study.

Scientists cited four main reasons for their problems accessing human embryonic stem cell lines: difficulty obtaining material transfer agreements, failure to acquire research approval from internal institutional oversight committees, cell line owners that were unwilling

(Continued on page 2)

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to share and federal policy considerations.

“Bureaucratic challenges may be inevitable in this ethically contentious and politically sensitive field, but policymakers should attempt to mitigate these issues by doing things like encouraging institutions to accept third-party ownership verification and providing clearer guidance on human embryonic stem cell research not eligible for federal funding,” said Levine.

The broad patents assigned to the initial inventors of the method used to isolate embryonic stem cells and numerous narrower patents claiming specific human embryonic stem cell-related techniques are also factors complicating access to human embryonic stem cell lines, Levine said.

Asked how many of the more than 1,000 existing human embryonic stem cell lines they used, 76 percent of the scientists reported using three or fewer lines; 54 percent reported using two or fewer lines in their research.

Stem Cell Lab World

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Production Assistants: Hal Leberry, Kimba Singer

Published 24 times a year
 DataTrends Publications, Inc., PO Box 3221
 Leesburg VA 20177-9093 USA
 Phone: 571-313-9916
 Fax: 703-771-9091
 Subscription: US\$345.00
 Site license (single site): \$1,475.00
 info@stemcellresearchnews.com
 http://www.stemcellresearchnews.com

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More than half of the 130 respondents cited access issues as a major reason they chose to use specific cell lines in their research.

“These results illustrate that many human embryonic stem cell scientists in the United States are not conducting comparative studies with a diverse set of human embryonic stem cell lines. That raises concern that at least some results are cell-line specific rather than broadly applicable,” Levine said. “Federal and state funding agencies may want to consider encouraging research using multiple diverse human embryonic stem cell lines to improve the reliability of research results.”

Embryonic stem cell lines are being used to develop new cellular therapies for various diseases, to screen for new drugs and to better understand inherited diseases. It’s crucial that diverse lines are available for this research to ensure that all individuals benefit from the results.

While availability was cited as the most common factor affecting scientists’ choices regarding which cell lines to use, other considerations included suitability for a specific project, familiarity with specific lines, a desire to reduce complications in the laboratory, cost, the extent of relevant literature and the preferences of scientists’ colleagues.

Three of the initial human embryonic stem cell lines derived at the University of Wisconsin in the late 1990s were the lines most commonly used by respondents. Cell lines H1, H9 and H7 were used by 79, 68 and 26 percent of respondents, respectively.

Scientists also reported using more than 100 other lines, but each of these was used by fewer than 12 percent of respondents.

“Other research communities in the life sciences have experienced material access problems and they addressed them, in part, by creating centralized information and data sharing hubs, including public DNA sequence databases, tissue banks and mouse repositories. The stem cell research community has taken promising steps in this direction, but this analysis should encourage the community to continue and, if possible, accelerate these efforts,” Levine said.

(Continued on page 3)

Results of the survey were published in the December issue of the journal *Nature Biotechnology*. Funding for the study was provided by the Kauffman Foundation's Roadmap for an Entrepreneurial Economy Program.

Citation: "Access to human embryonic stem cell lines;" Aaron D. Levine; *Nature Biotechnology*, Volume 29, Pages 1079–1081, 2011, published online 08 December 2011, DOI: 10.1038/nbt.2029

Abstract:

<http://dx.doi.org/10.1038/nbt.2029>

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BioTime Successfully Completes HyStem-Rx Preclinical ISO 10993 Studies

Alameda, Calif.-based BioTime, Inc. (BTX) announced the successful completion of ISO 10993 biocompatibility studies for HyStem-Rx.

The tests, as prescribed by the International Organization for Standardization for permanent implantable medical devices, are required by the United States Food and Drug Administration and European Union regulatory authorities prior to the initiation of clinical studies in humans. The results of these preclinical studies successfully demonstrated the safety and biocompatibility of HyStem-Rx.

"This is an important milestone in our commercialization effort and brings us closer to offering much-needed products to clinicians and patients around the world, beginning with the large markets in reconstructive and cosmetic surgery," said William P. Tew of BioTime. "Our HyStem technology forms the foundation for unique stem cell delivery products in both the adult and embryonic stem cell marketplace, including products manufactured using BioTime's ACTCellerate technology. Current research at leading medical

institutions has shown that HyStem is compatible with a wide variety of tissue types including brain, bone, skin, neural, cartilage, and heart tissues. Our next milestone will be the completion of manufacture of clinical lots under current good manufacturing practices, and an ISO 13485 certification audit by mid-2012, which will enable the initiation of clinical trials in the European Union by late 2012 with the goal of receiving approval to market HyStem-Rx in the EU for reconstructive and cosmetic surgery in late 2013."

In its first clinical application, HyStem-Rx will be used with autologous adipose cells to restore subcutaneous tissue lost as a result of injury, oncologic resection, or congenital defects. Restoration of the normal skin contour is an important quality-of-life issue, not only in elective cosmetic procedures, but also in reconstructive surgeries needed to repair deformities and traumatic injuries to the face and upper extremities. BioTime's plan is to bring HyStem-Rx to the medical market first in the EU, where the anticipated cost of the clinical trials would be relatively low. Once the use of HyStem-Rx in surgery is established in the EU, BioTime would address an even larger American market where there are approximately 4 million surgical reconstructive procedures performed per year.

HyStem-Rx is a proprietary biocompatible hydrogel that mimics the human extracellular matrix (ECM), a web of molecules surrounding cells that is essential to cellular function. When cells lacking the ECM or an ECM substitute are introduced into the body, they commonly die or fail to function correctly after transplantation. HyStem hydrogels are currently being used by researchers at a number of leading medical schools in laboratory studies of stem cell therapies to facilitate wound healing and for the treatment of ischemic stroke, brain cancer, vocal fold scarring, and cardiac infarct.

"BioTime's HyStem product line is one of four components in our near-term revenue strategy, which also includes Hextend revenues, sales of stem cell research products (including the ACTCellerate cell lines and associated products),

(Continued on page 4)

and planned near-term products being developed by our subsidiary OncoCyte Corporation,” said CEO Michael West. “These, combined with expected long-term revenues from the potentially very large revenue cell-based therapeutic products that are under development at our subsidiaries, provide BioTime with a balanced commercial strategy. The value of this balance is becoming apparent in the regenerative medicine community as competitors whose sole focus is on long-term therapeutic products find it challenging to raise the requisite capital to fund clinical development.”

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

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Advanced Stem Cell Technology

Article Describes Way To Control Differentiation Of Neural Cell Types

AMSBio (U.K.) has written a technical article about a new method to control and direct differentiation of physiologically relevant neural cell types using stem cell qualified reagents.

Stem cells have revolutionized our approaches to and understanding of neuroscience. The key to research success is the ability to control and direct differentiation into physiologically relevant neural cell types.

Controlling cell differentiation in a predictable way is a major challenge in stem cell research. The new method described within the article shows how to differentiate adult neural stem cells and pluripotent ES cells using 3D extracellular matrices and reagents from AMSBio, enabling researchers to gain a valuable insight into the stem cells they are studying.

Contact:

http://www.amsbio.com/brochures/Neuroscience_Tools_AMSBio.pdf

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Scientists Make The Case For Using Pig-Derived Stem Cells Rather Than Rodent Cells

Adult-Cell-Sourced Stem Cells Don't Form Tumors In Pigs

Researchers exploring the use of pigs as a source of stem cells say they have found a better way to determine the safety of future stem cell therapies than using rodent-based models.

Rat and mouse studies are likely inadequate for testing many human therapies, including pharmaceuticals, because 50 percent of all chemicals test positive as carcinogens in rodents regardless of their source or identity, according to Thomas Hartung, a professor in the Bloomsburg College of Public Health at Johns Hopkins University.

Hartung suggests these rodent studies may be no better than a coin toss. For example, some components in coffee appear to be carcinogenic in rodents, but in humans moderate coffee consumption may reduce the risk of cancer.

In 2010, Steve Stice and Franklin West of the University of Georgia introduced 13 pigs that have shown promise in unlocking the path to new therapies. The pigs recently produced another positive finding: adult-cell-sourced stem cells don't form tumors in pigs.

“Pluripotent stem cells have significant potential for stem cell therapies,” said West, an animal science researcher and assistant professor in the UGA College of Agricultural and Environmental Sciences. “However, tests in mice often resulted in tumor formation that frequently led to death.”

The formation of tumors has raised concerns about the safety of induced pluripotent stem cells, or iPSCs, and cells derived from these stem cells. Until now, all iPSC safety studies have been performed in rodent models.

“To address the concern, our research

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team studied tumor formation in pigs generated from pig iPSCs,” West said. “Brain, skin, liver, pancreas, stomach, intestine, lung, heart, kidney, muscle, spleen and gonad tissues from all 11 pigs tested showed no evidence of tumors.”

The absence of tumor formation in these pigs suggests that iPSCs can safely incorporate into tissues without tumor formation.

“Being able to safely use iPSCs without the potential of causing tumors is essential for this promising stem cell therapy to become a viable treatment option,” said Stice, a Georgia Research Alliance Eminent Scholar in the College of Agricultural and Environmental Sciences. “We now have graduate students working on making neural cells from the human and pig stem cells to help further the studies. The human stem cells were effective in a rodent model for stroke, but rodent studies are not rigorous enough to start human clinical trials.”

“Over 700 drug treatments have gone to human clinical trials for stroke alone based on findings in rodents and have turned out not to be viable in humans,” West said. “The pigs are much more human like, and they are going to be a much better model to study strokes.”

West is leading a cooperative project between the UGA Regenerative Bioscience Center and stroke researchers at Georgia Health Sciences University.

“This project will improve the speed and efficiency of treatment development for stroke and many other conditions and potentially reduce the number of nonhuman primates used in research,”

**NOTE: Archived content on
StemCellResearchNews.com**

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he said.

Additionally, Stice and West have now bred the pigs produced from iPSCs and have proven the stem cells did pass to the offspring. This finding opens the door for better animal-sourced tissue for human regenerative medicine such as islet cells that produce insulin for diabetic patients.

Using iPSC technology, the UGA Regenerative Bioscience Center is working with researchers at Emory University to make pigs whose cells from the pancreas would demonstrate decreased rejection in human treatments.

“The next step would be to put these pig insulin-producing cells into other animals, potentially dogs or cats suffering from diabetes, to see if it will produce insulin for them without being rejected,” Stice said. “So, it’s moving forward. Never as fast as we like, but it’s moving.”

Citation: “Brief Report: Chimeric Pigs Produced from Induced Pluripotent Stem Cells Demonstrate Germline Transmission and No Evidence of Tumor Formation in Young Pigs;” Franklin D. West, Steven L. Stice et al.; *Stem Cells*, 2011; 29 (10): 1640 DOI: 10.1002/stem.713

Abstract:

<http://dx.doi.org/10.1002/stem.713>

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Animal-Free Reagents Used To Create Clinical Grade Neurons From Skin Cells

Stem cell scientists have taken human skin cells, reprogrammed them to be pluripotent and then differentiated them into neurons, using animal origin-free reagents and feeder conditions throughout the process.

This is the first time scientists have been

(Continued on page 6)

able to derive potentially clinically usable induced pluripotent stem (iPS) cells and differentiate them into neurons in animal origin-free derivation and differentiation conditions using commercially available reagents to facilitate broad application, said Saravanan Karumbayaram, study first author and an associate researcher with the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA.

The Broad center researchers also developed a set of standard operating procedures for the process, so other scientists can benefit from the derivation and differentiation techniques performed under Good Manufacturing Practices (GMP) protocols. GMP protocols are tightly controlled and regulated so the cells created meet all the standards required for use in human beings.

“Developments in stem cell research show that pluripotent stem cells ultimately will be translated into therapies, so we are working to develop the methods and systems needed to make the cells safe for human use,” Karumbayaram said.

Conventionally, stem cells are grown on mouse fibroblast cells, which provide factors the cells need to flourish and grow. However, because animal products are involved, those cells have to be further tested for any contaminating animal-derived products before they can be used in humans.

Karumbayaram tried six different animal-free media formulations before arriving at a composition that generated the most robust pluripotent stem cells. He combined two commercial media solutions to create his own mix and tried different concentrations of an important growth factor.

“The colonies we get are of very good quality and are quite stable,” said Karumbayaram, who compared his animal-free colonies to those created conventionally using mouse feeder cells.

Efficiency did suffer. Fewer colonies were created using the animal-free feeders, but the colonies remained stable for at least 20 passages.

The resulting neurons started life as a small skin punch biopsy from a volunteer. Those skin cells were then reprogrammed to become pluripotent stem cells with the ability to make any cell in the human body. The iPS cells were then grown in

colonies and later coaxed into becoming neural precursor cells and finally, neurons.

The animal-free cells were compared at every step in the process to cells produced by typical methods, Karumbayaram said, and were found to be of very similar quality.

“We were very excited when we saw the first colonies growing, because we were not sure it would be possible to derive and grow cells completely animal-free,” he said.

Because the cells were grown in a special facility designed to culture animal-free cells, the testing and examination required to make clinical-grade cells should be much simpler, said William Lowry, study senior author and an assistant professor of molecular, cell and developmental biology in Life Sciences.

To date, at least 15 animal-free iPS cell lines have been created at the Broad Stem Cell Research Center.

“It’s critical to note that we are nowhere near ready to use these cells in the clinic,” Lowry said. “We are working to develop methods to make sure these cells are genetically stable and will be as safe as possible for human use. The main goal of this project was to generate a platform that will one day allow clinical translation of stem cells to the clinic.”

The study was published in *Stem Cells Translational Medicine*, 7 December 2011, early online edition.

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(Continued on page 7)

Stem Cells Used To Gain Insight Into Severe Childhood Epilepsy

Researchers investigating the fundamental cause of Dravet syndrome, a severe childhood epilepsy, have reprogrammed fibroblasts, a type of skin cell, from Dravet patients and generated patient-specific neurons that could help determine new therapies or better medications for the syndrome.

Jack M. Parent, M.D., associate professor of neurology at the University of Michigan, working in collaboration with Lori Isom, Ph.D., professor of pharmacology and Miriam Meisler, Ph.D., professor of human genetics, found that these patient-derived neurons showed increased excitability, abnormal neuronal behavior that can produce seizures.

This novel approach toward unraveling the pathophysiological mechanism behind Dravet syndrome was reported at the American Epilepsy Society's annual meeting.

Parent and his team obtained fibroblasts from both Dravet patients and unaffected controls and reprogrammed the cells to induced pluripotent stem cells (iPSCs) by gene transfer.

Forebrain-like neurons were generated from the iPSCs and studied for their electrophysical properties. The Dravet-derived neurons displayed a lower threshold for electrical activity, more repetitive firing, and increased firing frequency than control neurons.

"These findings indicate that patient-specific mutant Dravet cells can be reprogrammed to successfully model an epileptic-like phenotype with *in vitro* seizure-like activity," Parent said. "Besides providing new insight into disease pathogenesis, this approach using patient-specific cells should prove a valuable tool to evaluate potential new medications for Dravet syndrome and potentially other developmental epilepsies."

This approach should also have broader applications in screening new treatments for other neurological disorders, Parent said.

Dravet syndrome, also called severe myo-

clonic epilepsy of infancy (SMEI), is a rare genetic disorder with typical onset in the first year of life. It is a progressive condition characterized by mixed seizure types, frequently including life-threatening status epilepticus. Children with Dravet syndrome have poor language development and motor skills, and hyperactivity. Males are affected twice as often as females.

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Researchers Discover Safe Way To Repair Sickle Cell Disease Genes

Researchers have developed a way to use patients' own cells to potentially cure sickle cell disease and many other disorders caused by mutations in a gene that helps produce blood hemoglobin.

The technique uses cells from a patient's skin to generate induced pluripotent stem cells (iPSCs), which are capable of developing into various types of mature tissues, including blood. The scientists say their method, which repairs the beta-globin gene (HBB), avoids gene therapy techniques that can introduce potentially harmful genes into cells.

The new technique, which will soon be tested as a therapy in animals, also appears to be much more efficient than other methods tested to date, the researchers said.

"Our findings set the stage for the development of iPSC-based therapies for devastating genetic disorders such as sickle cell disease," said the study's principle investigator, Juan Carlos Izpisua Belmonte, a Salk Institute for Biological Studies professor in the Gene Expression Laboratory.

The researchers reprogrammed skin cells taken from a sickle cell disease patient into induced pluripotent stem cells (iPSCs), immature cells capable of developing into any type of bodily tissue.

Sickle cell disease is a group of inherited blood disorders caused by genetic mutations in the HBB gene, resulting in abnormal hemoglobin, the iron-containing protein that normally allows blood cells to carry oxygen. This causes red blood cells to

(Continued on page 8)

become hard and sticky and resemble a curved farm tool called a “sickle.” In the two leading disorders caused by HBB mutations, sickle cell anemia and beta thalassemia, red blood cells can’t effectively carry oxygen.

Symptoms of sickle cell disease include swelling of the hands and feet, pain due to clogging of blood vessels, anemia and stroke.

The disorders are most common among people of African, Mediterranean and Middle Eastern descent. One in every 500 African Americans and one in every 30,000 Hispanic Americans are born with sickle cell disease, according to the Centers for Disease Control and Prevention.

The disease can be cured with stem cell or bone marrow transplants, but there is a high risk that recipients of transplants will reject the donated marrow or cells, which can result in serious side effects and even death.

The researchers set out to devise a safe method to use iPSCs to correct the HBB gene in patients who have defective copies of the gene.

Because the iPSCs come from a patient’s own body, they should carry less risk for transplant rejection. Also, about 500 other disease-causing mutations have been identified in the HBB gene, so correcting the gene could potentially cure a multitude of HBB-related diseases worldwide.

However, traditional iPSC generation and gene therapy techniques have proven to be potentially unsafe, according to the researchers.

Many have used viruses to convert adult cells to stem cells and to carry a normal HBB gene to infect and repair hematopoietic stem cells that give rise to all blood cells.

But when these repaired stem cells are given back to patients, they can include unwanted genes (transgenes) that have become inserted into the host genome and disrupt the normal function of DNA. The technique is also inefficient, correcting only a small percentage of gene mutations, and transplantation success has proven rare in clinical trials testing gene therapy to treat beta thalassemia.

“We wanted to fix the mutation in such a way that it does not leave any unwanted traces in a patient’s genome,” SuzU.K.i said.

To do that, the researchers used a two-step approach. First, they took adult skin cells from a patient with an HBB mutation that causes sickle cell disease. They used six genes to coax these cells to revert to iPSCs, which could then be developed into blood cells.

The genes were introduced into the cells using a technique that avoids the use of viruses and insertion of transgenes into the cells’ genome.

Their next step was to repair the HBB gene mutation in the stem cells. To swap the defective gene with a normal copy in the iPSCs, the investigators used a modified adenovirus (common cold virus) that, unlike viruses used in other methods, does not replicate itself in the body and does not alter the host cells’ DNA. The viral genes were deleted and replaced with a DNA sequence that contained a normal HBB gene.

The modified virus then delivered the new genetic material inside the iPSCs, where the DNA region containing the broken gene was replaced with the sequence containing the normal gene.

“It happens naturally, working like a zipper,” Li said. “The good gene just zips in perfectly, pushing the bad one out.”

By replacing a relatively large region of DNA, the technique allows the scientists to fix many gene mutations at once, which suggests the method might provide a way to treat hundreds of types of HBB-related diseases. The correction of the mutant HBB gene was also highly efficient and the research team conducted multiple tests to ensure no errant genes were integrated into the genome.

The scientists now plan to make blood cells from the repaired stem cells and test their effectiveness in animals. If successful, this may lead to therapies for humans in which a patient’s stem cells will be reverted into iPSCs, then genetically repaired and transplanted back into the bone marrow of the same patient. If successful, the bone marrow will then produce all new blood cells, including normal hemoglobin.

If the technique proves effective, the researchers said, it might be used for treating other types of diseases caused by single gene mutations.

Citation: “Efficient correction of hemoglobinopathy-causing mutations by homologous recombination in integration-free patient iPSCs;” Mo Li, Juan Carlos Izpisua Belmonte et al.; *Cell Research*, December 2011; 21 (12): 1740 DOI: 10.1038/cr.2011.186

Abstract:

<http://dx.doi.org/10.1038/cr.2011.186>

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British Researchers Create First Animal Product-Free Clinical Grade hESC Lines

Stem cell scientists announce they have submitted to the U.K. Stem Cell Bank (UKSCB) their first clinical grade human embryonic stem (hES) cell lines that are free from animal-derived products, known as “xeno-free” stem cells.

The cells, which have the potential to become the “gold standard” lines for developing new stem cell-based therapies, will be the first deposited in the UKSCB based at the National Institute for Biological Standards and Control, under arrangements that will ensure they are freely accessible to the wider research community. The expectation is that these cells will be grown and processed by the UKSCB to provide stem cell stocks that will be used for clinical research and treatment to benefit patients.

Researchers said this is a significant milestone; this first batch of cells is the culmination of nearly ten years of research funded strategically by the Medical Research Council (MRC) that will keep the U.K. at the forefront of regenerative medicine.

Embryonic stem cells can be grown in the laboratory indefinitely while retaining their capacity to develop into specialized cell types, such as nerve or heart muscle cells, which can then be used in clinical trials. More than 20 ‘research grade’ stem cell lines have been provided by King’s College London to the UKSCB since it derived the first research grade hES cell lines in the U.K. in 2003, but the challenge to date has been to establish appropriate derivation and growing conditions for the cells without the presence of any animal products, such as porcine enzymes, bovine serum or mouse feeder layers.

Clinical use of hES cells is already being explored in a number of phase 1 safety trials, such as spinal cord injury and macular degeneration. However, the hES cell lines used in these trials were reclassified from “research grade” to “clinical grade” for specified short-term clinical studies in selected disease states, as a matter of expediency.

This route is not considered appropriate for the future of cell therapy because of the expense of the required testing and reclassification, and the significant risk of using cell lines derived on unqualified feeders, using unqualified reagents under undocumented envi-

ronmental conditions in the embryology and stem cell labs and storage facilities.

While it might be reasonable to incur additional risks for these early pioneering studies, it is not reasonable to accept these risks for the long-term future of cell therapy. Therefore the highest standard of xeno-free lines are urgently needed, and the development of these lines by King’s represents a major step forward.

The hES cells were grown from frozen embryos donated by patients who had previously undergone IVF treatment and no longer wished to use their remaining stored embryos. These embryos would otherwise have been discarded in line with HFEA requirements.

The team developed a comprehensive methodology and standards for derivation of the xeno-free hES cell lines that will be appropriate for studies in human subjects after suitable additional testing and processing by the UKSCB. Developed in line with these rigorous standards, researchers, physicians and industry can be reassured of the reliability of the seed stock – the essential base for translational applications. It is hoped that these standards will be recognized across academia, future users and policy agencies operating in and monitoring the field.

As the research that underpinned this work was funded by the MRC, the decision has been taken to submit these to the UKSCB for open-access therapeutic use for the public good. A number of additional xeno-free lines will follow shortly from King’s and from the stem cell team at the University of Manchester/Central Manchester NHS Trust, who have been similarly supported by MRC and have also developed clinical grade hES cells to submit to the UKSCB in the same way.

Contact: <http://www.kcl.ac.uk/index.aspx>

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New Lab Products

Comprehensive Range Of High Quality 2D Coded Tubes

Identifying a sample via a code on the tube can be done in a number of ways.

However the most reliable in terms of long-term identification and tracking of samples is via a 2D coding on the bottom of the tubes.

But not all 2D coded sample storage tubes, even those using the same coding system, offer the same storage performance.

Barcodes on Micronic 2D Data Matrix and 2D TraXis coded tubes are permanently laser-etched into the tube surface making them especially resistant to solvent attack and wear. Uniquely manufactured from a single component - the code in Micronic laser encrypted 2D codes cannot fade or peel off even when subjected to repeated handling and freeze-thaw cycles. Because code clarity will remain unchanged throughout the lifetime of a Micronic 2D coded tube - they offer unmatched secure sample traceability.

A new white paper available from Micronic examines factors affecting establishing a secure traceable stored sample including robustness of the tube coding, the purity of polymer used for manufacturing tubes and having effective means of sealing tubes.

Manufactured to industry-leading strict tolerances the precision and tube-to-tube consistency of Micronic sample storage tubes maximizes uptime when used with automated handling systems. Produced in an automated Class 7 clean room environment from additive-free, high purity polypropylene the long term integrity of samples stored in Micronic tubes is unmatched.

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

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Optimized PCR Plates For All Thermal Cyclers And Sequencers

Porvair Sciences Ltd. has unveiled PCR plates manufactured from polypropylene for extra rigid-

ity.

The high quality PCR plates are compatible with the majority of 96- and 384-well block PCR and sequencing instruments, including FAST sequencers.

Summarized in an easy-to-use selection guide, the Porvair PCR plate range of standard or low profile 96-well PCR plates are available in specific optimized formats (full, half or no skirt), with well volumes of 100-200 microliters. Designed for higher throughput assays, where samples are often at a premium, Porvair 384-well PCR plates offer a working well volume of only 30 microliters. To ensure full compatibility with robotic systems the 384-well PCR plates offer a full plate skirt and high rigidity to minimize distortion before and after thermal cycling. Black alphanumeric printing on all PCR plates ensures easy well identification.

Produced in Class 10,000 clean room conditions, the Porvair range of PCR plates are certified free of pyrogens as well as DNase and RNase enzyme activity enabling routine achievement of excellent PCR results. Porvair PCR plates are based upon a well design where the liquid meniscus comes below the plate surface eliminating sample carryover problems when using a plate lid.

Available in bulk packs of 50 individually wrapped plates – Porvair Sciences 96 –well and 384-well PCR plates reduce the cost of Polymerase Chain Reaction (PCR) analysis without compromising performance.

Contact: <http://www.porvair-sciences.com>

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Commercial Launch Of iCell Neurons For Neuroscience Drug Discovery

Madison, Wis.-based Cellular Dynamics International (CDI) on December 13 announced the commercial launch of human iCell Neurons for use in neuroscience drug discovery, neurotoxicity screens, and other health research. This is the first commercial availability of human neurons, or brain cells, created from induced pluripotent stem (iPS) cells in the quantity, quality, and purity required for life science re-

(Continued on page 11)

search.

iCell Neurons exhibit the typical physiological characteristics and responses of the neurons with which we are born. These neurons quickly form connective neuronal networks that are electrophysiologically active, making them useful in a variety of applications commonly used in neuroscience research, including cell viability, ATP production, oxidative stress, neurite outgrowth, electrophysiology, and synaptic neurotransmission assays. CDI's proprietary manufacturing capabilities enable the production of iCell Neurons in industrial quantities with greater than 95 percent purity.

CDI has successfully engaged in pre-launch collaborations with several pharmaceutical customers for validation testing and establishing disease-relevant neuroscience assays.

"We have been working with CDI for some time now and are very impressed with their iCell Neurons, which provide us with a unique model of pure and highly differentiated human neurons showing real potential for measuring functional neurotransmission," said Dr. Pascal Laeng, head of molecular and cellular pharmacology at Galenea Corp. "The preliminary data are very promising, and we look forward to continued collaboration with CDI to implement iCell Neurons in our high throughput assay of synaptic function."

"CDI's human iPSC-derived neurons, iCell Neurons, offer unprecedented opportunities for drug discovery and development," said Dr. Johannes Mosbacher, director of CNS electrophysiology at Actelion Pharmaceuticals. "The cells not only functionally express key ion channels and receptors but also form electrophysiologically active networks. These attributes of iCell Neurons help substantiate the possibility that these cells provide an exciting new human model of neuronal physiology that augments traditional ones, such as rat primary neurons and human neuronal cell lines."

iCell Neurons present a human platform that enables the modeling of healthy neuronal cells to improve the predictability of drug candidate efficacy and toxicity screens early in the pharmaceutical pipeline process.

"The human brain represents a complex organ that has consistently proven difficult to model in vitro, and this is partially reflected in the lack of effective therapeutics to treat neurological diseases and disorders," said Chris Parker, chief commercial officer. "Degenerative diseases, such as Alzheimer's, Parkinson's, and ALS, and genetic dispositions, such as Huntington's and muscular dystrophy, can also be

modeled to better understand these disease states for drug discovery and eventual therapies."

Because iCell Neurons are human cells, they better recapitulate human biology. These cells are better predictors of drug candidate responses than current cell models, including immortalized cell lines and primary neurons isolated from rodent tissues, which present significant limitations in biological relevance, reproducibility, and scalability.

"iCell Neurons are the third iPSC-derived product CDI has now commercially launched," said CEO Robert Palay. "We launched the first product ever developed from iPSC cells, iCell Cardiomyocytes, in December 2009, followed by iCell Endothelial Cells in September 2011. Based on strong intellectual property and exclusively licensed patents, we have developed a proprietary process to industrialize the manufacture of virtually any cell type in the human body. CDI is the first company to utilize stem cell technology to manufacture the vast quantities of high quality stem cells and tissue cells required to better understand human biology, revolutionize the drug discovery process, and develop cell-based therapies to treat human diseases."

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

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Spinovation Biologics Spedia-NMR Gains Momentum in Client Adoption

Spinovation of Nijmegen, The Netherlands, reports that there has been an increasing demand for Spedia-NMR technology, an analytical service that provides fast, fine-tuning of cell culture feeding strategy, delivering improved cell viability and higher product yield.

Spedia-NMR has shown itself to be faster and more reproducible than liquid chromatography (LC)-based methods for cell culture media analysis. Spinovation Biologics now provides NMR services to 20 major biotech companies, one of which is in the world top 10 Biopharma. The number of companies realizing the benefits of Spedia-NMR is increasing every month, with 25 more biotechs currently evaluating the

(Continued on page 12)

benefits of the service.

Spedia-NMR provides rapid, quantitative multiplex analysis of spent cell culture media, quickly identifying which feed components are most influenced by process change. Results include information on the production and accumulation of metabolites and toxic components.

Spedia-NMR is able to evaluate over 50 analytes at a time providing robust and cost efficient results with ideal linearity ($R \geq 0.99$) over a large dynamic range (from 10 μM to 0.5 M) and limit of detection at approximately 1 μM . The service provides a detailed analysis including volatile metabolites and can even identify unanticipated unknowns, saving the time and cost of multiple analyses.

“The increasing uptake of Spedia-NMR services by Biopharma and biotech clients reflects a high demand for high throughput, detailed analysis of bioprocesses,” said CEO Dr. Frederic Girard. “Our clients are using the Spedia-NMR data to optimize and standardize conditions in preparation for large-scale manufacturing of biologics, which they can do within a far shorter timeframe using our technology.”

Spinovation Biologics offers Spedia-NMR alongside a wide range of complementary analysis methods including LC-MS, LC-NMR, LC-SPE-NMR, LC-SPE-NMR-MS, for troubleshooting in bioprocess and performing simple to complex profiling and characterization of biologics and biosimilars (including peptides, proteins, oligo/polysaccharides). All services are available on a contract or pay-per-sample basis to suit individual client requirements.

Contact:

<http://www.spinovation-biologics.com>

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Thermo Fisher Scientific Introduces Searchable Tool for Diagnostic Applications

Rochester, N.Y.-based Thermo Fisher Scientific Inc. has introduced the immunoassay plate guide as a keyword rich, fully searchable online resource, as well as in a tablet PC format.

As a result of the keyword driven content, you can simply type a phrase into the search box to pull out all relevant sections. Furthermore, the interactive guide

allows you to navigate through the pages using click button arrows, or by typing the specified page number into the page window. You can also click directly on the contents page titles to be taken instantly to the desired page and insert virtual sticky notes to keep track of your thoughts. The user-friendly tablet PC format incorporates all of the same functionality, which is accessible on the move.

Providing in-depth detail on the range of Thermo Scientific Nunc immunoassay plates, the immunoassay plate guide provides an easy to use laboratory resource. For sensitive protocols, it is essential that you match the correct plate type to your assay to ensure that accurate, reproducible results are obtained for downstream analysis.

Contact:

<http://www.thermoscientific.com/oemdiagnostics>

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Defending Against Mycoplasma Contamination With Expanded PES Filter Line

Thermo Fisher Scientific said it has expanded its Nalgene 0.1 Micron PES Filter line with a new 1-liter unit, offering customers the broadest size selection on the market for 0.1 micron vacuum filtration of cell culture media to prevent mycoplasma contamination.

The new unit incorporates a large 90 mm diameter membrane and a proprietary Rapid-Flow membrane support plate to facilitate rapid, high-capacity filtration rates. The Nalgene PES 0.1 micron filter unit is ideal for use in academic, pharmaceutical and biotechnology cell culture labs.

Along with the new 1-liter unit, the Nalgene 0.1 micron PES filters are also available in 150 mL, 250 mL and 500 mL capacities. By choosing the ideal filter size for their application, customers can reduce costs, save storage space and avoid waste.

The Nalgene 0.1 micron PES units effectively filter media and buffers to protect against a loss of culture viability due to contamination, particularly mycoplasma contamination, which can destroy valuable cell cultures. While sterile techniques and routine

(Continued on page 13)

testing reduce contamination, 0.1 micron final filtration provides an enhanced level of protection. Additionally, the filters' low protein-binding PES membrane reduces the potential for removing critical components from the media during filtration, and low extractable levels ensure that the solution remains unchanged. Built to the well-known Nalgene quality standards, the guaranteed leak-proof filter bottle cap maintains the pH of filtered media.

The Nalgene 0.1 micron PES filter units provide the last line of defense against mycoplasma contamination while offering enhanced flow capabilities in a broad volume range.

Contact:

<http://www.thermoscientific.com/filtration>

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Imaging 8mm Deep: Further Into Tissue Than Ever Possible Before

Center Valley, Pa.-based Olympus on December 5 introduced another advanced 25x super-long-working-distance microscope objective designed to be used with the Scaleview-A2 clearing reagent - this one delivering vivid 3D image capture of structures 8mm deep, much further into contiguous tissue than was ever possible before.

The 8mm objective is the second high-performance optic Olympus has designed for the breakthrough Scaleview-A2 imaging technique first developed at the RIKEN Brain Science Institute in Japan. The company recently introduced a high-performance 4mm-working-distance 25x objective designed to be used with the Scaleview-A2 reagent.

The new 8mm objective, which has a numerical aperture (NA) of 0.9, may be ordered from Olympus now.

Both objectives have been optimized to be used with the Scaleview-A2 reagent and the Olympus FluoView FV1000-MPE multiphoton microscope to collect images. Together, they provide detailed, crisp images captured at unprecedented depths within brain and other tissues. Scientists envision the possibility of using the 25x, 8mm working distance objective and its companion 25x, 4mm objective with the reagent for developmental biology studies and for imaging and mapping the brain and other organs.

The Scaleview-A2 reagent is significant because most bodily tissues are opaque, making it difficult for researchers to see inside. The reagent literally makes tissue transparent and minimizes light scatter. When used together with either of the Olympus objectives, which are optimized for the reagent's refractive index, the system allows scientists to peer several times deeper into tissue. In the mouse brain, for instance, the RIKEN team has imaged neurons 8mm beneath the surface.

A further advantage comes from eliminating most tissue slicing. Until now, most optical microscopy techniques required slicing dead biological tissue into very thin sections, damaging the specimens and making it challenging to visualize how slices fit together. It was especially difficult to visualize how neural filaments connect in the brain. By eliminating most slicing, the connectivity of the brain and other organs can be imaged intact.

"I'm very excited about the potential," said Dr. Atsushi Miyawaki, part of the RIKEN research team in a recent interview with *The New York Times*.

Miyawaki's team is working on imaging the mouse brain as part of the worldwide Connectome project - a global effort to understand the structure, interconnectivity and function of animal and human brains. The reagent and objectives may help neuroscientists map the architecture of the mouse brain.

Contact:

http://www.olympusamerica.com/seg_section/seg_scaleview_a2.asp

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Muse Cell Analyzer Offers Multiparametric Analysis On A Single Platform

Billerica, Mass.-based EMD Millipore, a unit of Merck KGaA (Darmstadt, Germany), on December 5 announced launch of the Muse Cell Analyzer system for real-time quantitative assessment of cell concentration, cell health, apoptosis, and cell cycle with greater accuracy and precision than manual hemocytometry or image-based automated analysis.

By providing real-time, multi-dimensional information on cell populations, the Muse cell analyzer enables faster, more accurate decision-making, more productive workflows, and greater insight in to

(Continued on page 14)

cell health.

The Muse system delivers high-performance cell analysis using patent-pending, miniaturized fluorescent detection and micro-capillary technology which occupy one-tenth the space of a typical cytometer. Laser-based fluorescence detection of each cell event can evaluate up to three cellular parameters.

As a result, Muse provides accurate quantitative results compared to imaging-based systems, which only examine up to two parameters, are time-consuming and ultimately provide less quantitative data. The system is capable of analyzing both suspension and adherent cells from two to sixty μm in diameter. Intuitive software and simple touchscreen interface enable rapid set-up and analysis.

“With Muse, researchers can gain new insights into cell health with greater precision and accuracy than they have come to experience with existing cell analysis techniques and instruments, without the price barrier as the system is priced just above \$12,000,” said John Sweeney of EMD Millipore.

To further optimize workflows, the Muse Cell Analyzer is designed to work with all-in-one kits, specifically validated for robust performance on the system. Kits include cell count and viability, apoptosis and cell cycle and come with all the reagents necessary for proper sample preparation.

Contact: <http://www.millipore.com/muse>

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