

## MEETING REPORT

# Stem cells in drug discovery, regenerative medicine and cancer

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### Abstract

A report on the Stem Cells World Congress held in San Diego, USA, 24-25 January 2011.

The Stem Cell World Congress brought together scholars and experts from a wide array of stem cell research. Discussions covered a range of issues and topics, including basic science discoveries related to the use of neural progenitors and mesenchymal stem cells (MSCs) for the treatment of neurodegenerative disease, the legal aspects related to patent protection of stem-cell-based discoveries, the best practices for biobanking of cord blood, and the ethical considerations related to stem cell research. This report focuses on major themes of the meeting, with a focus on the stem cell topics related specifically to medical genomics.

### Stem cells in regenerative medicine

One of the primary focuses of the meeting was the use of stem-cell-based therapy in regenerative medicine, which aims to regenerate damaged tissues. Keynote presentations discussed research in the field of neurodegenerative diseases, such as Alzheimer's disease, Huntington's disease, and amyotrophic lateral sclerosis. Jan Nolte (University of California Davis, Sacramento, USA) suggested that stem cell therapy for neurodegenerative diseases represents a potential cure, compared with small-molecule-based therapy, which can ameliorate symptoms but not correct underlying genetic or structural problems. Nolte focused on Huntington's disease, an autosomal dominant disease that is linked to increased CAG repeats in the Huntington gene (*HTT*) on chromosome 4. Nolte is using a catheter-based approach to deliver bone-marrow-derived MSCs, which are programmed to secrete a small interfering RNA to downregulate mutant Htt protein.

She has found that MSCs home to sites of injury within the brain, have a 'neuro-protective effect', and can reverse injury through Htt downregulation. The MSCs do not form tumors, even 8 months after transplant into immune-deficient animals. Risk of tumor is one of the concerns in using human embryonic stem (hES) cells for regenerative medicine.

Larry Goldstein (University of California San Diego, USA) discussed the idea of using stem cells to model the genomic variation that is a contributor to human neurodegenerative disease. He said that developing cell-based therapies is critical for neurodegenerative diseases because 50% of the population over 85 years of age will develop Alzheimer's disease. He discussed using human induced pluripotent stem (iPS) cells derived from the fibroblasts of people with both sporadic and familial forms of Alzheimer's disease to identify genotype-phenotype correlation within the biochemical derangements typically observed in neurodegenerative disease. In addition, he presented the pre-clinical development of a cell-based therapy for amyotrophic lateral sclerosis using the H9 hES cell line differentiated into neural progenitors and astrocyte-like cells.

For the treatment of stroke patients, Marcel Daadi (Stanford University, Palo Alto, USA) presented the use of hES cell therapy to aid in motor function recovery. Neural progenitor cells derived from hES cells partially rescued the neurological deficits in experimental stroke animal models, specifically in the areas of strength, coordination, balance and other motor functions. Daadi showed that *in vivo* molecular imaging using functional magnetic resonance imaging (MRI) allows tracking of hES-cell-derived neural progenitors to the source of a brain injury.

Suzanne Berry (University of Illinois, Champaign, USA) presented work related to mesoangioblasts isolated from murine fetal aortic arch. Mesoangioblasts can differentiate into smooth muscle, skeletal muscle, and cardiac muscle. Berry used a Duchene muscular dystrophy mouse model system to show that mesoangioblasts incorporate into skeletal muscle to restore dystrophin protein levels. In addition, mesoangioblasts can differentiate into cardiac muscle *in vivo* and improve cardiac

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function, as measured by echocardiogram, in this model system.

### Stem cells in drug discovery

Joseph Frank (National Institutes of Health Clinical Center, Bethesda, USA) discussed the concept of cell tracking in cell-based therapies and described cell tracking as a 'key issue' for the US Food and Drug Administration in terms of approval for stem-cell-based therapies. Frank described cell-based therapies on a 'micromolar' scale given the number of cells injected compared with target organ cell mass. He used iron labeling *in vitro* to show the retention of 99% of the labeled iron in human hematopoietic stem cells. Iron-labeled cells can be identified using standard MRI protocols and can be followed for up to 6 months *in vivo*, and iron does not induce differentiation in stem cells. He presented a novel therapy adjunct in which a magnet is used to 'home' iron-labeled cells to a specific site *in vivo* using focused magnetic fields. In addition, he highlighted that pulsed, focused ultrasound improves local retention of stem cells.

Hakim Djabalah (Memorial Sloan-Kettering Cancer Center, New York, USA) presented work on a high-throughput drug discovery screen to identify small-molecule inhibitors and drivers of differentiation in hES cells. He said that given the complexity and difficulty of hES cell work, this strategy was not likely to yield significant targets in a cost-effective manner using current technology. Djabalah also presented preliminary data showing that iPS cells provide a more stable platform for drug discovery in terms of target identification and validation for both inhibitors and drivers of differentiation.

Stefan Jellbaur (University of California, Irvine, USA) and Enal Razvi (Select Biosciences, Sudbury, UK) presented a market analysis of stem-cell-based therapies and cancer stem cell research. One key issue related to stem cell research is that the most common hES cell lines published, the H1 and H9 lines, would be required for any study using a novel hES cell line to provide a known standard against which new lines can be validated.

### Stem cells in inflammation and cancer

Joni Ylostalo (Texan A&M Health Science Center, College Station, USA) presented a novel culture method for human MSCs using a 'hanging drop' system of cell suspension. In this suspension system, MSCs form spheroids, and these show a potent anti-inflammatory response (as measured by production of prostaglandin E2) compared with MSCs that are adherent to plastic in a standard culture system.

Mauricio Rojas (University of Pittsburgh, USA) showed that the anti-inflammatory response of MSCs can be used to prevent acute and chronic lung injury if the cells are used early in the injury cycle. Using a murine heterotrophic allogenic trachea transplant system, MSCs reduce obliterative bronchiolitis, a disease of chronic rejection that is a significant problem in lung transplant patients.

I presented work supporting the hypothesis that a stem cell phenotype is produced after the epithelial-to-mesenchymal transition in liver cancer. These findings are similar to recent discoveries in the breast cancer field, where the epithelial-to-mesenchymal transition has been shown to generate cancer stem cells.

### Conclusions

The 2011 Stem Cell World Congress covered a wide range of topics related to stem-cell-based therapy and discovery. Many of the presentations related to regenerative medicine focused on neurodegenerative diseases. One suggestion was that neuronal progenitors represent a potential default pathway of differentiation for hES cells. Critical barriers to successful implementation of stem-cell-based therapy for regenerative medicine include documentation of cell tracking studies during pre-clinical trials. Adult stem cells, such as MSCs, are being evaluated for their anti-inflammatory effect and as potential delivery vehicles for cell-based gene therapy. Lastly, iPS cells derived from patients with genetic diseases will provide a unique opportunity to explore genotype-phenotype correlation and may ultimately be used to validate genome-wide association studies.

### Abbreviations

hES, human embryonic stem; iPS, induced pluripotent stem; MRI, magnetic resonance imaging, MSCs, mesenchymal stem cells.

### Competing interests

The author declares that he has no competing interests.

### Authors' information

CBR is an Assistant Professor of Pediatrics and Pharmacology at Penn State College of Medicine. He manages an active stem cell and cancer stem cell laboratory and cares for children with intestinal and liver disease.

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