

## Breakthroughs in Stem Cell Research and Clinical Applications - Report of the SABPA Science & Technology Forum VIII



The topic for this year's SABPA Science & Technology Forum VIII was "Breakthroughs in Stem Cell Research and Clinical Applications". This year's event attracted over 250 attendees. The theme was selected since stem cell research is one of the most innovative and promising technologies for the treatment and prevention of human disease and this field has made enormous progress in the past few years.



Six investigators that are at the forefront of this field presented their latest findings regarding technical advances of stem cell therapies for treatment and

prevention of neurological diseases, spinal cord injury, type-I diabetes and cancer.

The morning session started with a keynote lecture from **Professor Lawrence Goldstein** from UCSD, a Howard Hughes Medical Institute Investigator and Director of the UCSD Stem Cell Program. Professor Goldstein is a strong advocate for stem cell research. He helped in writing the California proposition 71 that created a \$3 billion funding organization in 2005 to support human stem cell research in the state. Professor Goldstein stated that to move the promise of this field into clinical

application we need; 1) Scientific foundation, 2) New technology, 3) Funding, 4) Collaboration, 5) Effective clinical trials, 6) Investigator 'aggressive restraint', 7) Manageable regulation and harmonization of national and international guidelines and 8) Efficacy.

Professor Goldstein presented work on using human embryonic stem cells (ESCs) in his own laboratory for the treatment of neurological diseases including Alzheimer's disease (AD). His approach is novel - by not using animal models of the disease, but using ESCs. He is generating neurons that carry familial AD mutants to test several hypothesis of disease causation. He is also using reprogramming technologies to generate human neurons with sporadic forms of AD. Subsequent biochemical and cellular comparisons of human neurons carrying sporadic or familial forms of AD may yield an understanding of what components of the sporadic disease are defined by genetic characteristics. He discussed his collaboration with industry that provides innovative technologies, and highlighted that stem cell research is not a one man show, but requires effective collaboration if the technology is to move forward.

Dr Hans Keirstead, an Associate Professor and Director of the Bill & Sue Gross Stem Cell Center (UCI) and the Chairman of the Scientific Advisory Board of California Stem Cell, Inc. gave an overview of the clinical progress of his company and laboratory in the transition of stem cell technologies from the bench to the clinic. Dr Keirstead was the first to put human ESCs in a human trial and has developed FDA-compliant oligodendrocyte progenitor cells from human ESCs suitable for addressing oligodendrocyte loss and has developed technology to address pre-clinical efficacy and safety concerns. Dr Keirstead discussed motor neuron progenitor differentiation, and therapeutic development for the treatment of type I infantile Spinal Muscular Atrophy, a neuromuscular disease characterized by degeneration of motor neurons and chronic spinal cord injury. Dr Keirstead has a number of progenitor cells and technologies that are available to other researchers, again stressing the importance of collaboration.

Dr Dan Shoemaker, Chief Technology Officer of Fate Therapeutics, a local San Diego company talked about how Fate Therapeutics is interrogating stem cell biology to develop therapeutics based on modulating cell fate and to enable a new drug discovery paradigm with the Company's proprietary induced Pluripotent Stem Cell (iPSC) technology. Fate Therapeutics is applying leading expertise in stem cell biology and conventional drug discovery to develop small molecule and biologic drugs that: 1) activate stem cells in the body to stimulate healing and repair or block cancer growth; and 2) create and differentiate iPS cells for personalized cell replacement therapies and drug discovery and development. The Company's first therapeutic candidate (FT-1050) entered Phase 1b clinical trials in early 2009 in hematopoietic stem cell support (6-12 patient study). Recently, Fate Therapeutics was named one of the 50 most innovative companies in the World by MIT's technology review. The line for questions for Dr Shoemaker at the end of his talk reflected the immense interest from the audience regarding his company's research.

After a short coffee break, Dr Anne Bang, Director of Stem Cell Research at Novocell Inc., San Diego, described how her company has developed a process to differentiate human ESCs to endocrine cells, mimicking pancreatic organogenesis, specifically for the treatment of type-I diabetes. Dr Bang showed us some remarkable pre-clinical studies in mice demonstrating the effectiveness of a pancreatic islet stem cell therapy that is administered subcutaneously using a microencapsulating system. The pros of their system include that it is both robust and reproducible and functions in vivo and has a greater regenerative potential than adult islets. One drawback of the system is that the length of time required to reach function is 30-90 days, however this is not a significant problem for the subjects who have this debilitating disease.

Dr. Wendy Levin (MD), Associate Director of Oncology Translational Medicine, Pfizer Inc, gave an excellent summary regarding the journey of bone marrow transplants, a treatment that has become routine for many types of malignancies, yet with a relatively low cure

rate. The reason for the low success rate of bone marrow transplants is that they do not eradicate the 'cancer stem cell'. Dr Levin discussed the clinical development of the small molecule PF-04449913 that targets Smoothed, a G protein-coupled receptor protein encoded by the SMO gene of the hedgehog pathway and that eradication of the 'cancer stem cell' in combination with other therapies may help cure many types of cancer.

Dr. Yang Xu, Professor of Biology from UCSD, gave an insightful summary on the work of his laboratory. Professor Xu focused on the pathways that are critical to maintain genetic stability in mammalian cells, particularly ESCs. By using disease-specific human ESCs, his laboratory aims to elucidate the roles of tumor suppressors in maintaining genetic stability and suppressing tumorigenesis.

Dr. Julie Clarke from Stemgent, our gold sponsor of the event outlined the services provided by her company for both academic and industrial stem cell research. The talks were followed by an active panel discussion with the audience, led by Dr. Stephen M Chang (CSO, Stemgent).

The concluding remarks from this forum were that stem cell research is advancing at a rapid rate. Collaboration between academic and industrial sectors is pushing this advancement and further effective collaboration is needed if the technology is to move forward to the clinic.