

## CABS Expert Forum on Stem Cell Research

Reported by Wentao Zhang and Ruhong Jiang

Ever since the passage of California Proposition 71 that called for \$3 billion in public funding for stem cell research in 2004, San Francisco Bay Area has become the epicenter of stem cell research with a collection of world renowned researchers. It is only fitting that on September 13, over 150 stem cell researchers and enthusiasts gathered at the UCSF (University of California – San Francisco) Mission Bay campus for a forum on stem cell research.



This event was co-organized by the Chinese American Biopharmaceutical Society (CABS) and UCSF Association of Chinese Students and Scholars. Six high-profile forum speakers from academia, the biotech industry, and the legal and investment communities discussed a broad spectrum of topics covering stem cell research highlights, therapeutic applications, intellectual property and business-related issues.

**Dr. Deepak Srivastava**, Director of the Gladstone Institute of Cardiovascular Disease at UCSF, presented an overview of the current status of stem cell research and the exciting therapeutic opportunities that included tissue and organ repair, protein production, and studying mechanism of various diseases. He discussed some basic differences between embryonic stem cell (ESC) and adult stem cell. Although ESC can mature into all cell types (i.e. pluripotent), there is more ethical resistance for its broader use. Adult stem cell,

on the other hand, has no battling ethical issues but it can only develop into limited cell types. A recent breakthrough from the laboratory of Dr. Shinya Yamanaka of Kyoto University in Japan demonstrated that adult cells can be induced or reprogrammed by retroviral transfection of four transcription factors, followed by clone selection to produce pluripotent stem cells. Dr. Yamanaka, who is joining Gladstone later this year, demonstrates that the induced pluripotent stem (iPS) cells are similar to ESC in morphology, proliferation and teratoma formation, and germline-competent. Dr. Srivastava described that mice with early iPS cells eventually developed tumor, probably due to the oncogenic c-Myc, one of the four transcription factors used to generate iPS cells. Later progress allowed the generation of iPS cells without c-Myc, and the resulting chimeras do not develop tumors. Human iPS cells have also been demonstrated and Dr. Srivastava told the audience that Gladstone recently formed a bio-partnership with iZumi, a biotech startup funded by venture capital firms Kleiner Perkins Caufield and Byers and Highland Capital Partners, to explore the therapeutic use of the iPS cells.

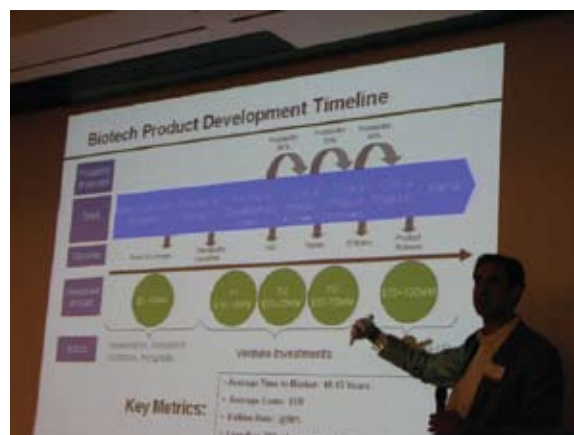
**Dr. Song Li**, associate professor of Bioengineer at University of California - Berkeley, discussed the bioengineering approaches to stem cells and his multidisciplinary research focus that involves stem cell biology, biomaterial and bioinstrumentation. He discussed mesenchymal stem cell (MSC) derived from bone marrow and its potential application in tissue repair. With low immunogenicity from the host, MSCs show self-renewal properties and can differentiate into many cell types. Dr. Li showed recent progress that mechanical factors such as fluid shear stress, mechanical strain and the rigidity of extracellular matrix can regulate the proliferation and differentiation of MSC's through various signaling pathways. Transplanted MSC's enhance angiogenesis and contribute to remodeling of the vasculature. MSC's showed some exciting therapeutic potential in a mouse hindleg repair model for nerve and spinal cord regeneration.

**Dr. Joe Gold**, a senior director at Geron Inc, a San Francisco Bay Area stem cell biotech company, discussed efforts made toward therapeutic applications of ESCs. Dr. Gold started his seminar with some practical considerations for stem cell-based human therapeutics, including cell scale-up, availability, potential immunological responses, safety, and economy. Availability in real time can be a daunting prob-

lem. For a heart failure, the patient undergoing a stem cell therapy would require an instant injection of at least 100 million cells. Even with cryopreserved cells, this scale will require coordinated work between the hospital who treats the patients and the company who manufactures the stem cells. A model that includes a master cell bank with multiple local working cell banks was discussed by Dr. Gold, and according to him, this model was used for Geron's product development of GRNOPC1, a cell based therapy for spinal cord injury. Safety is another major concern for stem cell-based therapies with many questions to be answered. How many pathogens (viruses, bacteria) one should screen? Where do cells go once injected? Will the stem cell cause tumor? And so on. Dr. Gold claimed that Geron submitted the longest IND filing, some 21,000 pages, to the U.S. FDA for its spinal cord injury therapy. However, many issues and uncertain ties exist in terms of developing and approving a cell-base therapy. In May, Geron announced that FDA had placed GRNOPC1 IND on clinical hold.

**Dr. Jie Zhou**, a partner specializing on patent law at Morrison & Foerster LLP, discussed intellectual property issues surrounding stem cells. Dr. Zhou emphasized the importance of IP to protect commercial value of products. Her presentation covered three most important IP issues in biotech industry including 1) procuring patent protection for the technology, 2) freedom of operation, and 3) enforcement of patent rights. For stem cell technology, Dr. Zhou, particularly pointed out the difference in patentable subject matter among USPO, EPO and UKPO on stem cells by giving the WARF patent application for human embryonic stem cells as an example. Dr. Zhou presented an example case between Merck vs. Integra to address how important of value of the research tool patents. The audiences were impressed by the many examples and valuable suggestions by Dr. Zhou.

**Mr. Jeff Karan**, MBA, is a senior partner with Proteus Venture Partners located in Palo Alto, California. With over 25 years of investment banking and corporate advisory experience, including twelve years at Morgan Stanley and Goldman Sachs, Mr. Karan briefly summarized challenges of investment in biotech industry in general and then focused on the challenges of investing in Regenerative Medicine particularly from many perspectives including R&D and manufacturing, regulatory and IP, reimbursement and right business model, etc. Mr. Karan also discussed the investment process of Proteus, cases for investing in Regenerative Medicine, and a brief introduction to Proteus. At the end of presentation, Mr. Karan announced that Proteus was expecting to close a \$225 million venture fund by the end of year--the first exclusively aimed at emerging stem cell companies. The new \$225M VC fund will aim for a dozen stem cell companies; Proteus Venture Partners plans to invest in 10 to 15 companies at \$10-\$20M per investment.



**Marie Csete**, M.D., Ph.D., Chief Scientific Officer at Californian Institute of Regenerative Medicine (CIRM), introduced that CIRM was established in early 2005 following the passage of Proposition 71 and is a state agency to make grants for stem cell research and regenerative medicine. Dr. Caset highlighted that the CIRM governing board had approved 229 research grants totaling more than \$614 million, making CIRM the largest source of funding for embryonic and pluripotent stem cell research in the world. Dr. Caset overviewed the awarding process and the upcoming initiatives including CIRM workshops in predictive toxicology and GMP; collaborative funding models with Genome Canada in cancer stem cell, etc. Dr. Caset also discussed funding research areas of interest in early translation research, disease team research awards, innovation awards and clinical programs. At the close, Dr. Caset pointed out that CIRM is working on a policy to address the IP issues.

The forum was well attended by scientists / students / postdocs from both the biotech industry and academia. It concluded a busy and successful 2007/2008 year of the CABS Science & Technology Committee, which organized three expert forums on special topics in drug discovery and development and three workshops in the drug discovery and development workshop series.