Exchange Award

Conference Title: Workshop on Improved Characterization of Mesenchymal Stem Cells for Clinical Trials

Principal Investigator: Curt I. Civin, MD

Co-Investigator: FDA - Steven R. Bauer, PhD

Workshop Date: May 8, 2013

Outcomes/Summary:

The M-CERSI conference on "Workshop on Improved Characterization of Mesenchymal Stem Cells for Clinical Trials " was held May 8, 2013 at the University of Maryland Baltimore campus in the Southern Management Corporation Campus Center located at 621 West Lombard Street. The program was organized by Drs. Curt Civin and Steven Bauer and co-sponsored by the University of Maryland School of Medicine's Center for Stem Cell Biology & Regenerative Medicine and Department of Orthopaedics, and the Food and Drug Administration. Over 130 participants attended from six different universities, two FDA centers (CBER and CVM), three other Federal Agencies (NIH, NIST, DoD), and several companies. Most participants were from universities, agencies, and companies within Maryland, but attendees from several other states and one foreign country were also present.

The two major goals of the conference were:

1. to assess MSC characterization and discuss methods that can be used to predict the quality, potency, and safety of MSCs,
2. to provide informal feedback regarding progress and future directions on the research conducted by FDA's MSC Consortium.

The workshop was conducted in two sessions corresponding to these two goals. The morning session focused on goal #1 was an open public workshop. The afternoon session on goal #2 was for invited participants, including the speakers and organizers of the meeting as well as members of FDA's MSC Consortium research project.

The morning session included brief introductions regarding the CERSI program as well as meeting overviews from Drs. Curt Civin (UMD), Franck Weichold (FDA) and Steven Bauer (FDA). Dr. Joseph Stains (UMD) served as moderator and did a great service keeping the highly packed morning session on schedule. Presentations from nine MSC experts were followed with a lively panel discussion on the themes that emerged from the morning session. Speakers presented on topics ranging from in vitro MSC assessment, to preclinical and clinical application of MSCs, and to application of systems biology and sophisticated computer imaging approaches for characterization of MSCs. Dr. Mark Pittenger (UMD) did an excellent job leading the panel discussion. Some of the prominent topics of discussion and emerging themes in MSC characterization included the following highlights:

- heterogeneity of MSCs is extensive due to different tissue sources of MSCs, different conditions of growth both in their local tissue environment and ex vivo, and different practices with respect to cryopreservation.
- MSCs may act through at least two basic mechanisms: first by elaboration of a large repertoire of biologically active factors that induce host responses which mediate wound repair and immunomodulatory activity of MSCs; and second, by more direct participation in tissue regeneration through incorporation. Increased understanding of the first mechanism is important for better characterizing and harnessing MSCs for clinical use, since many potential uses of MSCs currently under evaluation in clinical trials involve the immunosuppressive/anti-inflammatory functionalities of MSCs rather than their direct reparative capacities.
- the consensus characteristic MSC cell surface markers identified by the International Society for Cellular Therapy and widely used in the MSC community do not capture the phenotypic and functional heterogeneity of MSCs or serve as adequate biomarkers for either their immunomodulatory or their reparative capacities.
- progress is being made to identify MSC characteristics such as cell surface markers or gene expression profiles that are predictive of MSC biological functions.
- steady progress is being made in the clinical application of MSCs.
- novel approaches to MSC characterization using computer-based image analysis show promise in defining how physical properties of the microenvironment influence MSC growth and morphology.

The workshop agenda and brochure for the morning session are available:
http://www.pharmacy.umaryland.edu/centers/cersievents/msc/index.html
An archive containing slide presentations from the morning session is available:
http://www.pharmacy.umaryland.edu/centers/cersievents/msc/presentations.html

The afternoon session took place in a smaller meeting room at the Southern Management Corporation Campus Center. The speakers, panel chair, and organizers from the morning session heard presentations from each of the seven FDA laboratory groups in the MSC Consortium. Each of these researchers is part of the FDA's Center for Biologics Evaluation and Research (CBER), Office of Cellular Tissue and Gene Therapies (OCTGT), within the Division of Cellular and Gene Therapies (DCGT). Dr. Michail Alterman presented work on proteomics of MSCs. Dr. Raj Puri's laboratory presented research on gene expression analysis of MSCs. Members of Dr. Deborah Hursh's laboratory presented work on genetic stability and epigenetic profiling of MSCs. Dr. Malcolm Moos presented work on single cell analysis and systems biology approaches for MSCs. Dr. Brent McCright presented work on development of wound repair models for MSCs. Dr. Cheng-Hong Wei presented work on development of in vitro and in vivo immunosuppression models for MSCs. Dr. Bauer presented on development of quantitative bioassays for MSC characterization. Each presentation was followed by discussion of the project and a general discussion of the whole project followed the last presentation. The panel of experts expressed support for the project but also had many excellent suggestions regarding future directions for each PI and for the overall research project. Research managers from OCTGT and DCGT attended this session and expressed gratitude towards the outside experts and satisfaction that the feedback was significant and would be useful.

A web-based survey was sent to the participants after the meeting. The meeting ratings were quite favorable and comments were quite useful. For example, 69.4% strongly agreed and 27.8% agreed that the meeting content was appropriate and informative. Many comments were received from attendees who favored future meetings covering stem cell-related topics. Several comments acknowledged the high quality, expertise, and variety of the speakers.

Meeting planning and administration

Dr. James Polli and Anne Anonsen (UMD) were tireless and provided essential and excellent support for meeting logistics, speaker travel, lodging, and reimbursement, oversight and design of the web site including registration, posting of the agenda and slides, and generation and distribution of the meeting brochure and name badges.

MaDonna Perry provided outstanding and crucial support including booking of the venue, arrangements for catering, coordination with the parking facility, check-in for the morning and afternoon sessions, cooridination with IT support, and generation and conduct of the post-meeting survey. Fulliscia Morrison provided much appreciated help with these tasks.

Planning Committee

The planning committee identified speakers and topics for the workshop presentations and panel discussions, and initiated discussions of meeting logistics.
Curt Civin (UMD) Chair
Steve Bauer (FDA) Co-chair
Mark Pittenger (UMD)
John Fisher (UMD)
Malcolm Moos (FDA)
Deborah Hursh (FDA)
Patrick Lynch (FDA)
Mike Mendicino (FDA)

Conclusions

The workshop was well attended and met the goals of the original proposal. The organizers were very pleased with the high quality of the speakers, their presentations, the discussions, and the participation by attendees. The meeting web site serves as an excellent resource for the content of the workshop. There was enthusiasm expressed for future workshops in similar, stem cell-related topics. Drs. Civin and Bauer are extremely grateful for the hard work of all those who participated in the planning and conduct of the meeting and for the monetary and staff support from CERSI-UMD.