

NIH Bone Marrow Stromal Cell Transplantation Center

CHARTER

Bone marrow harbors within its stroma a population of cells [bone marrow stromal cells (BMSCs)] that have been shown to have a beneficial effect when administered directly to an injured tissue or via the circulation, in preclinical and clinical studies of a human diseases and disorders. BMSCs are reported to be immunosuppressive and immunomodulatory, and the positive effects of these cells are most likely due to the repertoire of cytokines and growth factors that they secrete, which may encourage local stem/progenitor cells to initiate repair. BMSCs can be readily obtained by biopsy, and can be easily expanded in culture. For these reasons, the NIH Bone Marrow Stromal Cell Transplantation Center is being established in order to develop a novel cell product for the treatment of a variety of human diseases and disorders.

This document describes the operating policies and administration of the NIH Bone Marrow Stromal Cell Transplantation Center (BMSCTC).

I. MISSION STATEMENT

The objective of the NIH Bone Marrow Stromal Cell Transplantation Center (BMSCTC) is to facilitate the use of clinical grade ex vivo expanded BMSCs for treatment of patients with a variety of human diseases and disorders.

Specifically, the mission of the BMSCTC is as follows:

1. To provide investigators with high quality clinical grade BMSCs that are prepared using procedures known to maintain their biological activities.
2. To assist clinical investigators in the preparation of clinical protocols through the development of boilerplate language for the cell portion of the protocol; in the preparation of FDA INDs through the development of a Master File, in collaboration with the CHI and/or with the use of contractors.

II. INFRASTRUCTURE

Overview

The BMSCTC will initially utilize existing space within the DTM/NIH CRC for the development of the cell product, with the possibility of expansion in the future. Activities during the first year will focus on building the infrastructure within the DTM, validation of ex vivo expanded BMSC properties through a number of assays, and finalization of the procedures. This activity will culminate in the development of a Master File submission to the FDA. Studies on labeling cells for non-invasive measurements will continue with the DTM and NIBIB.

Concomitantly, clinical protocols will be developed by investigators with the assistance of the CHI, and/or a consultant(s), with the goal of having at least one new protocol by applicant investigations in place by the end of the first year. During the second year, progress of the initiated clinical protocol(s) will be monitored, and two new protocols will be initiated.

III. ADMINISTRATION

Steering Committee - The Steering Committee will be composed of seven members, each representing a contributing institute, along with a member from the CC. Drs. Pamela Robey (NIDCR) and Harvey Klein (DTM/CC) will serve as Co-Coordinators. Other representatives will include Drs. Ronald Gress and Jonathon Vogel (NCI, one vote), Dr. Warren Strober (NIAID), Dr. Rocky Tuan (NIAMS), Dr. Joseph Frank (CC/NIBIB), Drs. Ron McKay, McFarland and Hallet (NINDS, one vote). The Committee will formulate the budget for the Center and will obtain the concurrence of the User Group, prior to submission of the budget to the Oversight Committee (see below). The Committee will closely monitor the operation of the BMSCTC and progress made towards reaching milestones. The Committee will meet at least quarterly during the first year to address issues that may arise during the finalization of the cell processing method, and to assess progress towards the goal of initiating at least one clinical trial by the end of year one. Subsequently, the Committee will meet biannually to assess progress towards bringing other protocols online and overall operation of the Center. In the event that more protocols are ready for initiation than can be handled in terms of generation of the cell product, or the need for protocol/IND support extends beyond resources available, the Committee will prioritize them based on the potential clinical impact and the severity of the disease or disorder to be treated. All Steering Committee meetings will be open to all Users in order to foster discussion, and obtain comments and suggestions aimed at improving the function of the Center. Minutes from all meetings will be prepared by the Co-Coordinators, and will be approved by the Steering Committee and User Group prior to submission to the Oversight Committee (see below).

User Group – The User Group will be composed of all investigators interested in the utilization of BMSCs either in the near or distant future. The User Group will be apprised of all activities of the BMSCTC and will be provided with ample opportunity for contributing comments and suggestions to the organization and operation of the BMSCTC during User Group meetings and by communication with the Steering Committee.

Oversight Committee – The Oversight Committee will be composed of a number of IC Directors and SDs. The Steering Committee will report to the Oversight Committee on the progress of the Center, and will submit plans for operation and budget details after discussion and general approval by the User Group to this Committee in a timely fashion so that adjustments determined by the Oversight

Committee can be easily implemented. The Oversight Committee has final authority on approving the budget for the BMSCTC

IV. OPERATION OF THE CENTER

Cell Product – The cell product will be generated by the CPL/DTM. Designated personnel in the DTM will provide the Steering Committee with quarterly status reports on progress made towards meeting the established milestones in generating the cell product. An evaluation of progress, with action items identified by the Steering Committee will be returned to the designated DTM personnel and distributed to the User Group.

Clinical Protocol Development – The Steering Committee will establish a relationship with the CHI (or establish contracts with consultants if needed) for the development of clinical protocols and FDA IND applications. Investigators will submit a request for cell product/protocol assistance to the Steering Committee. These requests will be reviewed by the Steering Committee, which if deemed appropriate, will submit the request to the CHI, or assign a consultant. A report of such action will be made to the Oversight Committee and to the Users Group. If needed, due to resource constraints, the Steering Committee will prioritize requests by a voting process, based on the clinical impact and graveness of the need for treatment of patients. Investigators should contact Dr. Patrick S. Riggins at the FDA early in the development of the protocol to gain information on points that the FDA will want to see addressed in a particular IND application. Investigators will, of course, submit protocols for approval to an appropriate IRB.

Clinical Trials – Investigators will carry out the approved trials within the infrastructure of their institute; i.e., clinical fellows, patient care coordinating and nursing care will not be financially supported by the Center.

Outside Collaborators – It is recognized that in some instances it may be necessary and beneficial to enlist outside collaborators who have expertise that is not represented here at the NIH (e.g., Orthopedists), in order to use the cell products in in order to broaden the range of therapeutic applications.

Databases – Currently existing databases will be evaluated for the appropriate storage of data generated by the fingerprinting of cell lots.

Staffing (New Staff - FTT (2 year initial appointment), renewable for a total of four years)

Staffing of the BMSCT will include existing staff within the DTM [including Drs. Stroncek, Hanh and others (TBA)] with the addition of a Staff Scientist in the Product Development Laboratory to scale up the procedures that have been developed, and a technician in the Cell Processing Laboratory for the actual

preparation of a cell product. A bioanalyst will also be appointed to carry out molecular fingerprinting of BMSCs grown in different culture conditions, and from different donors. In addition, at least one consultant will be identified and a contract will be put in place to assist investigators in the development of their protocols and IND submissions to the FDA. Actual performance of the clinical protocol will be within the institute of the clinical investigator.

V. FUNDING

The BMSCT will receive \$1.08 million dollars per year for a total of 5 years, derived entirely from the contributing institutes, with contribution in kind from the CC based on the involvement of the DTM. Yearly budgets will be submitted by the Steering Committee to the Oversight Committee on July 1st of every year. Funding decisions within the BMSCTC will be determined by the Steering Committee after discussion with the User Group. It is anticipated that the major funding decisions in year 1 will concern hiring of new staff, purchase of equipment to build the infrastructure within the DTM, and establishment of contracts for consultants, if needed. Thereafter, expenses would be primarily for the generation of autologous and non-autologous cells for use in an approved protocol(s). In the event that the budget for the first year must come to a vote of the Steering Committee, Dr. Klein will recuse himself. However, every effort will be made to gain unanimous consensus.

It is understood that the funding for the BMSCTC is to be used solely for the development of a cell product for use in clinical trials and will not be used for translational animal studies.