Stem cell research offers unprecedented opportunities in developing new medical therapies for debilitating diseases. Stem and progenitor cells have the potential to replace damaged or diseased cells and to restore vital functions. Although stem cell research is on the cutting edge of biological sciences today it is still in its infancy. To promote research in ‘cell-based therapy and regenerative medicine’, Department of Biotechnology, Ministry of Science and Technology, Government of India, proposes to support medical schools/institutes for establishment of specialized centres for cell-based therapy.

**Purpose of the support**

The primary objective of the support for creation of Specialized Centres of Cell-based Therapy is for promotion of multidisciplinary research to address clinically relevant questions. This can be achieved by integrating basic science research on stem cells and its application to clinical problem solving, thus the proposed centres would perform preclinical and clinical studies for cell based therapy. The centres are expected to concentrate on clinically relevant research, which however would include preclinical studies wherever necessary. The potential for safe new treatments can only be realized if preclinical and clinical research programs provide the basis for establishment of the new therapy.

Previously, it was thought that tissue-specific stem cells could only differentiate into cells of the tissue of origin. Recently, however, a series of studies has suggested that adult tissue-specific stem cells may differentiate into lineages other than the tissue of origin, thus exhibiting transdifferentiation. Bone marrow cells appear to have the capacity to repopulate many nonhaematopoietic tissues, such as neuroectodermal cells, skeletal myoblasts, cardiomyocytes, endothelium, hepatocytes, and epithelium of lung, gut, and skin. A novel multipotent adult progenitor cell isolated from bone marrow is reported to differentiate into cells associated with all three germ cell layers. Thus, bone marrow can be regarded as central repository for primitive stem cells that can repopulate somatic tissues.

Bone marrow, peripheral blood, and cord blood stem cells have been tried for treatment of various tissue disorders. While haematopoietic stem cells have been reported to transdifferentiate into other cell lineages including alveolar type 1 epithelial cells, bronchial epithelial cells, endothelial progenitor cells, etc., mesenchymal stem cells have been demonstrated to differentiate into a variety of non-haematopoietic tissues including bone, cartilage, tendon, fat, skeletal and cardiac muscle, and early progenitors of neural cells. In addition, mesenchymal stem cells may also promote haematopoietic stem cell engraftment. Adult skeletal muscle cells are being tried as a potential cell source for cardiac muscle cells for the treatment of heart disease. Cardiac and lung tissues are speculated to contain one or more progenitor cells that could be induced to proliferate and repair cellular damage.

Experiments in mice and animals are necessary but not sufficient for realising the potential of stem cells to develop tissue replacement therapies that will restore lost function in damaged organs. Because of the substantial biological differences between experimental animals and human development, data on experimental animals cannot be extrapolated to human. Therefore, much more

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knowledge on human stem cell biology is essential to make progress in the application of stem cell research to therapies for treatment for human diseases.

Creation of Specialized Centres of Cell-based Therapy is designed to address the need for facilities where basic and clinical investigators can transform validated hypotheses into clinical applications. The following are some of the preclinical tasks, which would precede cell-based therapy:

- Standardization of methods for isolation, culture, and storage of stem cells
- Development of standard operating procedures
- Ongoing process validation
- Provision of controlled good manufacturing practice (GMP) infrastructure.
- Controlled studies to monitor the delivery of cells and the use of appropriate controls.
- Safety monitoring
- Data entry.

**Organization of the Specialized Centres for Cell-based Therapy**

The key feature of the Specialized Centres for Cell-based Therapy (SCCT) will be to conduct comprehensive clinical research, beginning with preclinical studies which would facilitate obtaining clearance from the drug controller for conducting the Phase I–II clinical studies. Preclinical studies should be over within first two years and by the beginning of the third year of the programme clinical studies should commence.

The Task Force on Stem Cell Research will have primary responsibility for the general evaluation of the project proposals, facilitating the formulation and monitoring of protocols and evaluation of study results. Task Force may constitute subcommittees as and when necessary for evaluating or facilitating any particular task. For example subcommittees may be constituted to oversee research protocol (Protocol Review Committee), data collection and monitoring, reporting of outcomes such as clinical benefits, toxicities, adverse events, graft versus host disease, etc.

**Mechanism of support**

The DBT support for the establishment of Centre for Cell-Based Therapy is limited to a maximum period of 10 years. Under this policy the grant will be provided for 5 years initially which however can be renewed for another 5 years depending on the progress of the project.

**Eligibility and special requirements**

The objective of the Centre for Cell-Based Therapy is to stimulate multidisciplinary collaborative clinically relevant research on important public health problems. The translation of knowledge into clinical practice should be the primary goal of applications submitted in response to this initiative. Recent advances in the understanding of stem cell and progenitor cell biology, transplantation of autologous and allogeneic cells for the treatment of disease, the development of cellular and molecular imaging tools and markers for stem cells, the management of immune reconstitution after stem cell transplantation etc., offer potential novel approaches to clinical problem solving. Centres are encouraged to undertake multi-disciplinary approaches, to include projects that address more than one therapeutic area, and to propose clinical research projects leading to early phase clinical trials.

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The medical school/institute applying for the grant should have a significant number of high quality researchers in the specific area validated by their publications. It should provide physical infrastructure in form of space, electricity, water, etc. and should allow the faculty members to conduct research at the centre. The institute can recruit 2 or 3 young scientists in regular faculty positions dedicated for the project. Salary component of these young scientists will be reimbursed by DBT for initial 5 years which would be extendable for another 5 years after due process. After the expiring of the project, the institute should be willing to takeover the financial responsibility of the faculty.

The following are the special requirements:

1. Translation of findings from basic to clinical studies is an important focus of the Centre for Cell-Based Therapy; therefore, effort should be made to include both clinical and basic research in the project. The research has to be patient oriented.

2. Specialized Center applicants should provide a detailed data and safety monitoring plan for the clinical research proposed. This plan should address informed consent, recruitment, reporting of adverse events, patient safety, storage and analysis of confidential data, and dissemination of any research results.

3. The sponsoring Institute has to arrange annual meetings to encourage the exchange of information among the participating investigators, the cost of which can be included in the budget.

**Receipt of application and review schedule**

Application Receipt Date: 15 August 2005  
External Peer Review and Task Force Review Date: September/October 2005  
Release of sanction order of recommended centres: 31 December 2005

**Award criteria**

Award criteria that will be used to make award decisions include:

- Scientific merit (as determined by external peer review and Task Force review).
- Expertise and leadership qualities of the principal investigator.
- Collaborative interaction between clinical and basic research components of the required number of clinical projects, and plans for transfer of potential findings from basic to clinical studies.
- Adequacy of the environment for performance of the proposed research.
- Availability of funds.
- Programmatic priorities.

**How to apply?**

The Principal Investigators can apply in the DBT R&D/Programme support format available in the DBT website (www.dbtindia.nic.in). Twenty five hard copies of the proposal(s) along with soft copy as per above format should reach to Dr. B. M. Gandhi, Adviser, Medical Biotechnology or Dr. Alka Sharma, Principal Scientific Officer, Department of Biotechnology, Block-2, CGO Complex, Lodi Road, New Delhi 110 003. Any additional enquiry may be addressed at Telephone: 2436 0984/2436 3699; e-mail: gandhi@dbt.nic.in/alka@dbt.nic.in.