

Stem Cell Research- A Review on the Latest Indian Guidelines

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Abstract:

Stem cell research and treatments have been commenced in India with a fine swing. It is flourishing as a promising and looming area of research as the therapy aid in the regeneration of impaired or lost tissue or organ in a host. As the system of treatment is developing day by day, it is mandatory that the Government should put forth stringent rules and regulations in order to safeguard the public health. Stem cell therapy have been popularised for the fact that specialized cells in the body like nerve cells or blood cells can be developed from the stem cells derived from sources such as embryo and umbilical cord. The Guidelines developed by ICMR cater recognition for specific treatments and spare others stating that certain treatments are in still in ambiguous state and cannot be approved as therapy. There are several areas that are needed to be addressed in this area. This review summarizes the general aspects of stem cell research along with a concise study on the regulations of stem cell therapy in India.

Key Words: Stem cell therapy, Stem cell classification, Therapy regulations, Indian guidelines, Review procedures,

1. INTRODUCTION:

Stem cell medical care is publicised because it is the next relief for all ailments. The major logic which have brought the therapy into the limelight is due to the intensive capability that has been revealed by stem cells in cure of ailments typically regarded “degenerative, in curative and irrevocable” like polygenic disorders, heart ailments, neural structure injuries, Parkinson’s, Alzheimer’s disease has Stem cell studies programmes have been promoted in India by taking into account the hype and hope created by the same in the past decade. Approaches for boosting up stem cell research (SCR) are in its course of advancement. The most crucial component of the approach is the production of sufficient human embryonic stem cell (Hesc) lines. Implementation of stem cell medical care in regenerative medicine guarantee the improvement of human wellbeing by reviving the activities of cells and tissues that are impaired due to deterioration or trauma. There are several areas that ought to be carried into thought in stem cell research such as ethical, legal and social norms. Stem cells and their products constitute definition of ‘Drug’ as per the Drugs and Cosmetics Act 1940, and are classified as ‘Investigational New Drug (IND)’ or ‘Investigational New Entity (INE)’ once utilised for clinical applications. Last decade has observed the sudden growth of chaotic utilisation of stem cell based treatments despite regulating either their safety or curative effectiveness. This has paved way to the profiteering of exposed subjects. To resolve all the turmoil correlated with stem cell therapy the government with the joint effort of Indian Council for Medical Research (ICMR) and Department of Biotechnology (DBT) have fabricated ‘The National Guidelines for Stem Cell Research (NGSCR)-2017’. Based

on the response received during the public discussions, the document has been updated accordingly.

Investigation in human developmental science has paved way to the exploration of human stem cells, together with embryonic stem cells and adult stem cells. Approaches are developed for the *in-vitro* culture of stem cells, catering favourable circumstances for learning and perceiving human embryology. As a result, scientists can perform examinations geared toward deciding the mechanisms hidden within the reconstruction of single, dedifferentiated cell, the fertilized egg, into discrete cells constituting the organs and tissues of the human body. Despite it is impractical to forecast the conclusions, boundless advanced expertise in human developmental biology which carries impressive capability for therapies and remedies will be harvested by researchers and society. Stem cell studies organized by growing countries cite the chance to focus on modernization to native framework, build medical care a lot of value effective and facilitate within the economic development. Flourishing nations have attempted to exploit the ‘bioethical vacuum’ that has turn up once President Bush in 2001 called for a holdup on federal funding of human embryo stem cell research (Hesr). Grabbing the chance India have begun to plough money proportionately in several offered resources of leading technology and Hesr, within the aspiration to achieve economic success. Hindu nationalist regime in India (in the late 1990s) stirred up public and private monetary endeavour in the fields of IT and molecular biology. Interpretations of bioethical demur concerning the utilization of the embryo are laborious to search out, and appear to create no hurdle to the advance of Hesr. However though Hesr would bear asset to those tormented by Parkinson’s, Alzheimer and other ailments, the foremost vital health care facilities

appear to be elusive by an enormous part of their populations. Approach for advancing stem cell research is progressively taking structure.

2. GENERAL ASPECTS OF STEM CELLS:

Stem cells are precursor, unspecialised, dedifferentiated cells economical enough of self-proliferation, migration and differentiation. Stem cells in its basic form can be defined as the premature form of cells which are capable of generating mature cells. The fundamental characters that typify stem cells embody their ambiguous ability to refurbish on its own and drop their primary dedifferentiated state to turn into cells of varied clan. Stem cells thus have

an astounding potential to recover life. They can divide and increase their number in a brisk manner to give rise to brain, heart, spine, limbs, muscles, skin and everything else that comprises the human body^[1]. This is viable because they split symmetrical and / or asymmetrically. i.e. two daughter cells were formed from each stem cell, one of which retain its potential for differentiation and self-renewal, while the other cell direct by its own towards a given cell lineage, or they both preserve their original nature. Stem cells are able to refurbish on its own and yield mature cells with peculiar traits and activities by differentiating in response to some physiological stimulation.

3. CLASSIFICATION:

Fig. 1: Classification based on potential^[2]

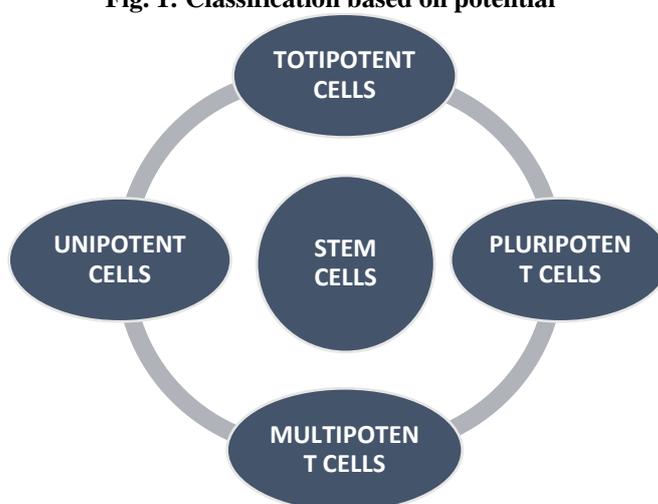


Table No.1: Definition of different types of stem cell based on potential.

TOTIPOTENT CELLS	PLURIPOTENT CELLS	MULTIPOTENT CELLS	UNIPOTENT CELLS
These cells develop in the initial stages of embryo growth, before blastocyst genesis, efficient of constructing an entire organism, along with all intra and extra embryonic tissues.	These cells which are capable to develop into any kind of cell but not into cells which result in the formation of embryonic structures such as placenta and umbilical cord.	These are hematopoietic cells, which have the capability to develop into platelets, RBC and WBC. They are capable to form a distinguishable number of cell types.	These cells can develop only into a single cell clan, are found in different body tissues. They act as cell reservoirs in different tissues.

Fig. No.2: Classification based on source^[3].

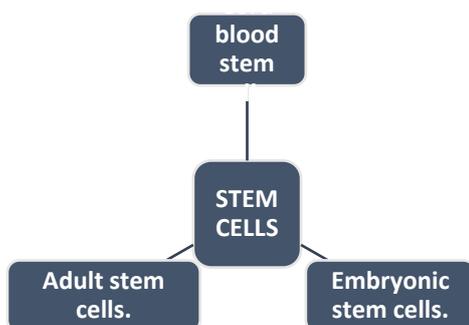


Fig.No.3: Government Departments involved in stem cell research.

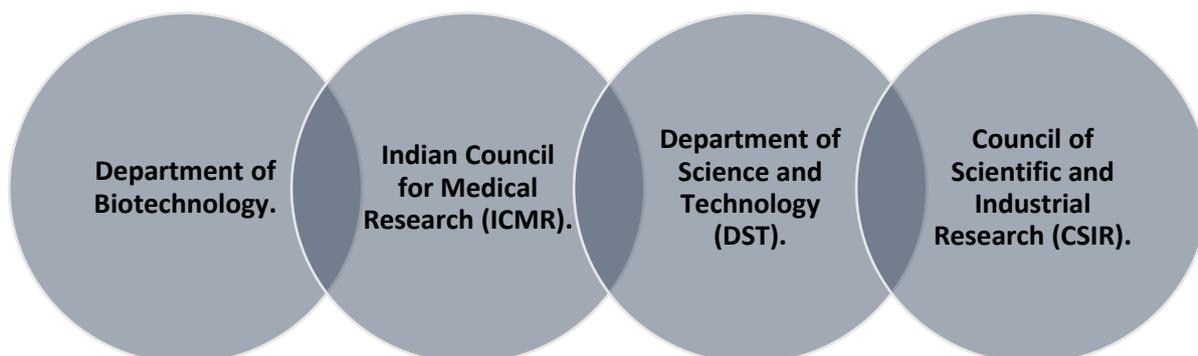
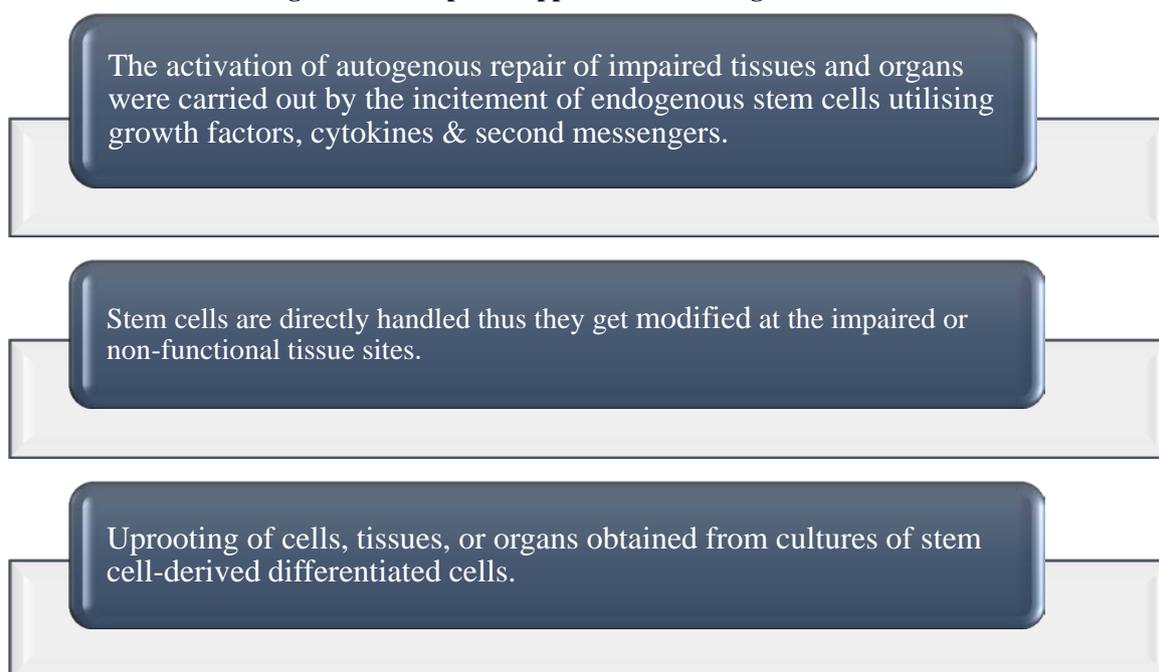


Fig.No.3: Therapeutic approaches for using stem cells ^[2].



4.0 STEM CELL RESEARCH IN INDIA:

India being a growing country with a rapid flourishing community of over 1.3 billion, still has a huge number of people thriving through economical scarcity and has scant approach to modern medicine. Contrarily with the largest group of English speaking scientific and technical professionals, India is regarded as one among the largest industrialized countries in global level excluding the United States. India is well entrenched with pharmaceutical industries and pursue to be the global pioneer in information technology area. India’s biotechnology and pharmacommerce are in a spot to register and promote pioneering technologies. Although at an inceptive phase, stem cell treatment is a swiftly thriving area in the Indian market, and besides there are over forty organizations and health institutions occupied in stem cell research all over the country ^[4].A distinct Task Force on ‘Stem Cell Research and Regenerative Medicine’ has been composed

to analyse the recommendations on the basis of their experimental merits. An institute of “Stem Cell Research and Regenerative Medicine” has been set up in Bengaluru. Guidance for “Stem Cell Research and Therapy” has been developed collectively by the Department of Biotechnology and Indian Council of Medical Research. Based on the observations gathered during public discussions (region-wise), the document has been revised accordingly.^[5] The Indian government is portraying a decisive part in supporting the growth of stem cell research. Department of Biotechnology lend explicit financial backing to proposed initiatives in this area and uphold each framework assembling and functional tasks such as clinical trials. Indian corporations have conjointly initiated to develop substances like ‘growth factors’ that are utilized in stem cell research at unquestionably diminished rates^[6].To lift the public-private cooperation endeavour in the nation, the DBT has proposed a novel program called Small Business

Innovation Research Initiative (SBIRI). SBIRI is to cater backing to high risk-pre proof-of-concept studies and the last minute evolution of studies in small and medium companies, led by pioneers with scientific backgrounds. Both the government and private industries have spent laboriously in research institutes learning stem cells. The preference of studies has lifted to a larger insistence on the clinical application of stem cells and development of a tissue culture project ^[4].

5 STEM CELL THERAPY:

For rational intentions, human embryonic stem cells are adopted in thirteen percentages of cell treatment strategies, while foetal stem cells are adopted in two percentage, umbilical cord stem cells in ten percentage and adult stem cells in seventy five percentage of the therapy. As indicated to the recent studies, the greatest significant therapeutic explanations of cell therapy have been cardiovascular and ischemic diseases, diabetes, hematopoietic diseases, liver diseases and orthopaedics. More than 25000 hematopoietic stem cell transplantations are carried out yearly for the cure of ailments such as lymphoma, leukaemia, immunodeficiency illness, congenital metabolic defects, hemoglobinopathies and many other serious disorders. The three types of therapeutic approaches followed for using stem cells are:^[2]

6. OLD INDIAN REGULATIONS REGARDING STEM CELLS:

Numerous Indian clinics are suspected of constructing fraudulent postulations regarding the effectiveness of an ample variety of stem cell medications and in few events furnish false declarations of approval from governing bodies. A collection of Guidelines for Stem Cell Research and Therapy (ICMR-DBT 2007) was furnished by the Indian Council of Medical Research (ICMR) and the Department of Biotechnology (DBT) conjointly in 2007. This 76-page document particularized accepted ethical regulations for study and procedures for formal committee authorization of stem cell activities and for their occasional observation. The matter was in line with mainstream bioethics in agreement of process and latent standards. The Guidelines imposed that clinical use of stem cells was not granted and that any use of stem cells in clinical framework must be part of clinical trial carried out after the authorization by a board assembled to manage stem cell activity the Institutional Committee for Stem cell Research and Therapy (IC-SCRT), the significant research ethics committee and the Drug Control General of India (DCGI). Scholars have recognized a disintegration of regulatory authority as a reason of dilemma for stem cell governance in addition to the unsanctioned condition of the 2007 ICMR-DBT guidelines. The ICMR is a segment of the Ministry of Health and Family Welfare, while the DBT is the segment of Ministry of Science and Technology. Perhaps the above mentioned dilemma cannot be considered as a crucial issue as such a structure also represents a persuasive manner of linking strength in intricate circumstances calling for numerous sources of competence. According to the current regulations, DBT is

an agency for financing preclinical and clinical R&D while ICMR funds research and furnish advices. The DBT do not disburse research activities taking place outside government-funded R&D programs. Its stem cell task force and committees overlook the DBT's own exploration studies omitting the clinical trials. International and national guidelines specify that clinical uses of stem cells must be as part of a clinical trial for studies carried out under the entrenched regulatory protocols ^[7].

7. REGULATIONS ACCORDING TO LATEST GUIDELINES:

Based on the 'National guidelines for stem cell research-2017' which was issued recently by ICMR and DBT provides information regarding the documents which need to get the consent from various regulatory authorities. This part deals with compulsory approvals from ICSCR, IEC and CDSCO before enlisting members for clinical trials.

- CTRI registration has been made obligatory for all Clinical Trial's adopting stem cells.
- IC-SCR registration from NAC-SCRT and IEC registration from CDSCO are inevitable for institutions to obtain consent to conduct clinical trials.
- Establishments are granted the approval to conduct clinical trial only after the registration with IC-SCR and IEC from NAC-SCRT and CDSCO respectively.
- Mandatory approvals are required from IC-SCR, IEC and CDSCO for clinical trials employing minimally manipulated autologous SSC's (ie. HSC's and MSC's) for non-homologous use of any indication or for homologous use of indications apart from those listed in Annexure III.
- Substantially manipulated stem cells are ought to have authorization from IC-SCR, IEC and CDSCO prior to the conducting of clinical trials.
- Prior approval from IC-SCR, IEC and CDSCO are mandatory for carrying out clinical trials including allogenic SSC's (with any degree of manipulation) and autologous SSC's with more than least and major manipulations.
- IC-SCR, IEC and CDSCO prior approval are compulsory for clinical trial using human pluripotent stem cells (hESC's or iPSC's) or their derivatives.
- CDSCO approval is required for any stem cell based product which is already approved and marketed outside India (or for simultaneous trial in India) provided it requires approval from CDSCO.
- A clearance from IC-SCR and IEC followed by approval from CDSCO are required for any clinical trial with a product predetermined to be authorized and marketed.
- Separate approval for individual elements and in combination is required from CDSCO proceeded by clearance from IC-SCR and IEC for tissue designed or combination output ^[8].

8. MECHANISM OF REVIEW PROCEDURES:

- Discrete tracking and reviewing system is crucial at both the organisational and national levels.
- The National Apex Committee for Stem Cell Research (NAC-SCR) which scrutinizes and oversees research activities and bring out strategies for clinical studies have been instituted.
- The authorisation and supervision of researches at institutional level is carried out by the Institutional Committee for Stem Cell Research (IC-SCR).
- The particular regulatory board shall confirm that the analysis, authorisation and scrutinizing of the research activities should be in agreement with the National Guidelines.
- Obligatory establishment of IC-SCR and enrolling with NAC-SCRT.

9. THE NEED FOR REGULATIONS:

According to the professional speculation, “stem cell therapy”, unlike the other medicine practice needs to be consistent to be used economically. The economic management of stem cell therapy is clearly defined by ICMR but the clinics bolstering the same are utilizing the loophole that there are no sufficient regulations for the law about the same in the country. Once the law is entrenched, the centres which operate stem cell therapy would fall in line with the law. The primary reason which pulls back the advancement of stem cell research centres in India is because the people are not dire about the previously mentioned therapy. The radical reason behind this is the affordability factor. Only one in 1000 can manage to take the medication, so there is no desperate demand for the same. Unlike United States, India does not have the brisk based science to conduct the Human research. The Government have brought in rigorous guidelines while performing stem cell research.

Studies on human members including cells and tissues extracted from human embryos, foetuses or any alternative origin must shield human rights, safety, dignity, and basic freedom. They offer distinct clinical assets as reported through controlled clinical trials, there are equitably startling peril for its usage. The stem cell collection, processing, storage and clinical application lift explicit attention.

10. CONCLUSION:

The thriving universal concern in stem cell research and therapy authorize advancement of a rigorous regulation and surveillance simultaneously with means to strengthen public knowledge and perception. Special exertions should be created to uphold fair availability to the profits of stem cell research. Intellectual property regimes for stem cell research ought to set conditions that don't impede key studies or saddle future product advancement. It is crucial that there be a public that's civilized and familiar concerning the ethical and policy considerations raised by stem cell research and its applications informed public

discussion of those perplexity should essentially be on the adopting of the science correlative with the stem cell research, and it should captivate a broad cross-section of society¹⁰¹. It is crucial for the inhabitants to engage in a full and sophisticated manner in the civic policy speculations concerning the progress and application of the novel technologies that are possible to possess serious public brunt. National authorities are pro-active in promoting and upholding this area. However there are numerous challenges still existing in the stem cell regulations such as the Government have imposed restraints on stem cell banking and therapeutic use in order to safeguard the patients receiving treatments. The government intent to hamper exploitation and commoditization of resources through the new guidelines.

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