Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 7, Issue, 04, pp.15213-15218, April, 2015

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

PLANNING AND DESIGNING OF A STEM CELL CENTRE IN A TERTIARY CARE HOSPITAL

Dr. Sameer Mehrotra and *Dr. Sunil Basukala

Department of Hospital Administration, Armed Forces Medical College (AFMC), Pune, Maharashtra

ARTICLE INFO

Article History:
Received 29th January, 2015
Received in revised form
15th February, 2015
Accepted 23rd March, 2015
Published online 30th April, 2015

Key words:

Stem Cell Centre,
Research,
Laboratories,
Guidelines.

ABSTRACT

Background: Stem cell based therapies have been hailed as futuristic medicine that holds promise of curing some of the currently untreatable diseases. As stem cells can be grown and transformed into specialized cells with characteristics consistent with cells of various tissues such as muscles or nerves through cell culture, their true use in medical therapies has been proposed. There are several medical, ethical and legal issues that need to be regulated by a national authority. Some countries have resolved this issue by drawing up National Guidelines and regulatory mechanisms for the use of stem cells for research. In India the Department of Biotechnology in collaboration with Indian council of Medical Research has come up with appropriate regulations and guidelines for conducting stem cell research.

INTRODUCTION

Humans in their relentless pursuit to defeat death and disease have always been looking to new and innovative tools in their arsenal. Along with urbanization and development, new and some existing diseases have been affecting mankind with renewed vigor. Stem cells although have been since 1960s, but their increasing value in the management of various disease has been realized very lately. Although there are various arguments for their increased use and otherwise, it is gradually being realized that stem cell therapy is here to stay. It is thus apt that the necessary infrastructure including physical facilities, planning and designing of such Centre is scientific so that the optimum benefit is derived from this great boon to mankind. Stem cells are cells found in most, if not all, multi – cellular organisms. They are characterized by the ability to renew themselves through mitotic cell division and differentiating into a diverse range of specialized cell types. Research in the stem cell field grew out by findings by Canadian scientists Ernest A. McCulloch and James E. Till in the 1960s (Becker *et al*., 1963 and Edward *et al*., 2001). There are two broad types of mammalian stem cells including the embryonic stem cells that are found in blastocysts and adult stem cells that are found in adult tissues. In developing embryo, stem cells can differentiate into all of the specialized embryonic tissues.

Corresponding author: Dr. Sunil Basukala
Department of Hospital Administration, Armed Forces Medical College (AFMC), Pune, Maharashtra

In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing specialized cells, but also to maintain the normal turnover of regenerative organs, such as blood, skin or intestinal tissues. As stem cells can be grown and transformed into specialized cells with characteristics consistent with cells of various tissues such as musclesor nerves through cell culture, their true use in medical therapies has been proposed. In particular, embryonic cell lines, antilogous embryonic stem cells generated through therapeutic cloning and highly plastic adult stem cells from the umbilical cord blood or bone marrow are touted as promising candidates.

Stem cell based therapies have been hailed as futuristic medicine that holds promise of curing some of the currently untreatable diseases. Use of stem cell research has been controversial especially with reference to the use of human embryos for obtaining stem cells (Lanza *et al*., 2004). There are several medical, ethical and legal issues that need to be regulated by a national authority. Some countries have resolved this issue by drawing up National Guidelines and regulatory mechanisms for the use of stem cells for research. In India the Department of Biotechnology in collaboration with Indian council of Medical Research has come up with appropriate regulations and guidelines for conducting stem cell research (Siminovitch *et al*., 1963).Although there has been some focus on the above mentioned issues, there is very little attention provided to the planning and designing aspects of the laboratories involved in the stem cell research and therapeutic activities and thus no guideline/ norm is available of this issue.

The built environments and its various aspects have a tremendous impact not only in undertaking satisfactory performance of activities but also in ensuring the safety of patients and the staff (Svendsen and Ebert, 2008 and Guidelines of Stem Cell Research and Therapy, 2007).

MATERIAL AND METHODS

A systematic review of various studies related to Stem Cell Centre was performed. Certain exclusion and inclusion criteria were framed to select the articles for the study. The standard data base for searching the articles were used. Guidelines available on the subject and the search material were studied and analyzed.

Facility planning for stem cell centre

Physical Facilities (Treleaven and Barrett, 2009; ISSCR, 2003 and ISSCR, 2003)

The authorities in the field of stem cells suggest that a functional Stem Cell Centre should have following sections:

a) Stem cell Collection laboratory
b) Stem cell Processing and production laboratory
c) Stem cell Preservation laboratory
d) Stem cell Preservation laboratory
e) Core blood Bank
f) Stem cell Therapy Centre

However, international Societies for stem cell research (ISSCR) and Australian stem cell Centre elaborated it further and recommends the following comprehensive facilities for a stem cell Centre:

a) cGMP regulated clean rooms
b) Processing laboratories
c) Production laboratories
d) Core laboratories foe cell sorting and isolation
e) Tissue Culture laboratory
f) Biochemistry and molecular biology laboratory
g) Media preparation facility
h) Centralized wash- up facility for glassware and instruments
i) Administrative offices and workstations
j) IT support Centre
k) Conference hall
l) Stem cell clinical trial room
m) Cafeteria
n) Training laboratory
o) Storage spaces

The facility to have dual power back up, central monitoring system, advance fire system with alarm system and sprinklers, automated temperature control, information security architecture, manned security system with limited access protocols. The stem cell banks should have provisions for maximum safety against natural calamities like rains, floods and earthquakes to endure safety of preserved samples.

Laboratory area: (ISSCR, 2003)

It should be present inside the facility, the laboratory area must be divided into 3 to 4 clean rooms of different classes, based on the kind of processes that need to be carried out. The details are as under:

a) General laboratory: class 1,00,000 clean room
b) Processing laboratory: class 10,000 clean room
c) Tissue culture laboratory: class 10,000 clean room
d) Cellular Expansion area: class 10,000 clean room

Open cell handling procedures must be performed in class 100 environments. However UK stem cell bank and Newcastle University recommend cell processing laboratories should be upgrade class B (class 100, IOS grade 5) clean rooms.

Storage area

The stem cells in Cryo-bags are stored in tanks that are cooled by vapors or liquid nitrogen. Liquid nitrogen is less subject to fluctuations in temperature. The storage temperature is maintained at -196 C. the computer system constantly monitors and tracks stem cells at all times. The tanks have inbuilt trolleys, for shifting in classes of any calamities (Gorin, 1992; Aird *et al*., 1990 and Stiff, 1991).Basic services (FACT-JACIE, 2010 and UNDP/World Bank/WHO) infrastructure of the Centre should be planned according to the services provided. The basic infrastructure facilities include:

a) Quality waste supply for analytical purpose
b) Analytical work area
c) Specimens/ samples / slides storage facility including cold storage
d) Record room
e) Facility for cleaning of glassware
f) Waste disposal facility including Biomedical waste
g) Fire safety equipment
h) Separate area for staff for hand washing, Waiting and storing food, drinks
i) Communication facility with other Centre
j) Transport of specimen/ samples

Backup power supply

More procedures are carried out in steps and in cyclic fashion at prespecified time. Therefore, there should be no interruption in power supply to the incubator and to other essential services in the Centre. Given the power supply situation in India, it is, therefore, imperative that a power back up in the form of Ups systems or a captive power generation system is available full time (UNDP/World Bank/WHO).

Steps for Vermin Proofing

Adequate steps should be taken to the whole Centre vermin proof, with suitable traps for preventing insects and other forms of unwanted creatures entering the Centre. This essential detail should be planned at an early stage because no pesticide can be used in a fully functional Centre, as it could be toxic to the cells and other specimens.

Hospital support services to stem cell centre (FACT-JACIE, 2010 and Carr *et al*., 2007)

A stem cell Centre should also consists of designated inpatients and outpatients treatment facilities with trained staff.

Under mentioned hospital support services should be present close to a stem cell Centre, having a transplantation Programme.

a) Routine laboratory support
b) Molecular laboratory support
c) Blood bank support
d) Diagnostic and interventional support
e) Nuclear medicine
f) Specialized laboratory support for HLA typing

Ancillary media services (Treleaven and Barrett, 2009 and FACT-JACIE, 2010)

Services of following departments should be available to stem cell Centre to any emergency and complications of transplant Programme:

a) Intensive care unit
b) Accident and Emergency department
c) Day care Centre
d) Operation theatre
e) Infectious disease department
f) Nephrology department
g) Pulmonary medicine, Psychiatry and Phycology
h) Gastroenterology department
i) Radiation oncology
j) Surgery
k) Cardiology
l) Endocrinology
m) Urology

Other Services

Occasionally services of other departments like Gynecology, Dermatology, Ophthalmology, Anesthesiology and Neurology may be required. Pharmacy should be available with 34 hour service. A BMT transplant registry is also required in case of transplant program (Treleaven and Barrett, 2009).

A preclinical animal experimentation facility

Should be nearby. The facilities for research are imaging facility, in – vitro research GLP grade laboratory and their associated facilities and services (Guidelines of Stem Cell Research and Therapy, 2007 and Treleaven and Barrett, 2009).

Apheresis facility

A convenient and reliable apheresis facility should be part of the Centre. A minimum of two cell separator should be present, out of which one functions as a backup. Apheresis facility should have provisions for emergency resuscitation at all times in immediate vicinity (Treleaven and Barrett, 2009 and FACT-JACIE, 2010).

Planning of areas based on traffic in the facility (Treleaven and Barrett, 2009)

A well designed stem cell Centre should have an unrestricted area and restricted area as detailed below (Fig 1). Some of the spaces mentioned below could be combined(that is, the same space may be used for more than one purpose). However, the space provision for restricted area cannot be combined with those for the unrestricted and vice versa.

The unrestricted area

A reception and waiting room for patients

This room at the entrance of the facility shall act as reception cum registration area and waiting area. Hence, requisition forms and reports are disbursed

A room with privacy

A room with privacy for interviewing and examining the patients. Adequate measures must be taken to ensure that history taking and examination are carried out in strict privacy, maintaining the dignity of patients. In case a male doctor examines a female patients, there must always be an attendant present. The room must be equipped with an examination table.

General purpose clinical laboratory

This laboratory must be equipped to carry out basic laboratory tests.

Store room

A well-stocked store for keeping essential stock, especially those items that have a long lead time. Facilities must be available for refrigeration for items like media and non-refrigerated conditions for storing needles, catheters, petri dishes.

Record room

Record keeping must be computerized as far as possible so that date is accessible foe analysis at a later date. A user friendly software Programme should be selected for maintaining patient records, treatment carried out, outcome and follow up.

Autoclave room

A separate facility must be used for sterilizing and autoclaving

Toilets along with facilities for differently able persons

Toilets for staffs

The restricted area

The restricted area will house the clean rooms, cryopreservation area and related facilities. Entry to a clean room must be strictly controlled and access should be through a change room having wash hand basin and an anteroom (HICPAC, 2003). The restricted area must be air- conditioned where fresh air filtered through HEPA filters is circulated at an ambient temperature of 22-25 °C.

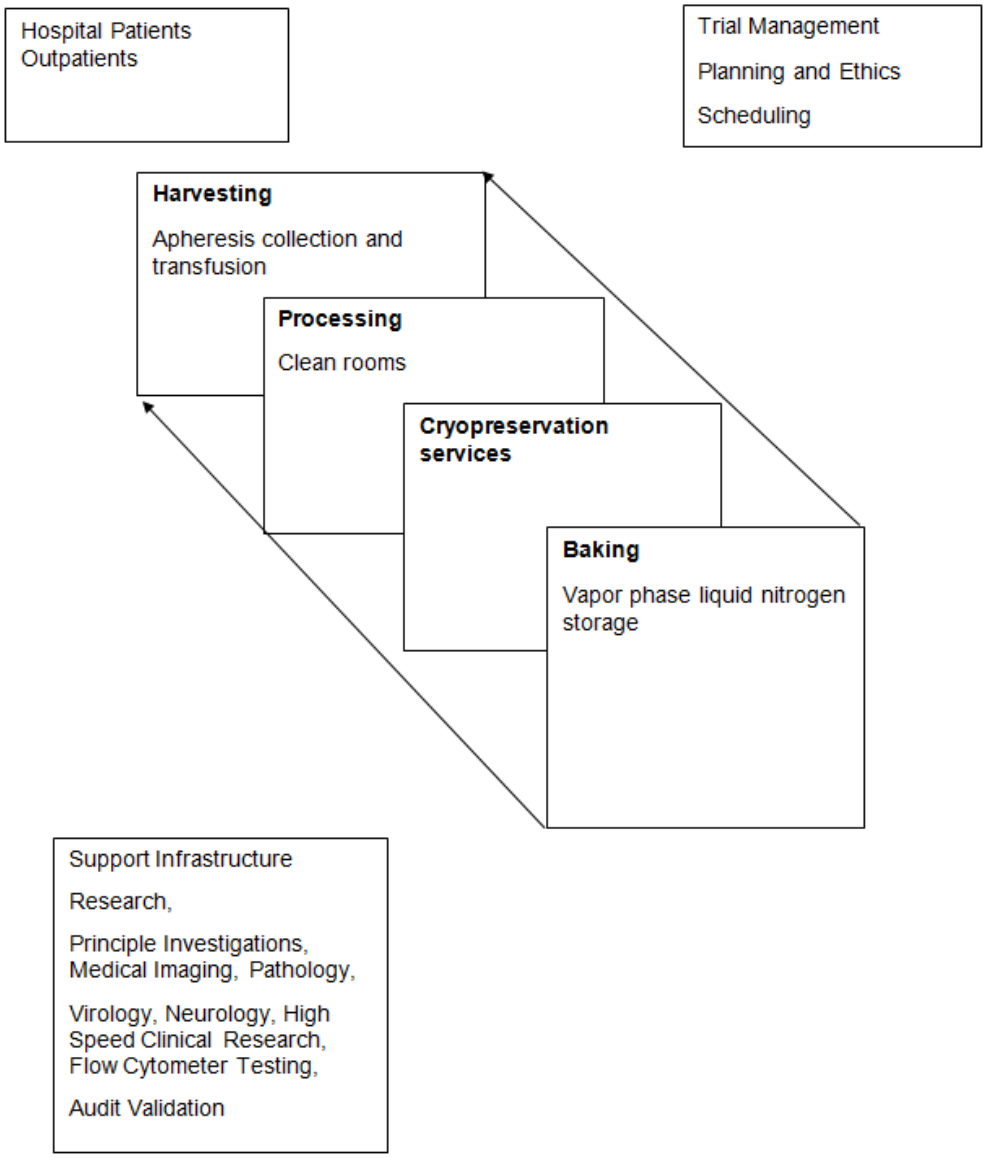

Fig. 1. Stem cell processing in a Centre

Staffing requirements of a stem cell centre (Guidelines of Stem Cell Research and Therapy, 2007; FACT-JACIE, 2010 and HICPAC, 2003)

Indian guidelines for stem cell research and therapy lay down following job position for a Centre

a) Head/ officer in-charge
b) Collection or processing facility head
c) Collection or processing facility medical head
d) Program head
e) Quality management supervisor
f) Technicians

The training, continued medical education and quality management should be a continuous process and should be documented.

Essential qualifications

Qualifications, experiences and job profile of some of the key staff is as under

a) **Laboratory in charge:** This individual should have relevant doctoral degree or is qualified and experienced in cell processing facility. He may also serve as medical head. Individual is responsible for all procedures and administrative operations if the cell processing facility, including compliance with standards.
b) **Facility medical head:** This individual is a licensed physician and is directly responsible for the pre collection evaluation of the donor, final approval of the donor for the collection, care of any complications arising from collection and compliance of the collection facility with standards
c) **Collection facility in charge:** this individual is responsible for all technical procedures and administrative operations of the collection facility. Preferably should have a doctoral degree or qualified by post-doctoral training. Should have 01 year experience in collection procedures should have performed 10 collection procedures.
d) **Processing facility in charge:** he is responsible for all technical procedures and administrative operations of the

processing facility. Preferably should have a doctoral degree or qualified post-doctoral training or has experience for the scope of activities carried out.

e) **Program head:** this individual is the licensed physician responsible for all administrative and medical operations of the clinical transplantation program, including compliance with standards.

Associated staff: other important associated staff required for smooth functioning of a Centre is as under:

a) **Apheresis staff:** A duly qualified and experienced medical director is essential for apheresis facility. Medical director should have a trained and experienced medical staff for care of patients undergoing apheresis (Treleaven and Barrett, 2009).
b) **Apheresis coordinator:** A coordinator is responsible for maintain the apheresis waiting list and its smooth functioning
c) **Product processing staff:** The facility must have a medical director as in-charge. Ideally, there, should be a minimum of two individuals with experience to be able to independently undertake cellular product manipulation and cryopreservation.
d) **Social service:** undergoing a stem cell therapy is a major life event for the patient and the family with significant social, psychological and financial implications. The social workers should see every patients and their family pre-HSCT, during and post HSCT.
e) **Clinical and diagnostic staff.** The Centre may require services of other hospital staff such as microbiologist, embryologist, pathologists and radiologists.

Providers of the following services should be available in stem cell Centre

a) Cleaning and housekeeping
b) Maintenance and repair
c) Environmental services
d) Engineering services
e) Information technology
f) Security

The roles and responsibilities of the staff should be clearly outlined. A Programme for technical training and updating of skills on a regular basis should be in place. The Centre should maintain a personnel file of all the technical and non- technical staff employed and conduct periodic staff evaluation. The actual numbers of staff will depend on the number of annual procedure performed.

Transplant staff

The ASMBT recommends that each Centre have a transplant team that includesa 'program director' and at least one other physician experienced in transplant medicine. For collection, Services of anesthesiologist is also required. The director should be board certified and have two year experience or one year training in transplant medicine. Physicians should maintain knowledge and skill levels by an appropriate continuing education program (ASCTA, 2009). The continuity of nursing care is also important, since the majority of care is actually delivered by the nurses. A single coordinating nurse is invaluable. There should also be a backup system for all personnel essential to Programme. Training of Centre staff mostly occurs through mentoring by experienced people in concerned field. Continuous education for stem cell Centre staff should be carried out and documented, annual professional society meetings and participation in intramural journal clubs should be promoted. Documentation of a laboratory staff member's proficiency in performing clinical procedur.es should be recorded and updated regularly.

Indian Scenario

Government of India realizes the future possibilities due to stem cell research and has allocated more than Rs.300 crore over the last five years towards research in stem cell technology. Since, the Programme is government funded, it focuses on diseases that affect millions of Indians rather than exotic diseases. The Indian Council of Medical Research (ICMR) and the Development of Biotechnology(DBT), New Delhi have started National stem cell initiatives to priories research funding and focus on clinical applications. The national task force on stem cell established in April 2005, is taking these plans forward. The key components of the Indian strategy are, creation of centers of excellence, virtual network of centers, generation of adequate human Embryonic Stem Cell (hESC) lines, human resource development through training and overseas fellowships etc.

Conclusion

Stem cells are derived from embryos, fetal and adult tissues. Today, they have acquired mystical status as they are master organizer of all the living organisms and can give rise to any tissue in the body being the carriers of the immortal DNA. The stem cells center is the nerve center of research, storage and therapy and involves almost all branches of medical sciences. However, the only clinical therapy approved is bone marrow therapy and no other stem cell therapy involving adult, fetal and embryonic cells has been approved world over. Although much hype and exaggeration exist, the estimate of market size of 90 billion by 2015, gives hope to million not responding to conventional treatment.

REFERENCES

Aird, WC., Labopin, M., Gorin, N. and Austin, JH. 1990. Long-term cryopreservation of human bone marrow. Blood; 76 suppl1: 525

American Stem Cell Therapy Association. ASCTA. Lab Practises Guidelines Version 1.0, 2009.

Becker, AJ., McCulloch, EA. and Till, JE. 1963. Cytological demonstration of the clinical nature of spleen colonies derived from transplanted mouse marrow cells. Nature; 197: 452- 4

Carr CA, *et al*. MRI Tracking of Systematically Administered Bone Marrow Stem Cells. Journal of Molecular and Cellular Cardiology, 2007, Vol 42 No 6.

Edward, BD., Lister, J. and Law, P. 2001. hematopoietic stem cell therapy. Churchill Livingstone; 688-712.

FACT-JACIE, 2010. International standards accreditation Manual, 4th edition, version 4.2.

Gorin, NC. 1992. Cryopreservation and storage of the stem cells. In: Areman E, Deeg H, Sacher R, editors. Bone Marrow and stem cell processing: a manual of current techniques. Philadelphia: Davis.

Guidelines of Stem Cell Research and Therapy, 2007. Department of Biotechnology & Indian Council of Medical Research.

Handbook of Good Laboratory Practises. UNDP/World Bank/WHO

http://www.Australianstemcellcentre.org

ISSCR, 2003. "Stem cell research regulations in the European Union". International Society for Stem Cell research, October 17.

Lanza, R., Gearhart, J. and Hogan, B. 2004. Regulations and Ethics of Stem Cell therapy. In: Handbook of stem cells, Volume. Elsevier Academic press; 747-93.

CDC and the Healthcare Infection Control Practises Advisory Committee (HICPAC) U.S. Department of health and Human Services, Centre for Disease Control and Prevention (CDC) guidelines for Environmental Infection Control on Healthcare facilities, Atlanta, 2003.

Siminovitch, L., McCulloch, EA. and Till, JE. 1963. The distribution of colony-forming cells among spleen colonies. *Journal of Cellular and Comparative Physiology*, 62; 327-36

Stiff PJ. Simplified bone marrow cryopreservation using dimethyl sulfoxide and hydroxyl-ethyl starch as cryoprotectants. In: Gee AP, editors. Bone Marrow processing and purging: a practical guide. CRC press, Boca Raton, 1991.

Svendsen, CN. and Ebert, AD. 2008. editors. Encyclopedia of stem cell research. SAGE; Vol 1& 2

Treleaven, J. and Barrett, AJ. 2009. Hematopoietic Stem Cell Transplantation in Clinical Practice. Churchill Livingstone.

****