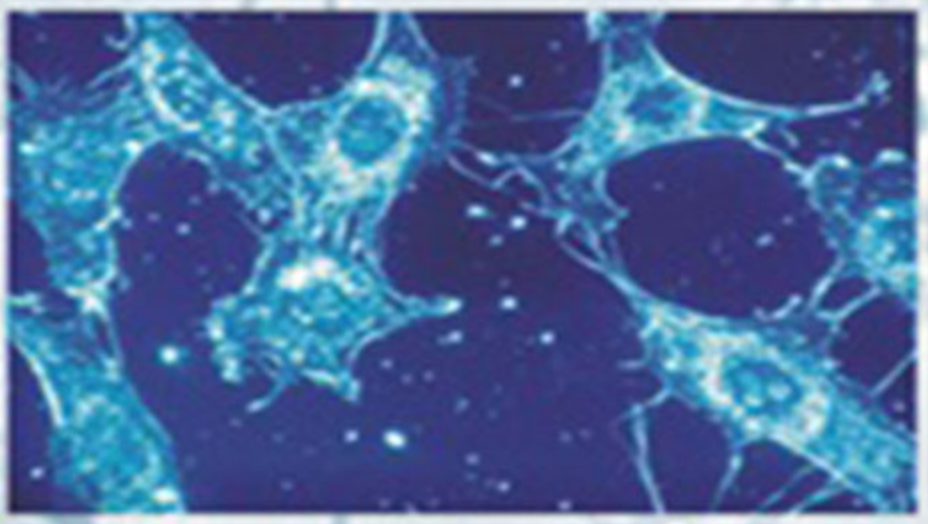
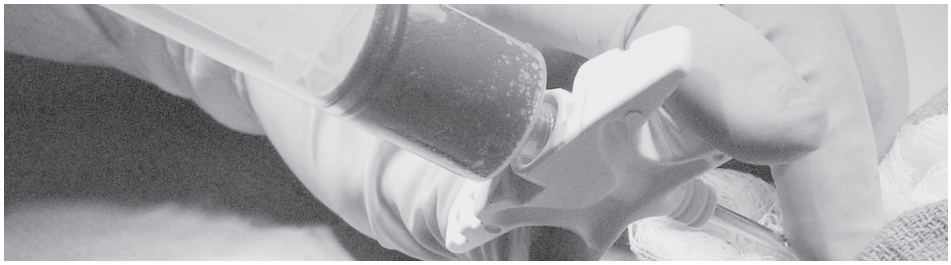


Regenerative Medicine

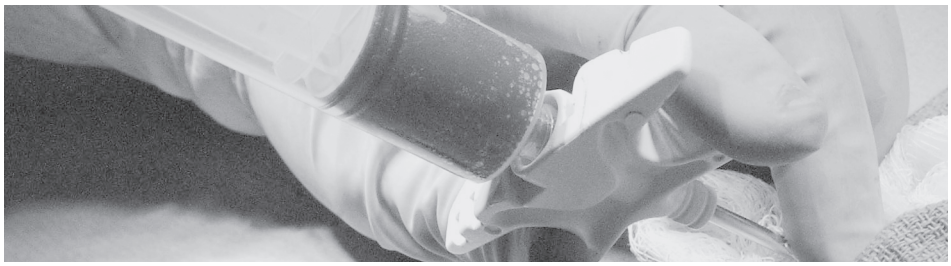
Stem Cells and Their Applications

K.R.S. Sambasiva Rao
K. Ananda Krishna

Regenerative Medicine



Regenerative Medicine: Stem Cells and Their Applications



K.R.S. Sambasiva Rao
and
K. Ananda Krishna

Center for Biotechnology
Acharya Nagarjuna University
Guntur 522 510
Andhra Pradesh, India

Foreword

Discovery of the human embryonic stem cells by James Thompson from University of Wisconsin, USA in 1998 and the subsequent controversy it generated, leading to a ban on embryonal cell research in USA, has made "stem cells" the most discussed scientific subject all across the globe. Lay person even in the remote areas are aware of stem cells, even though their information may be erroneous. Another fallacy it has generated is that 'stem cell' refers only to embryonic stem cells. Those of us carrying out stem cell research for over three decades, find this situation surprising when even regulatory bodies believe in the fallacy.

Stem cells were discovered in the seminiferous tubule by LeBlond and co-workers nearly a hundred years before. However, the stem cell concept and the foundation of stem cell biology was laid by Prof. Lazlo Lajtha, a pathologist by training at the Paterson Institute of Cancer Research, Manchester, UK. Using the haematopoietic tissue, bone marrow, he showed a hierarchy of stem cells which maintained blood cell production throughout the life

of an individual. Later, several researchers showed that stem cells were present in skin, intestinal lining and other tissues where the functional end cells had short life span and needed to be replaced constantly. These stem cells had a unique property, that of self renewal and when they divided, unlike other somatic cells, resulted in two cells, one of which would remain a stem cell, whereas the other would gradually lose the self-renewal property and differentiate into progenitors which divided several times to give rise to the functional end cells. The best studied stem cell system is the haematopoietic stem cells and the male germ cells as well as the embryonic stem cells.

Pioneering work of Prof. Mc Culloch and Till, both Canadian researchers in 1961 using the mouse model, showed that bone marrow from inbred mice donor could be transplanted into a recipient, whose bone marrow was destroyed, resulting in complete reconstitution of the haematopoietic system. This paved the way to transplantation of marrow in human subjects, by Prof. Donnel Thomas, at Seattle. He successfully cured a thalassaemic patient by transplanting marrow from a normal HLA matched donor. Bone marrow transplantation is the first clinical use of stem cell, because it is the stem cells from the donor marrow which reconstitute the haematopoietic system of the recipient.

Allogeneic bone marrow transplantation is the most important clinical use of stem cells to treat diseases caused by defective stem cells in the haematopoietic tissue. Bone marrow transplantation is a well established clinical procedure over 40 years. Some of the prominent diseases that can be treated successfully are as follows:

(i) Leukemia

(ii) Anemia

(iii) Thalassaemia

(iv) Myelodysplastic syndrome

An important advance in the clinical use of haematopoietic stem cells is the discovery of clinically useful stem cells in the umbilical cord blood, which can be easily collected without harming the child or mother, at the time of child birth. Hal Broxmeyar at the Memorial Sloane-Kettering Centre, New York showed that the umbilical cord blood contains significant number of stem cells which have the same properties as the haematopoietic stem cells from the bone marrow. Several other researchers in many laboratories including the Cancer Research Institute, Tata Memorial Centre, made similar observations,

which lead to enormous effort to investigate whether umbilical cord blood derived stem cells were clinically as efficient as the bone marrow derived cells, in reconstituting the haematopoietic system. In 1989 Elaine Gluckman in France performed transplantation using umbilical cord blood stem cells and successfully treated a child with Fanconi's Anaemia.

Several diseases such as Parkinson's result due to degeneration of functional end cells. Till date, these diseases remained incurable. However, clinical observation in patients show that bone marrow contains stem cells which are capable differentiating into non-haematopoietic cells, when they are present in the novel tissue environment. This is called 'transdifferentitation' and the property of changing their fate is 'plasticity'.

'*In vitro*' and animal experiment have show that these stem cells can be used in humans to regenerate lost tissues such as neurons. Some of the applications which are already in clinical use are as follows:

1. Revascularization in limb ischaemia.
2. Regeneration of hepatocytes.
3. Corneal reconstruction using the limbal stem cells.
4. Healing of non-fusing fractures.
5. Regeneration of cartilage in joint disease.
6. Revascularization of the myocardium following ishaemia of coronery artery.
7. Spinal cord injuries.

Several other diseases like Parkinson's and Type 1 diabetes will soon follow.

The umbilical cord blood because of its higher content of very primitive stem cells with high degree of plasticity is expected to be more important compared with bone marrow or other sources. The cord, which contains about 1 in 200 mesenchymal stem cells is an exciting new source of stem cells which has great promise. The embryonic stem cells have even greater potential, however, they have also the defect of becoming tumour.

In conclusion, stem cells from the adult tissue as well as embryonic are on the way to revolutionize medicine by becoming the most important tool of "Regenerative Medicine".

The book entitled "*Regenerative Medicine: Stem cells and their applications*" by Prof. Sambasiva Rao and his colleague is an useful contribution to the student community pursuing advanced studies in Medical Biotechnology. The book is well researched and uptodate in information. It is well presented and easy to comprehend. Prof. Rao has brought his long experience in teaching Biotechnology to post graduate students to make it a valuable contribution towards curriculum development.

I sincerely hope that student and young researchers make full use of this valuable book.

Dr. S.G.A. Rao
Founder President
Society of Regenerative Medicine and Tissue Engineering
#117, Venkateshwaranagar, Jakkur Post, Bangalore – 560 064
Tel: 91-080-65652220/28462175
Email: srbiotechnology@gmail.com, sgarao@yahoo.com

Preface

Stem cells are the undifferentiated cells that play a major role in regenerative medicine. These cells have the ability to self-replicate and transform into an array of specialized cells in the human body. In future, stem cells can be used to treat a wide variety of medical conditions and diseases. For instance, they can be used to produce insulin-secreting cells for the treatment of type I diabetes, to generate liver cells for patients with liver failure, to treat neurodegenerative disorders like Alzheimer's and Parkinson's disease, to cure myocardial infarction *etc*. Thus, we envisage a possibility to restore the normal functions with the application of stem cells.

Stem cell therapy is a cutting-edge technology and a breakthrough in the field of regenerative medicine. The principal objective underlying the writing of "Regenerative medicine: *Stem cells and their applications*" was to emphasis on this rapidly growing area of science. The book on "Regenerative medicine: *Stem cells*

Regenerative Medicine : Stem Cells and their Applications

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Author : K R S Sambasiva Rao And K Ananda Krishna