

**MARKET**

India is one of the few countries in the world pursuing stem cell research. But regenerative medicine, comprising stem cell therapy and tissue engineering is at a nascent stage in India. Today, increased focus on R&D and demand for better and healthy life has made it possible to receive stem cell therapy, in combination with gene therapy, for diseases caused due to physical trauma like spinal cord injuries or even for degenerative conditions like Parkinson's Syndrome. According to Datamonitor, while the global stem cell therapy market is projected to be worth more than \$30 billion, the Indian stem cell market is likely to be worth \$540 million by 2012. Until recently, the promise of stem-cell therapy centred around the ability of stem cells to alter into virtually any kind of cells. But researchers are finding that stem cells may have other healing effects. In recent studies, scientists have observed stem cells acting as anti-inflammatory agents, reducing swelling and even scarring when administered to injured tissue.

With diseases like Parkinson's Syndrome taking a toll on human life, the need for stem cell therapy is also increasing. K V Subramaniam, President and CEO, Reliance Life Sciences, informs, "In our estimate, by 2011 about 164.4 million patients suffering from



As on date more than 25,000 cord blood samples have been processed and stored in India alone, and growing a pace of about 25 percent year-on-year. Globally more than a million such samples have been stored and more than 10,000 such stores samples being released for therapy to save patients from over 75 life threatening diseases

Mayur Abhaya Srisrimal  
Executive Director  
LifeCell International

diabetes, cardiovascular disorders, neurological disorders, burns and wounds, osteoarthritis, osteoporosis, bone, cartilage (joints and replacements), liver disorders, congenital abnormalities and neoplasms would benefit from stem cell therapy in India. Presently, stem cell therapy has good potential in ocular, cardiovascular, and neurological disorders."

**Regulatory power**

Internationally, cord blood banks are regulated by several regulatory agencies of which the most notable ones are the American Association of Blood Banks (AABB), and the Foundation of Cellular Therapy (FACT). In India, the Indian Council of Medical Research (ICMR), issued national guidelines for stem cell research and therapy in November 2007. Standards for processing and storage of cord blood are described in the national guidelines and at present is governed by the Drug Controller General (India) DCG (I), under the general scope of blood banks. However, Mayur Abhaya Srisrimal, Executive Director, LifeCell International, points out, "As of today these guidelines have yet to become law and hence any violations of the same cannot be punished. Nevertheless, these guidelines act as a moral binding for companies who work along ethical practices, and would thus set the tone for research and therapy in India. One of the key tenets of this guideline is that all work done in the area should be registered with the National Apex Council for Stem Cell Research and Therapy (NAC-SCRT), though the implementation of the same is decentralised, and managed at the institutional level."

Adds Subramaniam, "Though the regulatory environment in India is, by and large, conducive to stem cell research, there is still a need for regulation of individual investigator (doctor) initiated cell based therapies, as these tend to be conducted in variance with international standards of clinical trials and cell processing and the imponderables on safety and efficacy are not scientifically addressed. Outcome of these initiatives are also not published in international peer-reviewed journals and presented in international conferences of repute." He adds that in the absence of such regulation, stem cell therapies can become analogous to beauty parlour procedures, which will be counterproductive and risky for patients.

**Stem cell research in India**

According to various estimates, there were more than 40 institutions and hospitals engaged in some form of embryonic and adult stem cell research in India during 2007. Currently, most of the research effort seems to be directed at ophthalmic and cardiology related stem cell based therapeutic options. However, banking of cord blood is a mushrooming ancillary industry that feeds the growing stem cell research industry in India, states Jumana



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Barnagarwala, Head-Healthcare Consulting, Principal Consultant, Datamonitor. The first private cord blood bank was launched in 2002 by Reliance Life Sciences. Although cord blood banks are supposed to be registered with the DCG(I)'s office, there is still very little regulation in this market. In 2004, the Department of Biotechnology (DBT) was requested to focus more on treatment of genetic disorders using stem cells by a parliamentary committee. Despite that, very little progress has been made in terms of actual clinical trials for therapeutic use of stem cells.

However, going ahead, Barnagarwala informs that 2009 will witness the launch of India's first ever clinical research facility for stem cells and regenerative medicine at Hyderabad. This initiative has been jointly established by the Centre for Cellular and Molecular Biology (CCMB) along with Nizam's Institute of Medical Sciences. With this initiative there could be increasing numbers of clinical trials using stem cell based research in the coming years.

Speaking on research in India, Jyothsna A Rao, Research Director, CRYO Stemcell Karnataka, avers, "The

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Indian stem cell segment, which is restricted to basic research, is yet to make significant strides in the field, which could tentatively lead to ground breaking discoveries. The clinical scenario is more heartening as there are a few groups (companies/hospitals) going ahead with clinical applications of stem cells and offering it as treatment option to deserving patients.

There are many licensed banks operating in the country such as LifeCell International, Reliance Life Sciences, Cryo-Banks International, Karnataka Cryo-Stem, Cord Life, etc. to name a few. These are all private banks which store the cells on behalf of the clients who pay for the service. Recently, Jeevan Blood Bank launched a public stem cell bank wherein the cord blood is donated for public use, but would have a fee charged at the time of retrieval of the same for therapy. Srisrimal adds, "As on date more than 25,000 cord blood samples have been processed and stored in India alone, and growing a pace of about 25 percent year-on-year. Globally, more than a million such samples have been stored and more than 10,000 such stores samples being released for therapy to save patients from over 75 life threatening diseases."

**Controversy's child**

Stem cells are indefinitely a possible solution to many unsolved problems, however, it has always been embroiled in controversies over the ethical aspect of stem cells especially to the use of embryonic stem cells and embryonic germ cells gleaned from abortions, because both require the intentional destruction of a human embryo or foetus.

It is believed that best stem cells come from growing embryos, since they are totipotent i.e. they are capable of developing into all other stem cells present in the body. Also because these are naive cells not being exposed to any carcinogens or environmental stress, thus making them in theory a preferred choice for treatment. But one question that always remains unanswered is how ethical is it since most research has been conducted on

embryonic stem cell lines—cultures of cells derived from four-five days old embryos, or fertilised cells.

Rao says, "In view of research interests, embryonic stem cells are more plastic; hence have more value in regenerative medicine. She elaborates conversely that it

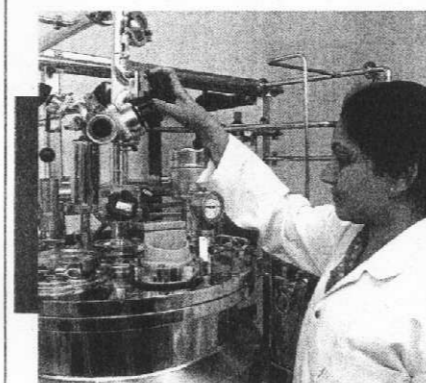
is also known that these cells also need to have an HLA match for transplantation and are known to form tumours in mice models. Hence, in the present scenario, it will be difficult to claim that they are more usable than adult stem cells. We think that as the

Government has not come up with proper guidelines, it would not only be unwise to use embryonic stem cells, but also unethical."

However, Srisrimal retorts by saying, "Of course the current process of obtaining stem cells from embryos is unethical if specific attempts

are made to obtain them, but would, however, pass the ethical muster if they are obtained as waste from in vitro fertilisation (IVF) clinics where several eggs are fertilised but wasted. With good regulatory controls, the unethical practices may be managed well as the benefits

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► far outweigh the cons." He adds that at LifeCell International they use stem cells from bone marrow, cord blood, cord matrix, menstrual blood, and adipose tissue and have an in-house ethics committee which regulates the manner in which they seek tissues for harvesting of stem cells, and have guidelines for informed consent from individuals, and also work with the ethics committees at various institutions from wherein these procedures are conducted for obtaining the stem cells.

Another issue that has occupied the limelight for the past few years has been the topic of cloning human beings. The perception is that conducting human cloning experiments is either acting as god or a breakthrough in the scientific field, making it a hot topic for debate. Irrespective of the ill effects of human cloning, it is difficult to overlook the benefits it holds in the form of enabling infertile procreation, getting a breakthrough in treating dangerous disease etc.

One such example is the recent success story of Dr Geeta Shroff from Delhi. She created a stir when she used embryonic stem cells to help a quadriplegic Australian patient, Perry Cross, a man who was permanently connected to a ventilator, to breathe on his own.

Barnagarwala informs, "While human cloning is not allowed in India, embryonic stem cell research can and has been conducted all over the country. Foetal or placental stem cells are being used for research or treatment, however, very strict regulations govern the procurement of such tissue—for instance medical termination of pregnancy cannot be attempted in order to procure foetal tissue. Further, the identities of the donor and the recipient cannot be revealed to each other."

Further, she states that though most governments and regulators across the globe are fairly cautious about the use of stem cells in therapeutics; this has still not deterred private set-ups in India from experimenting on patients. "This may act as a double-edged sword—on one hand it may attract foreign patients who would like to give stem cell based therapeutics a try but are restricted from doing so in their own countries; on the other hand, since these 'experiments' have not been backed by adequately designed clinical trials they are likely to fail as well," Barnagarwala cautions.

**Current studies and future course**

In spite of all these controversies, research on stem cells has proved to be of great importance. Some of the notable stem cell-related research that has taken place in India include treatment of ocular surface disorders using limbal stem cells; improved stem cell preservation using banana lectins; *in vitro* differentiation of human embryonic stem cells into neural and non-neural lineages; generation of human embryonic stem cell lines; transplantation of haematopoietic stem

cells; isolation and characterisation of mesenchymal and liver stem cells etc, lists Barnagarwala.

Cryo-stem Cell, Karnataka, is in the forefront of stem cell research, banking and clinical applications of adult stem cells including bone-marrow and cord-derived in India. They are mainly concerned with clinical applications of stem cells, enriched bone marrow and umbilical cord blood, and mesenchymal stem cells (bone-marrow and cord-derived). "Our research centre, in collaboration with various hospitals in the country, is conducting clinically-relevant research on stem cell differentiation and tissue engineering. The knowledge gained from these research effort can be incorporated in future stem cell therapeutic regimens," informs Rao.

"Lack of adequate regulation is the major stumbling block in India and this is likely to discourage global companies and international patients from seeking therapeutic options based on stem cell research originating in India. For instance, obtaining informed consent from donors; adequate storage facilities and the status of the contract between donor and the bank are grey areas that have not been sufficiently legalised in India," points out Barnagarwala.

The Indian regulatory environment is quite supportive of stem cell research. However, Subramaniam states, "The primary hurdle that organisations in this area face is in terms of availability of talent given that stem cells science is a frontier area. With increasing number of universities and colleges in India incorporating stem cell studies as part of

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Research Director  
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Karnataka

Looking ahead, LifeCell has set up a dedicated stem cell clinic for therapeutic purposes named TRICell at the Sri Ramachandra Medical College in Chennai. Initially, the facility had been handling hemato-oncological disorders that are curable using either bone marrow or cord blood stem cells. Apart from this, to expand the application of stem cells TRICell had also initiated clinical trials for diseases such as critical limb ischemia using point-of-care medical devices such as bone marrow aspirate and concentrate (BMAC) from Harvest International, USA. Srisrimal adds, "Recently, we set-up a research lab for clinical grade expansion of stem cells to achieve the required dosage necessary for successful treatment, at a cost of over Rs 5 crore. In the next two years an outlay of additional Rs 10 crore has been earmarked for advancing these stem cells into clinical trials, and also introduction of additional banking services from novel tissue sources such as the menstrual blood, cord matrix, and adipose tissue."

**Government's role**

While India has some advantages in the stem cell research arena, like the technology to identify and segregate stem cell lines and qualified and well-trained scientists to carry this research to the next level in terms of actual therapeutic use, there are a number of drawbacks to this currently disorganised and relatively unregulated market. These include lack of resources to fund and execute large-scale studies and fragmented state of current research groups that do not adequately leverage each others' know-how and facilities.

their undergraduate programmes, the talent crunch is expected to ease at working levels. Also, organisations involved in stem cell research are investing in knowledge enhancement programs by encouraging their researchers to take up value added training programs in international centers of excellence."

Judicious financing of good projects will ensure a guaranteed position in the field of regenerative medicine. Government should take active interest in making proper guidelines for stem cell research. Rao informs, "However, there is an intrinsic drawback in their dealings as a few known investigators are prone to be awarded with these grants whereas new players with no known 'coterie' to belong to end up at the wrong end of the stick. This leads to stagnation of ideas and inbreeding, resulting in a lopsided picture." Further, she feels, Government grants must be given to all deserving candidates and not to the same people over and over again. The time taken for all the process to end is also very long and it is very impractical to wait for their decision.

Agreeing on the same, Srisrimal adds, "Government has spent very little funds till date for stem cell research in India. However, it has shown its commitment to the industry by announcing the setting up of a dedicated stem cell research and therapy clinic at Hyderabad, which is set to open late next year. The main factor that hinders the development of further work in India is the need for a policy framework that needs to mature into law." ■

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