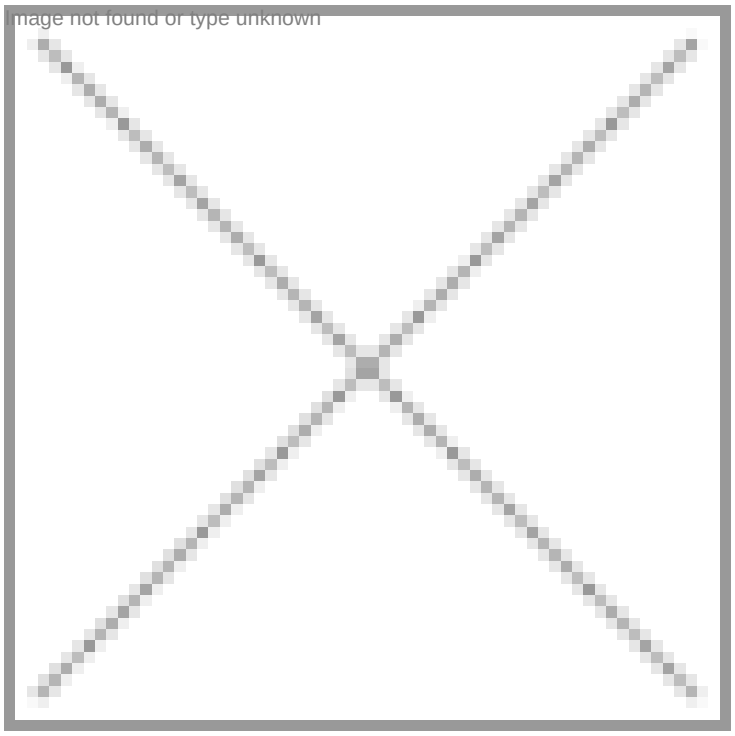
BioSpectrum
the business of Bio & Health Sciences

Stem cell research still at modest levels

06 August 2007 | News



Stem cell research still at modest levels

There is a lot of talk about stem cells in India, yet the research here is at modest levels.

In May this year, Bangalore-based Manipal Hospital announced a major breakthrough in the treatment of Parkinson's disease using stem cell therapy. It presented the case of Andrew Kisana, a US national. The doctors at the hospital said that the patient's bone marrow was harvested at the regenerative medicine department and the mesenchymal stem cells were injected into the part of the brain, which was affected because of Parkinson's disease. Kisana had received three injections. This was the first time such a major effort was attempted in India for treatment of Parkinson's disease. Kisana was suffering from the degenerating disorder for 15 years. After undergoing intensive drug therapy, lesion and deep brain stimulation (DBS), he had come to Manipal Hospital.

"The successful recovery of the patient would give hope to scores of Parkinson's cases which affects one percent of the population. The condition largely manifests in cases above 50 years, but there are younger people being affected. Stem cell therapy now gives such patients a new hope. However, we need to observe the long term clinical effects in larger number of patients to decide whether it is primary or secondary or supplementary treatment option for degenerative disorders," said Dr NK Venkataramana, director, Manipal Institute of Neurological Disorders.

The hospital's regenerative medicine department is currently carrying out clinical trials in stem cell therapy in 15 spinal cord injury patients besides researching in the use of stem cells in patients of heart attack and leg ischemia, said Satish Totey, chief scientific officer of Stempeutics Research (the regenerative medicine research arm of the hospital).

Ramesh, a patient with spinal cord injury, was treated with stem cell injection. "After the treatment I am able to pass urine and can move my hands. My sensations have also come back," he said.

Stem cells provide deeper insights into embryonic development and can be magic bullets to cure such debilitating diseases such as Parkinson's and Alzheimer's or and they can aid pharma companies in early stage screening of drugs, thus cutting on costs and bringing life-saving drugs to the market faster.

So the question is, where do we stand now on stem cell research? Specifically, what is the status of the ethics and policy debate? What can we hope to be accomplished on stem cell research and in regenerative medicine? What is the capacity for the researchers to make reproducible and meaningful clinical progress? And what is a sensible government policy that can take into account both the ethical considerations as well as the hopes for medical progress?

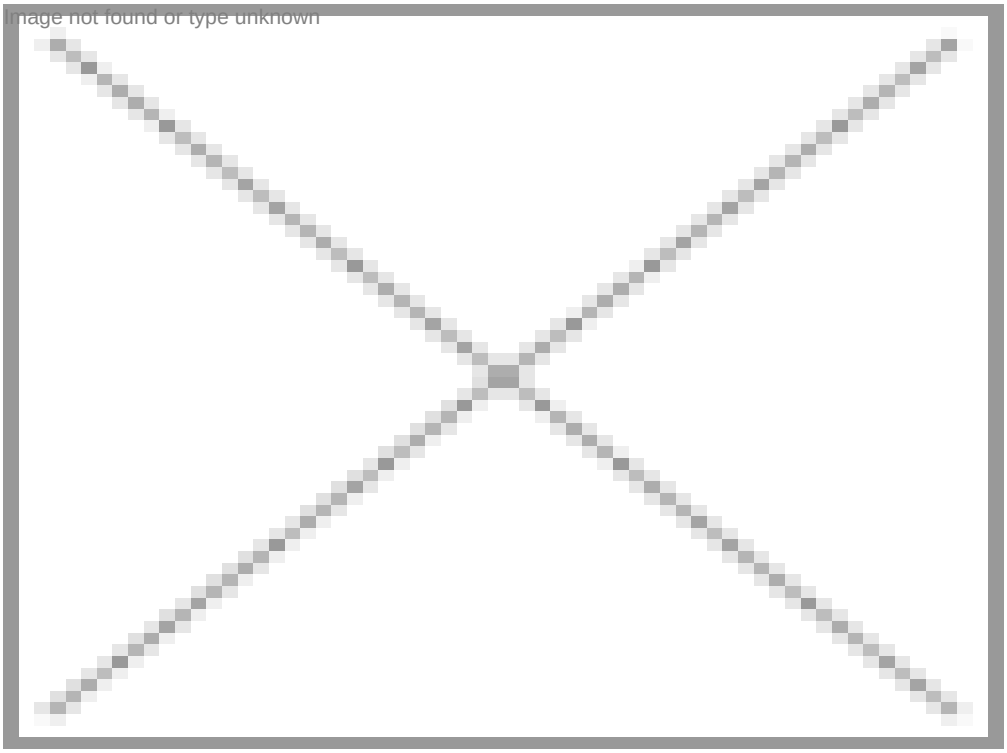
The unanimous feeling is that India is well positioned to emerge as a significant player in the global stem cell research area. India is particularly interested in the clinical application of stem cells in ophthalmology, cardiology, diabetes, and spinal cord repair. There is also keen interest from big biotech companies in the US, Canada and the UK, in joint venture projects with Indian researchers.

The Indian Council for Medical Research allows the use of fetal cells up to 14 weeks of pregnancy. The big question, however, is how will these cells be put to use a few years down the line, and how well will the stem cell banks that are coming up maintain them, in the absence of specific guidelines.

The CCMB has a collaboration arrangement with the Deccan Medical College (DMC) for liver stem cell research. The DMC and the Japanese Nichi-in Centre for Regenerative Medicine, which has developed a gel that preserves stem cells, are ready to undertake human trials using stem cells in end-stage liver failure patients.

The CCMB has also done work with the LV Prasad Eye Institute in growing corneal limbal cells, which help in repairing the damaged corneal tissue and restoring vision. Doctors have successfully performed more than 200 such procedures. CCMB is also working with Biological E on the use of cord blood cells and is venturing into newer areas. It has simultaneously built up facilities that can aid industry and other research institutes. For example, its Nuclear Magnetic Resonance (NMR) imaging facility being set up with the help of the Department of Science and Technology (DST), would allow imaging of cells and enable an insight into the effects of drug molecules at the cellular level. This would obviate the need to sacrifice animals for scientific experiments. It has also developed transgenic gene models of mice, for conducting drug trials.

Overall, research efforts by the scientific community or industry are still at modest levels, though a few major groups are working in specific areas.



The LV Prasad Eye Institute, Hyderabad has been putting research in adult stem cells to good use. Here doctors take about one millimetre limbal tissue from the healthy eye of the patient, culture them on an appropriate surface and graft it on the diseased eye. Such limbal stem cell treatment is available in only two other countries- the US and Taiwan.

AIIMS has claimed reasonable progress in therapeutic stem cell research work. Using bone marrow mononuclear cells, it has initiated clinical trials on about 40 patients. The focus is on treating muscular dystrophy, spinal cord injury, cerebral dysplasia, heart tissue damage, diabetes and motor neuron disease. AIIMS has marked a global first in pioneering stem cell medicine by the "injection method", for reviving heart muscles, placing the institute right at the top of the world's medicine map.

LifeCell, a stem cell banking and research company in India, has enrolled 3,000 expectant women for stem cell banking in just 20 months of operations, thereby creating a landmark in the stem cell industry. LifeCell has 18 stem cell collection centers across the country, which have collected 3,600 samples so far. And it plans to increase the number to 31 by March 2009.

Mumbai-based Reliance Life Sciences and Bangalore-based National Centre for Biological Sciences (NCBS) for being among the ten elite research institutions in the world invited by America's National Institute of Health (NIH) to take part in the federally funded research on embryonic stem cells. While the Reliance Life Sciences has isolated stem cells which are in various stages of development, the NCBS was in possession of potential stem cell lines which are yet to be characterized.

At NCBS, Dr Mitradas Panicker is working on embryonic stem cells and neurostem cells forming neurons. On the other hand, Reliance Life Sciences is committed to spending another $200 million over the next five years to reap the benefits of stem cell research. Reliance Life Sciences has characterized 10 stem cell lines including two neural SC lines, dopamine producing neurons and neurons for stroke patients.

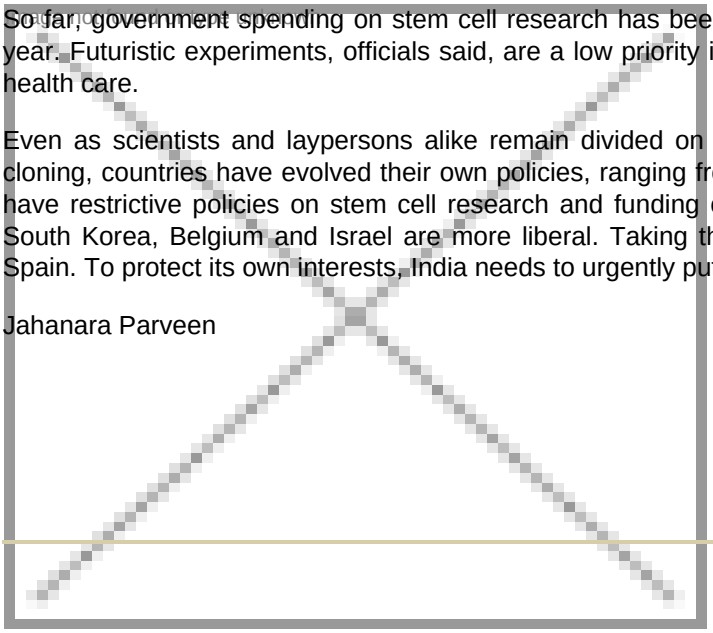
Dr Balkrishna Matapurkar, a surgeon at New Delhi's Maulana Azad Medical College, has pioneered a stem cell based technique for the regeneration of tissues and organs. He already holds a patent for this innovative technique.

"Although India is ahead of most countries in stem cell research, the work here is still in its infancy. Indian players are building expertise in the field of stem cell research and at the same time the DBT is playing a significant role in encouraging the researchers and is trying hard to fund people in the field" said Dr Mitradas Panicker. Indian scientists worked on stem cells successfully, using corneal stem cells to treat retinal damage and goat stem cells to address liver ailments, studying stem cells from mouse embryos and using umbilical cord blood stem cells to treat genetic blood disorders.

So far, government spending on stem cell research has been limited; about $200,000 was budgeted for such programs last year. Futuristic experiments, officials said, are a low priority in a country in which millions of people have no access to basic health care.

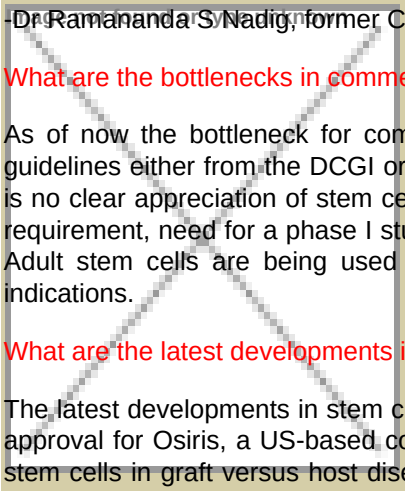
Even as scientists and laypersons alike remain divided on the hype, hope and ethical issues surrounding stem cells and cloning, countries have evolved their own policies, ranging from permissive to restrictive. For example, the US and Germany have restrictive policies on stem cell research and funding owing to ethical issues. In contrast, the UK, Singapore, Japan, South Korea, Belgium and Israel are more liberal. Taking the middle ground are countries such as Australia, Canada and Spain. To protect its own interests, India needs to urgently put in place a carefully-thought-out policy in this area.

Jahanara Parveen



"India should encourage adult stem cell usage for various life threatening diseases"

-Dr Ramananda S Nadig, former COO, Stempeutics Research



What are the bottlenecks in commercialization of stem cells?

As of now the bottleneck for commercialization of stem cells in this country is the lack of clear guidelines either from the DCGI or the ICMR. While everyone is going gaga about stem cells, there is no clear appreciation of stem cells as a new biological entity, clarity on pre-clinical animal testing requirement, need for a phase I study in humans and a blue print on how to get them to the market. Adult stem cells are being used in bone marrow transplants without a clear OKAY for various indications.

What are the latest developments in stem cell research?

The latest developments in stem cell research is the fact that the US FDA has accorded a fast track approval for Osiris, a US-based company, to conduct a phase III study of the use of mesenchymal stem cells in graft versus host disease. Based on the results of this study, there is every likelihood that Osiris would be permitted to market these MSCs. The fact that the US FDA has accorded this status to MSCs is significant and will probably pave the way for many other drug authorities to consider permitting such trials.

What according to you is the most significant breakthrough in stem cell research and application?

The most significant breakthrough in stem cell research as of now is the fact that we have understood the phenomenal potential of adult mesenchymal stem cell use in various indications. The initial response is very encouraging and the subjective improvements seen in our patients will have to stand the scientific scrutiny of well planned proof of concept studies before stem cells are accepted by physicians practicing evidence based medicine.

What's your view on the stem cell research legislation in India?

We in India seem to be waiting for either for the US FDA or the European authorities to lead and formulate stem cell guidelines before we have our own plans. While the recommendatory efforts of the ICMR and DBT are laudable, we still do not have concrete guidelines on clinical trials with these new biological entities. The time is ripe for us to get our act together and have an interim plan that will permit organizations like Stempeutics go ahead with the Phase II proof of concept studies, analyze the results and strategize our regulations.

I strongly feel that we in India should encourage adult stem cell usage for various life threatening diseases for which we have as of now no clear cure and regenerate hope amongst those suffering.

Hasthana Rajappa

Stem cell policy, guidelines being discussed

India is rapidly emerging as a hub for stem cell research with the market for stem cell research in India estimated to be about $540 million by 2010. However, we are yet to have a policy on the same lines, but it may soon become a reality.

Draft guidelines for stem cell research were formulated jointly in 2006 by the Indian Council for Medical Research (ICMR) and the department of biotechnology (DBT) under the ministry of science, New Delhi. These guidelines address both ethical and scientific concerns such as destruction of human embryos to create human embryonic stem (hES) cell lines, potential for introducing commodification in human tissues and organs and possible use of technology for germline engineering and reproductive cloning.

Principles

The guidelines state that any research on human beings, including human embryos, as subjects of medical or scientific research or experimentation, should adhere to the general principles outlined in the "Ethical guidelines for Biomedical research on Human Participants issued by the ICMR in 2006. The principles include essentiality of research with potential health benefits, respect for human dignity and rights, individual autonomy with respect to informed consent and privacy of the individual concerned. It also takes into account beneficence with regard to improvement of health of individuals and non-maleficience with the aim of minimization of risk and maximization of benefit.

Monitoring mechanism

All institutions and investigators carrying out research on human stem cells should be registered with the National Apex Committee for Stem Cell Research and Therapy (NAC-SCRT) through Institutional Committee for Stem Cell Research and Therapy (IC-SCRT). All clinical trials with any stem cell will also need to have prior approval of IC-SCRT and the Drug Controller General of India (DCGI) for marketable product and shall be registered with NAC-SCRT. Any International collaboration shall also have prior approval of NAC-SCRT or a respective funding agency as per its procedure or the health ministry's screening committee.

Categorization of stem cell research

The research on human stem cells is categorized in three areas depending on the source of stem cells and the nature of experiments.

Permissible: It includes in vitro studies on established cell lines from any type of stem cell and in vivo studies with established cell lines from any type of stem cell. In vivo studies can be carried out on experimental animals (other than primates) using fetal/adult somatic stem cells from bone marrow etc provided appropriate consent of the donor is obtained. Establishment of new human embryonic stem (hESC) from spare supernumerary embryos is also allowed with appropriate consent from the donor. All the above studies need the prior approval of IC-SCRT. Once a cell line is established it needs to be registered with the IC-SCRT and NAC-SCRT.

Restricted: This includes the creation of a human zygote by IVF, CNT or any other method with the aim of deriving a hESC line. A specific justification stating that the creation of the zygote is critical and essential for the research would be required and only then would it be approved by the NAC-SCRT through IC-SCRT. It also includes clinical trials sponsored by MNCs involving stem cell products imported from abroad, studies on chimeras where stem cells from two or more species are mixed and introduced into animals including primates at any stage of development. Further research involving introduction of human embryo stem/germ/somatic cells into animals at embryonic or fetal stage of development for studies on pattern of differentiation and integration of human cells into non-human animal tissues is also restricted. Only when there is a strong scientific justification would such a research be approved.

Prohibited: It includes transfer of blastocysts/human embryos generated by SCNT/parthenogenetic to a human or non-human uterus; research involving the directed non-autologous donation of stem cell lines to an individual; research in which any cells of a pluripotent nature are combined/grafted with a human or non human embryo/ foetus. Also embryonic stem cell research involving in vitro culture of any intact human embryo for longer than 14 days is not permitted nor is research involving introduction of embryonic cell into human or non-human primate blastocyst.

Cord blood stem cell banking

The guidelines allow for clinical use of cord blood stem cells. All cord blood banks have to be registered with the DGCI as per the guidelines of the blood banks. Purpose of banking should be explained to couples interested in storing cord blood. For this, standard operative procedures for collection, transportation, processing, storage, preservation and clinical use of umbilical cord blood should be laid down with approval of the IC-SCRT along with a detailed protocol of isolation and characterization of stem cells. Several other points need to be taken into consideration as per the ethical guidelines of ICMR.

Approval for derivation of a new hESC line

When approving proposals for derivation of a new hESC line whether from spare embryos or embryos created for the purpose, only those proposals shall be approved that show that they would help develop methods to detect abnormalities in embryos before implantation, will increase knowledge about serious diseases, develop methods of therapy for diseased or damaged tissues or organs. The research teams for the same should have appropriate expertise and training in derivation, characterization and culture of ES cells.

Procurement of gametes, blastocysts or somatic cells

The IC-SCRT should review the process of procurement of gametes, blastocysts or somatic cells for the purpose of generating new hES cell lines. In this respect, consent for donation of supernumerary embryos should be obtained from each donor at least 24 hours in advance. Blastocysts made through IVF specially for research purposes and gametes and somatic cells donated for development of hESC lines derived through SCNT or by parthenogenesis or androgenesis should also have approval of IC-SCRT.

Banking and distribution of hES cell lines

The draft guidelines adhere to key ethical principles that focus on the need for consent of donors and a system for monitoring adherence to ethical, legal and scientific requirements. It is necessary to ensure that the hESC were obtained ethically and with informed consent of donors, were well characterized and screened for safety and the conditions under which they were stored meet the current standards of good lab practices (GLP), good manufacturing practice (GMP) and good tissue practice (GTP). Also institutions planning to bank hESCs should establish uniform guidelines to ensure that donors of material give informed consent through a process approved by the IC-SCRT.

Use of stem cells for therapeutic purposes

There is no approved indication for stem cell therapy as a part of routine medical practice, other than Bone Marrow transplantation (BMT). Hence all stem cell therapy other than BMT shall be treated as experimental. It should be conducted only as clinical trial after approval of the IC-SCRT/IEC and DGCI (marketable products). All experimental trials shall be registered with NAC-SCRT. Also the centers carrying out stem cell clinical trials and the agency/source providing such cells for the trial should be registered with NAC-SCRT through IC-SCRT/IEC.

Draft guidelines

Draft guidelines were discussed on November 7, 2006, jointly by both the committees of the DBT and ICMR in a meeting organized by the DBT, when it was decided that there should be an Annexure on "Laboratory standards for cell collection and processing for research and therapy. The DBT then organized a meeting of the joint committee of ICMR and DBT on July 16, 2007 at Bangalore to discuss the Annexure on "Laboratory standards for cell collection and processing for clinical use." The document is being circulated amongst the members of the joint committee and based on the comments received by the members, it will be finalized. The draft guidelines will then be hosted on the ICMR/DBT website inviting comments from the general public.

Shalini Gupta