Stem Cells, the Future Therapy

10 March 2009 | News

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With progress at different levels, stem cells are showing potential for commercial success and significant business opportunities.

Advances in biological sciences and the development of human stem cells are today bringing new hope for the treatment of many diseases such as Parkinson's, diabetes, heart diseases and cancer, as well as injuries for which there has previously been no effective treatment. Stem cell research and the accompanying enabling technologies have virtually exploded since embryonic stem cells were first isolated in 1998. Many of the enabling and complementary technologies impacting stem cells are also catching up.

Induced pluripotent stem cells or iPS cells have been a big breakthrough in the stem cell research arena. Dr Thomson and his team of researchers successfully reprogrammed the human adult skin cells to act like human embryonic stem cells. The breakthrough it is said is likely to change the course of action making research on embryonic stem cells redundant, given that iPS cells are remarkably similar to human embryonic stem cells. Besides researchers can skirt all the ethical issues related to human embryonic stem cells (hES) and can make as many iPS cells they need for research.

Progress in stem cell research is now astounding and over 2,000 research papers on embryonic and adult stem cells are being published in reputable scientific journals every year. While embryonic stem cell research has yet to yield any clinical trial result, adult stem cells are already being used in treatments for several conditions including leukemia, Hunter's syndrome and heart disease.

The beginning

In the early 1900s European researchers realized that the various type of blood cells e.g., white blood cells, red blood cells and platelets all came from a particular "stem cell". However, it was not until 1963 that the first quantitative descriptions of the self-renewing activities of transplanted mouse bone marrow cells were documented by Canadian researchers Ernest A McCulloch and James E Till.

Research into adult stem cells in animals and in humans has been ongoing since this time, and bone marrow transplants--actually a transplant of adult stem cells--have in fact been used in patients receiving radiation and chemotherapy since the 1950s.

Developments in biotechnology in the 1980s and 1990s saw the introduction of techniques for targeting and altering genetic material and methods for growing human cells in the laboratory. These advances really opened the doors for human stem cell research.

Then in 1998 James Thomson, a scientist at the University of Wisconsin in Madison, successfully removed cells from spare embryos at fertility clinics and grew them in the laboratory. He launched stem cell research into the limelight, establishing the world's first human embryonic stem cell line which still exists today.

Since this discovery, a plethora of evidence has emerged to suggest that these embryonic stem cells are capable of becoming almost any of the specialized cells in the body and therefore have the potential to generate replacement cells for a broad array of tissues and organs such as the heart, liver, pancreas and nervous system.

Market overview

The possibilities for stem research are truly endless, and yet unpredictable. In this nascent, but rapidly growing field of stem cell therapies, products are taking time to reach the commercialization stage. However, the market potential for stem cell therapies is assumed to be very huge. And according to a Business Insights report, the market for stem cell products and services is forecast to grow almost three-fold from $24.6 billion in 2005 to $68.9 billion in 2010 and during the last few years over 2,000 US patents claiming stem cell technologies and applications relevant to health care were published. It also mentions that the proportion of stem cell patents claiming applications in hematology decreased after 1999, while the proportion of patents claiming applications in neurology, type 1 diabetes, cardiology and drug screening increased dramatically in the last few years and over 100 companies with proprietary human adult stem cell technologies and products have been identified.

Indian scenario

Stem cell research in India gained attention when the US Department of Health disclosing its interest in funding stem cell research in two Indian Centers--the Reliance Life Sciences and the National Center for Biological Sciences. The National Center for Biological Sciences had been working on stem cells for quite long and has three documented stem cell lines.

India has no clear policy regulating stem cell research but the country has its fair share of research going on--though blazing success stories from India are yet to come by. Also, the Indian regulations are by far more relaxed than some other countries in the region. The Indian regulatory environment is quite supportive of stem cell research. "However, there is a need for regulation of individual investigator 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," said KV Subramaniam, president and CEO, Reliance Life Sciences.

In India several scientific departments and institutions of the government, such as Department of Biotechnology, Department of Science and Technology, Indian Council of Medical Research and Council for Scientific and Industrial Research are promoting stem cell research. The priority areas of research have been identified through discussions at various forums on basic and applied sciences.

Among the various programs being supported in embryonic and adult stem cells research in India are: establishment ofhESC lines, use of limbal stem cells for repair of ocular surface disorders, isolation; purification and characterization of hematopoietic, mesenchymal cells among others.

Reliance Life Sciences is developing a wide range of novel research-led, autologous and allogenic cell therapies and tissue-engineered products to get into regenerative medicines business. Under the "regenerative medicine initiative", the company has several groups who work in areas such as embryonic stem cells, ocular stem cells, haematopoietic stem cells and skin and tissue engineering.

One of the newest companies in stem cell research in India is Stempeutics Research Private Ltd, a Bangalore-based company focused on research, therapeutics and therapy in the field of regenerative medicine. Dr BN Manohar, president, Stempeutics confirms that the company has developed cell characterization for purity and identity by flow cytometry, functional assay for multipotency, process validation for manufacturing, large scale cGMP complaint up-scaling of mesochymal stem cells and quality control testing and quality assurance.

Stempeutics has also established cell and tissue manipulation facilities at Bangalore, Manipal and Kuala Lumpur inMalaysia.

"India has massive potential for stem cell research as there is a very good environment and we have things going for us," he added.

Another major institute involved in stem cell research in India is the Stem Cell Biology Department at NIRRH, Mumbai headed by Dr Deepa Bhartiya. The LV Prasad Eye Institute, based at Hyderabad caught the headlines recently when its doctors succeeded in transplanting a stem cell derived cornea to a patient who had lost his cornea - a treatment option available only in the US at the time. The Maulana Azad Medical College, Delhi is yet another major institution involved in stem cell research.

The future of stem cells

Experts predict a rapid progress in adult stem cells and slower but intense work with embryonic stem cells. It is hoped that,by that, by 2020, researchers will be able to produce a wide range of tissues using adult stem cells, with spectacular progress in tissue building and repair. In some cases, these stem cells will be actually incorporated into the new repairs as differentiated cells.

The future may also see some exciting new pharmaceutical products in the pipeline. These drugs may, for example, activate bone marrow cells and encourage them to migrate to parts of the body where repairs are needed.

And experts predict that along the way there will be a number of new biotech companies folding, as a result of good investment into adult stem cell technology. The emergence of cord blood banking itself has created more than a dozen companies globally in a span of 2-3 years.

Cord-blood cell transplants are becoming common as a therapy for diseases of the blood as scientists are finding that stem cells from umbilical cord blood may be able to grow into other kinds of cells as well. Such advances are casting cord blood, previously regarded as medical waste left after childbirth, in a new light. Today doctors use cord blood cells to treat about 70 diseases, mostly anemias or cancers of the blood, such as leukemias and lymphomas.

A yet another area of future research concerns the delivery of stem cells to the tissues in which they are needed. Current practice involves either the injection of stem cells directly into the targeted tissue, or injection of the stem cells into the bloodstream without any guarantee that they will actually find their way to the appropriate tissues. Targeted delivery would ensure that the therapeutic stem cells are introduced to the organs and tissues that need them, where they need them.

Jahanara Parveen

Reproductive Engineering Using Stem Cells, a Panacea for Infertility

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—Dr. Chander P Puri, CEO, Yashraj Biotechnology Limited

Over the last few decades, we have witnessed exemplary advances in science especially in the arena of biotechnology, an umbrella term covering a wide range of scientific applications for the benefit of mankind. Till very recently, biotechnology-based endeavors had been aimed to discover new methods to produce biomolecules in vivo or in vitro with the intent of using them for detection or treatment of various pathologies afflicting humans or animals.

Now biologists are facing another challenge, a very threat to the perpetuation of human life i.e. infertility. Although at this juncture, infertility statistics worldwide are not alarming, these incidences are steadily intensifying. This has compelled biologists to take the onus for devising innovative ways to preserve fertility or treat infertility. And in this pursuit, they have been immensely benefited by the legacy of almost 30 years of in vitro fertilization techniques leading to a groundbreaking discovery of embryo or adult cell derived stem cells. Embryo derived primitive cells or embryonic stem (ES) cells are endowed with a potential to give rise to every tissue type in the body, hence it was envisaged that two indispensable progenitors of a new life i.e. eggs and sperm could also be generated from these cells outside the human body. This hypothesis so far has proven well-grounded and efforts in this direction have not been futile. Researchers at the University of Pennsylvania, US, have been able to develop mouse eggs in vitro from few ES cells grown separately. Male germ cells have also been derived from mouse ES cells and these cells have resulted in live births.

It has been demonstrated that premeiotic and haploid germ cells derived in vitro can successfully fertilize oocytes, produce embryos and live pups. However, the animals born of the fusion of the in vitro developed male germ cell and the normal oocyte were found to be infertile, abnormally large and had stunted growth, probably due to genetic defects arising during the creation of the sperm. While further research is needed to obviate the possibility of genetic or epigenetic errors accruing during the ex vivo creation of male and female gametes, these success stories in mouse, have enthused researchers to generate human gametes in vitro. Studies indicating the expression of egg and sperm specific markers in spontaneously differentiating human ES cells in vitro have strengthened the belief that the derivation of gametes is feasible from human ES cells.

Studies are also being undertaken to develop germ cells or gametes without using embryonic stem cells. Porcine fetal skin–derived stem cells have been induced to differentiate into oocyte-like cells within follicle structures. The potential of bone marrow stem cells has also been explored in treating male infertility in mouse models. Researchers at the Harbor-UCLA Medical Center observed the characteristics of germ cells in the bone marrow stem cells which were injected into the testes of infertile mice. Although these germ cells did not differentiate fully into sperm, these studies highlighted the relevance of other factors or cellular signals required for complete differentiation of sperm.

The recent finding that some human embryonic stem cell (hESC) lines display greater propensities to differentiate along certain lineages than others suggests that some ESC lines could produce gametes more efficiently that others. Establishing the right micro-environment where germ cells can thrive naturally among other fetal gonadal cells will be the key. Indeed, the factors that support germ cell development have been found to be useful in enhancing the derivation rates of germ cells from

ES cells. Considering the limitations of adult cell derived stem cells and the ethical issues associated with ES cells, attempts have been made to develop stem cells from adult differentiated cells.

Researchers have identified several genes that can dedifferentiate adult cells into stem cells. These dedifferentiated cells, called iPS cells can be reprogrammed into the cells that eventually become eggs and sperm and this may open up new vista for the treatment of infertility using patient-specific cells. However the major challenge in translation of these research observations for human use is how to generate high quality germ cells in the lab. Germ cell derivation remains very inefficient process with less than one of one million starting cells becoming a germ cell. The poor efficiency of this process has been attributed to the failure of meiosis and/or the simultaneous activation of both male and female germ cell programs in ESC-derived gametes resulting in meiotic catastrophe. There are many uncertainties and dangers associated with the use of iPS also. As the process of reprogramming involves viruses for gene delivery, it potentially increases the likelihood of genetic abnormalities and cancers. Research endeavors are in full swing to surmount the obstacles currently being encountered in generation of immature and mature gametes.

It is hoped that with the ex vivo generation of human sperm and egg, infertility will soon become ‘a thing of the past’. The eggs and sperms created in vitro may help people who lose such cells because of age or certain pathologies such as cancer or ovarian disorders. These techniques will also have appealing spin-offs such as reproductive cloning of farm animals.