STEM CELL INNOVATION SYSTEM IN INDIA: EMERGING SCENARIO AND FUTURE CHALLENGES

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Abstract: The present paper is an attempt to explore the emerging stem cell innovation system in India. It is contended that the social capital in terms of linkages of various sorts can no longer be ignored to strengthen the innovation system and that the co-evolution of technology and institutions is yet to emerge. It seems that given the nature of complex technologies involved, there is a greater need felt for R&D and training collaboration and hence linkages of various types are taking place. For shaping futures for a balanced growth of this sector, the institutions in India will have to be geared towards greater coordination, promotion of greater knowledge flows at national as well international levels. This paper also analyses the strengths and barriers in the development of rapidly growing stem cell research in India along with future challenges.

Keywords: *stem cell research; India; sectoral system of innovation; linkages.*

INTRODUCTION

In recent years Stem cell has emerged as a sector with potential to treat a wide range of debilitating diseases and disability. Stem cell innovations have become a major focus not only for government policy initiatives and investment but have also heralded benefits for both health care and biotechnology industries. Globally, the stem cell industry is a billion dollar market. The global market size for stem cell therapy in 2006 was estimated to be US $26 billion and is projected to reach US $96 billion by 2015 (Business Standard, 2008) and consequently stem cell

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research is becoming increasingly competitive. Research in the United States, European Union and Asia is moving apace with increasing level of government support (UKSCI report, 2005). The stem cell sector has witnessed a rapid growth worldwide. This is reflected from the fact that merely in a four-year period, the figure for number of firms has increased from 33 (Laysaght and Hazlehurst, 2003) to 166 during 2002-06 (Martin et al., 2006).

Given the huge "disease burden" (Darr et al., 2007; Reddy et al., 2005), the need for cell therapy, diagnostics and medicines, the claim of the stem cells need to be exploited to the fullest. Countries across the world have evolved their own policies to take advantage from the stem cell development.

India has also taken significant steps to establish an advantageous position in global stem cell market. Indian stem cells market is growing at a rate of 15 percent per annum and is expected to hit US $540 million by the year 2010 (Express Pharma, 2007). The government of India is very much supportive of the stem cell research, which is clear from the fact that the government has invested US $500 million during the period 2004-2007. The private players have not lagged behind and have made significant investments (Express Pharma, 2007). Thus, it is not surprising that India is projected as a global player in this sector.

However, given the nature of stem cell research that involves complex technologies also demands a commensurate R&D support. Transforming basic scientific research into viable therapeutic applications requires significant amount of funding, human resources and infrastructure. Simultaneously commercialising of R&D requires rigorous clinical testing and consumer demand.

Stem cell research does involve several contentious issues posing challenges of socioeconomic, political and ethical in nature. The commercial path of stem cells entails trust of international scientific, industrial and financial communities. If trust disappears market vanishes (Salter et al., 2007). It has become most crucial after the South Korea's Hwang affairs. In this back drop, the present paper has attempted to analyse the stem cell sector in India using sectoral system of innovation as an analytical framework. The main thrust of this paper is to trace out the linkages among different players in Indian stem cell sector, along with an overview of stem cell research in India.

The paper is divided into 6 sections. Section 2 deals with the analytical frame work. Section 3 discusses the structure of stem cell research in India. Role of institutions is highlighted in section 4. Section 5 explores the emerging scenario of stem cell research in India, Finally, it is contended that the social capital in terms of linkages of various types can no longer be ignored to strengthen the innovation system and that the co-evolution of technology and institutions is yet to emerge.

ANALYTICAL FRAMEWORK

The present study is carried out from a perspective of the sectoral system of

innovation (SSI) without assigning any causal priority as against other perspectives like the national innovation system (NIS) or international system of innovation (ISI) (Desai, 2009). The innovation system in any country consists of Institutions (laws, regulations, rules, habits, etc.), the political process, the public research infrastructure (universities, research institutes, support from public sources, etc.), financial institutions, skills (labour force), etc. that affect how it generates, disseminates, acquires and applies knowledge. "To explore the technological dynamism of innovation, its various phases, and how this influences and is influenced by the wider social, institutional, and economic frameworks has been the main focus of this type of analysis"(Fagerberg, 2005). Tapping global knowledge is another powerful way to facilitate technological change through channels such as FDI, technology transfer, trade, and technology licensing. The NIS approach that rightly recognized the interactions between socioeconomic, political and institutional factors within the national boundaries has not only visualized its crucial role in the developing countries but also the increasing significance of international cooperation in the catching up process (Freeman, 1995). However, the relationship between NIS and ISI has been de-emphasised. There are other scholars (Desai, 2009; Fromhold-Eisebith, 2006) who perceive the effective linkages between the NIS, regional innovation system and ISI as beneficial for evolving balanced science, technology and innovation policies for the developing countries. Without assigning any causal priority to any of these levels, it is argued that these linkages would provide adequate understanding of the interactions between the international institutional factors, R&D collaboration, migration and return migration of knowledge workers and other linkages.

Many scholars pursuing sectoral system approach view the interactions between: a) knowledge & technology domain; b) actors & networks; c) institutions and d) learning as essential components for innovation (Malerba, 2005). According to them the successful innovation is heavily dependent upon the role of 'organisation' (firms as well as non-firm organisations) and the prevalent 'institutions' (rules of the game). Firms are viewed as key actors in the innovation process. However firms do not innovate in isolation. In the innovation process firms interact with other firms as well as non-firms organisation. Here institutions play an important role in their linkages. The linkages are viewed as key elements of the innovative and production processes. Moreover, the SSI perspective provides a focus on the sectoral specificities like in this case the challenges of the special raw material that is being used. It is in the preceding context that the structure of stem cell research in India is analysed.

STRUCTURE OF STEM CELL RESEARCH IN INDIA

India is an emerging player in the stem cell arena. The research and therapeutic applications of stem cell has been growing rapidly in recent years. In 2000 there were very few authored papers in terms of stem cells by Indians, but by the beginning of

2007, in a single year, there were around 100 authoring papers, as shown by the Web of Science database (Chakraborty et al., 2009). In terms of publication India is placed under top 10 countries of the world (see figure 1). During the period 2006-10, Indian scientists published 412 papers in the area of stem cell. Out of these, there were 142 internationally collaborated papers and the major collaborators were from USA, Japan, France, Canada and the UK (ISI Web of Science, 2011). India's growing strength in the field of stem cell is also reflected by its significant patenting activity compared to other emerging players (Table 1). Indian stem cell market is growing rapidly with promising stem cell therapies. India is seen as a potential player in the global stem cell market by offering cost effective treatments in comparison to developed countries. There are significant numbers of research laboratories, hospitals and firms that are active in this area (Greenwood, et al., 2006; Lander et al., 2008; Sharma, 2009) and a few universities have also taken initiatives.

Most of research in the area of stem cells is being carried out through public sector especially government research laboratories. Presently, more than 40 academic institutions and research laboratories including government and private hospitals are involved in stem cell research. At least twenty private firms are also active in this area. Most of them are engaged in the area of stem cell cord blood banking. The reason might be that stem cell cord blood banking requires less expertise in comparison to technologies required for the embryonic and adult stem cells.

Research laboratories

Stem cell research is mostly being carried out by public research laboratories in India. The focus is mainly on the adult stem cell research. Different research laboratories are engaged in different areas of adult stem cells. In comparison to adult stem cells, a few research laboratories are working in the area of embryonic stem cells, even after the favourable environment compared to the western countries.

Institute for Stem Cell Biology and

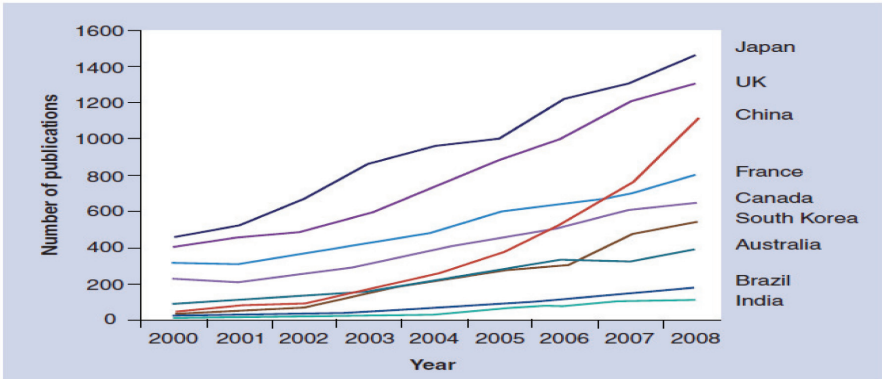

Figure 1: Publications in Stem Cell Research (2000-2008)

Source: McMahon et al. (2010)

Table 1: International comparison of the number of stem cell patents granted by the USPTO (Based on inventor country and/or assignee country)

Rank	Country	1994-2003		1994-1998		1999-2003	
		Patents	Share	Patents	Share	Patents	Share
1	United States	672	73,93%	469	74,92%	203	71,73%
2	Canada	41	4,51%	24	3,83%	17	6,01%
3	Japan	37	4,07%	23	3,67%	14	4,95%
4	Germany	29	3,19%	24	3,83%	5	1,77%
5	France	25	2,75%	16	2,56%	9	3,18%
6	Great Britain	19	2,09%	17	2,72%	2	0,71%
7	Israel	18	1,98%	13	2,08%	5	1,77%
8	Italy	16	1,76%	11	1,76%	5	1,77%
9	Switzerland	10	1,10%	5	0,80%	5	1,77%
10	Netherlands	9	0,99%	6	0,96%	3	1,06%
11	Australia	6	0,66%	5	0,80%	1	0,35%
12	Russia	5	0,55%	3	0,48%	2	0,71%
13	India	4	0,44%	1	0,16%	3	1,06%
14	Austria	3	0,33%	1	0,16%	2	0,71%
15	Belgium	2	0,22%	2	0,32%	0	0,00%
15	China	2	0,22%	1	0,16%	1	0,35%
15	Korea	2	0,22%	0	0,00%	2	0,71%
15	Norway	2	0,22%	1	0,16%	1	0,35%
15	Sweden	2	0,22%	1	0,16%	1	0,35%

Source: Glänzel et al (2004).

Regenerative Medicine (inStem) is an autonomous institute recently established by the Department of Biotechnology (DBT) in Bangalore. It is viewed as an India's first dedicated institute for the research in stem cells in the country (Sharma, 2009; Times of India, 2009). The aim of inStem is to provide a single platform for scientists and clinicians to work together in the area of stem cell biology and regenerative medicine. It is working in collaboration with Centre for Stem Cell Research at Christian Medical College (CMC) Vellore, a centre engaged in translational stem cell research. It is also engaged in promoting public-private partnership with the help of another newly established Centre for Cellular and Molecular Platform Technologies (C-CMAP), Bangalore. Soon after the inception inStem announced the launch of a collaborative research programme with the Institute for Integrated Cell Material Sciences, University of Kyoto, Japan. The National Centre for Biological Sciences, Bangalore is also involved in this collaborative research programme. In addition inStem has also signed a MoU with US-based California Institute for Regenerative Medicine to develop a jointly funded research project.

National Centre for Biological Sciences (NCBS) Bangalore is one of the leading research laboratories in the country. It is active in embryonic as well as adult stem cells. Its three human embryonic stem cell (hESC) lines are eligible for National Institute of Health (NIH) funding. However at present it is not available for the researcher (NIH website).

Jawaharlal Nehru Centre for Advance Scientific Research (JNCASR) is a multidisciplinary research institute in Bangalore. Research scientists at this

centre have derived two human embryonic stem cell (hESC) lines which are deposited in the UK stem cell bank. These cell lines are available for the research community to do further research. The stem lines were derived from the discarded embryo obtained from Bangalore Assisted Conception Centre (BACC), Bangalore. The NCBS was also a part of this collaborative project (Inamdar et al., 2009). The JNCASR website shows that "this project will be part of the International Stem Cell Initiative 2 (ISCI) project to identify the common genetic changes that occur in hES lines on prolonged culture. This will be the first time that India is represented on an ISCI project (http://www.jncasr.ac.in/newsview.php?id=51)".

Centre for Stem Cell Research (CSCR) is supported by the CMC, Vellore and the DBT, Government of India, located in the CMC campus. The centre is interested to understand human diseases and develop stem cell based therapies for some of the diseases. It has set up four goals for the stem cell based research and therapy (http://www.cscr.in/): a) to have scientific faculty involved in basic research that will have translational potential, mostly with adult stem cell at present; b) To develop a training programme for students and scientists who will contribute to the manpower required for this field in the country; c) To develop cellular and animal models of diseases to test hypothesis generated from our understanding of stem cell biology and d) To clinical trials with stem cells produced under current good manufacturing practice (GMP) conditions. In 2009 a scientist at CSCR has succeeded in the creation of induced pluripotent stem (iPS) cells. This is seen as a path breaking research in India where adult stem cells are modified in such a way that they can behave like embryonic stem cells. India is the fifth country after Japan, US, China and the UK in terms of developing this technology (Menon, 2009).

National Centre for Cell Sciences (NCCS), Pune has conducted animal and preclinical research for pancreatic regeneration using bone marrow stem cell. NCCS scientists are interested in the clinical trials for diabetes. They are in the process to establish a team of clinicians, scientists, and patients for conducting the stem cell based trials (Lander et al., 2008). NCCS has also developed the deposition facility for stem cell lines. Two hESC lines developed by the National Institute for Research in Reproductive Health, Mumbai has been deposited in NCCS (Sharma, 2009)

Centre for Cellular and Molecular Biology (CCMB), Hyderabad is also one of the leading research laboratories in the field of stem cells. It has set up a stem cell facility centre in association with Department of Science & Technology (DST) and Nizam's Institutes of Medical Sciences (NIMS), Hyderabad. The facility centre will work in both basic and applied research. The role of NIMS is to provide patient pool for the CCMB (The Financial Express, 2006). CCMB has started a collaborative cardiac stem cell transplantation project with NIMS. The other partners of this project are Madurai Kamaraj University and The Wellcome Trust Sanger Institute UK (The Financial Express, 2009).

Central Leather Research Institute, Chennai is presently focused on "engineering tissue by seeding scaffolds with stem cells" (Lander et al., 2008:12). It is interested in to have collaboration with private sector to further development of their research findings (Lander et al., 2008).

National Brain Research Centre, Manesar is active in the area of neural stem cells. The centre is also working in the area of embryonic stem cell research.

Institute of Immunohematology, Mumbai conducts research in the field of Haematopotic stem cells. It has two US and two Indian patents and it filed one US and Indian patent respectively. (Personal communication, Dipika Mohanty)[1]

Hospitals

In India quite significant numbers of public and private hospitals are involved in stem cell research and therapy. They are involved in both basic and applied research. They are also offering various kinds of stem cell based therapies to the patients. Hospitals have linkages with the various stem cells firms and research laboratories. In this way knowledge flows from basic researcher to the clinicians.

India's one of the largest research-intensive hospital, All India Institutes of Medical Sciences (AIIMS), New Delhi conducts basic and applied research. They are also involved in clinical trials and pilot treatments. The Stem Cell Facility was established in 2005. AIIMS is working in the area of adult and cord blood stem cells. Limbal, Haematopotic, Mesenchymal, Cancer and Epidermal stem cells is the main focus. It offers various therapies to the patients. So far more than 300 patients are under gone stem cell transplantation for various diseases (Express Healthcare, 2007). It is also active in the research on umbilical cord blood banking. AIIMS has developed an in-house umbilical cord blood bank for this purpose (The Hindu, 2009).

Sir Ganga Ram Hospital, New Delhi is active in stem cell transplantation. It has tied up with Life Cell a cord blood banking firm based in Chennai for the stem cell therapy (Lalchandani, 2006). It was reported that the doctors at this hospital have treated at least 60 patients through stem cell based therapy by the beginning of the year 2011 (Jha, 2011).

Sankara Nethralaya, an eye hospital based in Chennai is working in the area of corneal and retinal stem cell research. Recently it has obtained a process patent internationally for growing stem cells of the cornea on synthetic gel which claims to be useful in the stem cell transplant (The Times of India, 2010).

L V Prasad Eye Institute (LVPEI) is a non-profit hospital located in Hyderabad. It started work in the area of stem cells in the year 2001 focusing on the corneal and limbal adult stem cells (Mason and Manzotti, 2010). LVPEI has developed its own ocular surface reconstruction method. Over the years LVPEI has been treated 750 patients with the overall success rate of 67 per cent. It was stated that some of the patients

were treated free of charge (Lander et al., 2008; Vemuganti and Sangwan, 2010). The treatments at LVPEI are supported by the DBT, the Hyderabad eye research foundation and the Champalimuad foundation.

However, the work of LVPEI was criticised by an international team of ophthalmologist for using animal/human materials during transplantation (Schwab et al., 2006).

The Nu Tech Mediworld is a private stem cell therapy clinic run by an obstratrician Dr. Geeta Shroff in Delhi. Dr Shroff claims to treat over 800 patients from 35 different countries using embryonic stem cell for the disease conditions like spinal injuries, eye disorders, diabetes, cardiac problems, and Parkinson's disease. She also emphasised that all of her patients have shown improvement without any adverse effects. Dr. Shroff has filed a patent claiming that "Terminal disease and other disorders or conditions that may be treated or ameliorated according to the present invention include, without limitation, cancer, liver and kidney disorders, nervous system disorders, skin disorders, autoimmune disorders, genetic disorders, eye disorders, musuloskeletal disorders, fertility and reproductive disorders and cardiovascular disorder" (WO 2007141657 20071213). Altogether her patent application listed nearly 80 diseases which may be treated by this new invention (Sipp, 2011). It is pertinent to highlight that though she has filed a patent but has refused to publish her findings in peer reviewed journals and consequently offers national and international concern (Amelia, 2007; Cohen and Cohen, 2010; Khullar, 2009).

Firms

Reliance Life Sciences Pvt. Ltd. (RLS), Mumbai, Stempeutics Research Pvt. Ltd., Bangalore and Nichi-In Centre for Regenerative Medicine (NCRM), Chennai are leading firms in India which are active in the different areas of stem cell research i.e. embryonic, adult and cord blood stem cells.

Reliance Life Science Pvt. Ltd.

RLS is the initiative of Reliance group, one of the largest private sector enterprises in India. It is engaged in embryonic, adult as well as cord blood stem cells.

RLS is playing a key role in developing the stem cell technology in India. It has three US and five Indian patents in the field of stem cells (USPTO & IPO data base). Its seven hESC lines are eligible for US federal funding along with NCBS, Bangalore. However the cell lines developed by RLS are yet too categorised.

RLS has collaborated with different government research laboratories and hospitals for the stem cell research. It deposited its embryonic stem cell lines at NCCS Pune that can be obtained from the NCCS for the research purpose. Similarly stem cell facilities are offered by the RLS in collaboration with NCBS, Bangalore.

In the area of ophthalmology it is collaborated with AIIMS, New Delhi and

Aditya Jyot Eye Hospital, Mumbai for the clinical trials. It has collaboration with Sir Hurkisondas Nurrotumdas Hospital, Mumbai for cardiac stem cells. RLS provides its services to hospital in extraction of stem cells from bone marrow (Dutta, 2006). The RLS has set up stem cell research laboratory at this hospital for the purpose.

RLS is carrying out clinical trials for application of stem cell-based therapies for stable vitiligo, non-healing diabetic ulcers, Parkinson's disease spinal cord injury and autologous stem cell conjuctival graft. It has developed some stem cell products in recent years. For example a) ReliNethra to cure corneal blindness; b) ReliHeal – G, (biopolymeric hydrogel wound management product) which claims to useful in early wound healing by promoting migration of new epidermal cells across the wound surface and c) CardioRel for heart attack (Bisserbe, 2010).

RLS has been offering ReliCord™ programme for umbilical cord blood banking. There are two types of services under this programme: a) ReliCord 'S' Sibling Donor Program, and b) ReliCord 'A' Allogenic, voluntary donor program. It has recently launched India's first cord banking services under the Relicord 'M' program, which stores umbilical cord derived mesenchymal stem cells.

Stempeutics Research Pvt. Ltd.

Stempeutics Research Pvt. Ltd. is a group company of Manipal Education and Medical group India. It is basically based in Bangalore, however it has also a small group in Manipal (India) and Kuala Lumpur (Malaysia). Stempeutics focuses on adult and embryonic stem cell research. In adult stem cells it is basically focusing on mesenchymal stem cells (MSCs) derived from sources like bone marrow, adipose tissue, Wharton's jelly and dental pulp. Its main goal is to develop stem cell based products i.e. drugs. Currently the main focus of Stempeutics is on MSCs derived from bone marrow which reached at the stage of clinical trials. The MSCs derived from other sources like adipose tissue, Wharton's jelly and dental pulp at the moment is at basic research level.

Presently Stempeutics is conducting clinical trial for the four indications: a) Mayocardial Infarction; b) Critical Limb Ischemia; c) Cerebral Stroke and d) Osteoarthritis. The first two is being conducted in India and the rest in Malaysia. The trail in India which was started in 2009 for Critical Limb Ischemia (CLI) is figure out as India's first true stem cell trials approved by the Drug Controller General of India (DCGI) (Jayaraman, 2009). It has completed initial phase I/II clinical trial in April 2010 and now came up with a product named "Stempeucel-CLI". For marketing of its different stem cell products, Stempeutics has signed a MoU with India's leading pharmaceutical company, Cipla.

In addition to above mentioned clinical trials, Stempeutics recently obtained DCGI approval for phase II clinical trial for chronic obstructive pulmonary disease, liver cirrhosis, osteoarthritis and diabetes mellitus (http://www.stempeutics.com/).

As per information provided on company's website it has filed 13 patent applications in India and 6 PCT applications. It has been recently received a patent in India on "*An in vitro human embryonic model and a method there of*" for potential application in toxicological studies and drug screening. Stempeutics aims to market its products in the European and North American markets.

Stempeutics' stem cell facility centre in Malaysia has been awarded the Bionexus Status by the Malaysian Biotechnology Corporation. BioNexus Status provides certain rights to the companies mentioned within the BioNexus Bill of Guarantees. Some of these rights are: a) freedom of ownership; b) freedom to source funds globally; c) eligibility to receive assistance for international accreditation and standards and d) a strong intellectual property regime. Stempeutics also has received National Pharmaceutical Control Bureau approval in Malaysia which facilitates the way to go in nearly 20 other countries which come under the purview of the Organisation of Islamic Conference without any further clinical trials (Biospectrum, 2011).

Stempeutics, with the support of the Malaysian Biotechnology Corporation in April 2008, launched the Stem Cells Operational & Professional Excellence (SCOPE) programme in Malaysia. This SCOPE programme is basically related to talent creation in the field of stem cells.

The Manipal Institute of Regenerative Medicine which is also a part of Manipal group helps Stempeutics in enhancing the knowledge base in the area stem cell research.

Nichi-In Centre for Regenerative Medicine

NCRM is an Indo-Japan join venture firm. It is spin -off from Nichi-In bio-Science Ltd. It is established in 2005. NCRM mainly focuses on autologous adult stem cells. Limbal, Haematopotic, Mesenchymal Liver and Corneal endothelial precursors stem cells. They are not conducting any research work either on embryonic stem cells or umbilical cord blood stem cells. It works in collaboration with different institutes in Japan which include both public and private. The institute in Japan either prepares the basic materials or technology for the NCRM. It is active in collaboration for either research or clinical application of stem cells.

In India it has collaboration in both research and clinical application of stem cells in different areas with different hospitals and institutes. The collaboration is basically for two purposes. The first one is in the area of stem cell research and second one for the stem cell treatments. In stem cell treatment collaboration, NCRM provides services such as stem cell isolation and NK cells expansion etc. to the hospitals based on MoU. The responsibility of the NCRM is limited at the service stage and documentation of the same only. The hospitals take care of clinical assessment, harvesting and application of stem cells.

NCRM is also engaged in academics and various training programmes in the

area of stem cells. It has started a PhD programme in the area of stem cell in collaboration with Acharya Nagarjuna University, Guntur, Andhra Pradesh in the year 2008. For its PhD student NCRM has launched a web-based training programme in regenerative medicine with the help of University of Toronto. This training programme will cover areas like organ failure, stem cell biology, ethics and translation (The Hindu, 2008).

Academic Institutions

Some of the universities in India either started courses on stem cell biology or engaged themselves in stem cell research.

For instance, Special Centre for Molecular Medicine, Jawaharlal Nehru University (JNU) New Delhi in their Pre-PhD course included a topic on 'Stem cell research and its application in human health'. School of Life Sciences at JNU is also interested in multipotent adult progenitor stem cell research (JNU Websites). Guru Gobind Singh Indraprastha University, New Delhi included the topic 'Stem cells in health care' in the curriculum for the master of technology degree (Greenwood et al., 2006). University of Madras, Chennai started one year PG Diploma in 'Molecular cell biology and stem cell technology' in the Department of Zoology.

University of Delhi is engaged in the study of basic mechanisms of stem cell function in association with Indian Institute of Nuclear Medicine and Allied Sciences, New Delhi (Lander et al., 2008). Research on neural stem cells is progressed at University of Hyderabad.

Acharya Nagarjuna University, Guntur is recognised the first Doctorate programme on stem cells in the country at Nichi-In Centre for Regenerative Medicine, Chennai.

Sri Ramachandra University, Chennai in collaboration with Life Cell a stem cell bank company, established 'Tri Cell' stem cell centre for the research on stem cell therapy related to hematological diseases. These are the efforts by the private players to enhance their knowledge base through interaction with the universities. Universities are also benefited by their strong infrastructure.

Apart from these, several hospitals who also provided graduate and post graduate degree to the medical students, also engaged in developing knowledge about stem cells, such as AIIMS, New Delhi and CMC, Vellore.

ROLE OF INSTITUTIONS

The Indian government is viewed as a dominant player in encouraging stem cell R&D activity and innovation in the country. This is evident from the new National Health Policy, 2002 that lays emphasis on equity, ethics and the futuristic concerns. These concerns are also reflected in the new health research policy (ICMR Bulletin, 2004) that accords high priority to emerging scientific developments such as modern biotechnology (genomics, human genetics, new drug development and stem cell research). Some of the

important actors in the National Health Research System are the DBT, Indian Council of Medical Research (ICMR), Department of Science & Technology (DST) and Council of Scientific and Industrial Research (CSIR). Out of these DBT is sharing a major responsibility.

DBT is currently supporting more than 55 stem cells programme at various research laboratories including hospitals in India. City clusters programme is promoted by DBT to take advantage from the clinical application of stem cell research. Delhi, Vellore, Pune, Bangalore and Hyderabad are included in the city cluster programme. The main aim of the city clusters programme is to share information, explore collaboration between basic researchers and clinicians. The focus is also on emerging policy issues discussion. The stem cell city cluster programme at Bangalore will consist of the Indian Institute of Science (IISc), NCBS, Banglore, Manipal Hospital, CMC Vellore and one local company. For the training in embryonic and adult stem cells DBT has established a centre at NCBS & JNCASR, Bangalore.

DBT has formulated the strategy for the development of stem cells. The key components of DBT strategy are;

- Development of skilled and brilliant pool of scientists;
- Establishment of Centre of Excellence in basic science institutes, medical institutes and selected animal institutes;
- To establish an autonomous stem cell institute in India;
- To organise world class science conferences/meetings;
- To provide opportunity of overseas training to young people;
- Supporting public-private partnership research in R&D area and
- Promote global partnerships.

Government of India has started an exchange programme with the University of California to train Indian university faculty and students in stem cell research. In this programme faculty will be trained in California and the faculty member of the University of California will come to India to train Indian Students (Indiainfo, 2008).

In India, stem cell research is largely governed by the DBT, ICMR and DCGI. DBT and ICMR have jointly prepared the Guidelines for Stem Cell Research and Therapy in November 2007. The Guidelines is approved by the Law Ministry and subject to the approval by the Cabinet (Pandya, 2008).

The guidelines classified stem cell research in to three categories, a) Permissible; b) Restricted; and c) Prohibited research area. These guidelines are perceived largely as permissive. It allows hESC, therapeutic cloning and chimera studies subject to the approval of the committees. To review and monitoring of the stem cell research and therapy, the Government of India is formulated two committees. The committee at National level is called as National Apex Committee for Stem Cell Research and Therapy

(NAC-SCRT) and at the Institutional level the committee is named as Institutional Committee for Stem Cell Research and Therapy (IC-SCRT).

Clinical research is very important part of the stem cell science. The safety and efficacy is essential for clinical research. For the stem cell clinical research DBT has constituted four separate committees: a) Human Studies Committee; b) National Bioethics Committee; c) Task Force on Stem Cells and Regenerative Medicine; d) Programme Advisory Committee.

International collaboration

Recently, India has become a major destination of FDI in R&D. This may not be due only to deregulation of economy but also because of strengthening of India's innovation system. The Government of India now permits 100% FDI under the automatic route for both 'research and development services' as well as 'health-related services'. However, harmonisation in international collaboration might be required, as the Draft ICMR Guidelines provide that, 'Collaboration will be permitted only after the joint proposal with appropriate MoU is approved by the Health Ministry's Screening Committee following clearance by the Apex Committee'.

In the area of stem cell research, Johnson & Johnson and Novo Nordisk are the two players to have liaised with specialists for basic research work. Johnson & Johnson has tied up with Neuronyx for adult derived stem cell research for applications in cardiovascular therapies. Novo Nordisk is working with its wholly owned subsidiary Zymogenetics in the generation of beta cells for transplantation and "stem cell factors" for oncology and blood and immune system applications.

EMERGING SCENARIO OF STEM CELL SECTOR IN INDIA

This section is based on an on-line survey. The questionnaire was sent by e-mail to the leading scientists/policymakers and entrepreneurs, engaged in various areas of stem cells in India.

Focus areas of Stem Cell Research

During the survey it was found that Indian Stem Cell sector is dominated by the adult stem cells. This has revealed greater interest towards the haematopotic stem cells & bone marrow mononuclear cell followed by neural, mesenchymal and liver stem cells (Figure 2).

In response to the questions regarding preference in stem cell sector, most of the respondents showed their inclination towards the development of strategies and techniques for stem cell therapies in comparison to extraction and characterisation of stem cells as potential or business goal (Figure 3).

Preference for raw materials

The development of any sector is very much dependent on the availability of raw materials. In this field, the problem is not so much of the adult and cord

blood stem cell as it is of the embryonic stem cell. During the survey, it was found that Indian stem cell scientists prefer IVF embryos for the research where the ethical issues are not so ticklish (Figure 4).

Patenting

Patenting is a crucial factor that determines what gets commercialised and by whom. The Indian scientists/entrepreneurs are more interested in patenting than publication of their research materials. Out of the total respondents, 80% indicated patenting as their first preference while only for 66.7% publication was the first preference. This reflects dominance of Zimanian mode over Mertonian mode of science. The response also revealed that the stem cell lines and preparation have more potential for patenting than stem cell culture methods and growth factors. 43% of the scientists/entrepreneur ranked the stem cell and preparation as the first choice, while 36% preferred stem cell culture methods and 21% the growth factors as their first preference (Figure 5).

Collaboration in stem cell sector in India

In order to inquire about the collaboration, scientists/ entrepreneurs were asked their engagement, it was discovered that 85.7 percent research institutes/firms have some kind of collaboration with others.

On the interest of their collaboration it was revealed that they are more or less equally like to have collaboration with national public as well as private research institutes. On the question of international institutes they showed their interest more in public research institute in comparison to private research institutes. The preference is also equal in the case of national and international universities. Public hospitals are more preferable than private hospitals for collaboration.

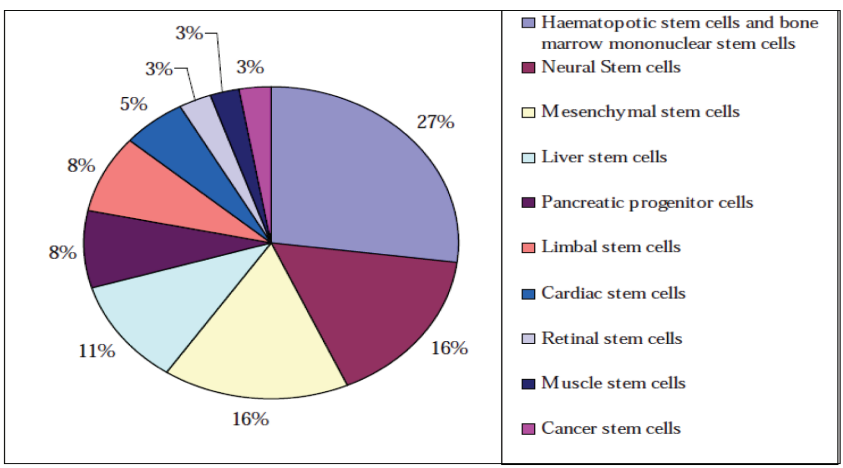

Figure 2: Area of Adult Stem Cells

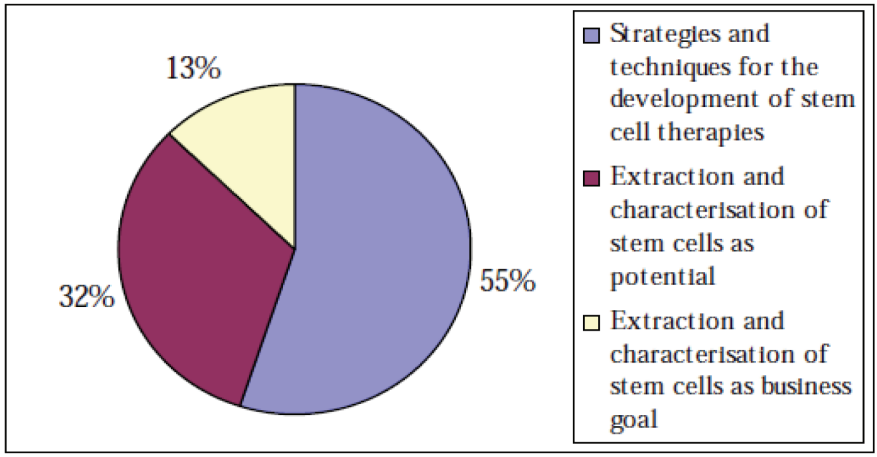

Figure 3: Preference in stem cell sector

It is observed from this analysis that preference for collaboration depends very much upon the nature of organisation and it varies according to their mandate. For example a leading eye hospital who is working in the area of retinal and limbal stem cells does not prefer any type of collaboration with any other hospitals. Similarly a firm in India which is spin-off from a foreign firm prefers collaboration with international public and private research institutes. It also showed their interest in private hospitals, the reason here might be for the clinical trials.

The scientists associated with public research laboratories in India gave importance to the national and international research institutes/universities for the collaboration. No one was interested in collaboration with any kind of hospitals.

The survey also tried to investigate the challenges of collaboration. Most of the scientists/policymakers and entrepreneurs believed that lack of shared vision and organisational structure are the main challenges of collaboration followed by other factors like maintaining access to additional funding, delayed accomplishments and increased competition between groups (Figure 6). The questions were also asked to rank the advantages of collaboration. On an average the general opinion was that meeting technical know-how is one of the most important advantages of collaboration. Lowering R& D and human resource managements ranked a second followed by market access and government connections. Only a few indicated collaboration with the suppliers as important and to a certain extent.

Barriers to commercialisation

Indian stem cell sector is at an early stage of development. Hence, it is at this stage that it is meaningful to identify the critical barriers in the commercialisation process. The survey has revealed that the Indian stem cell sector is facing shortage

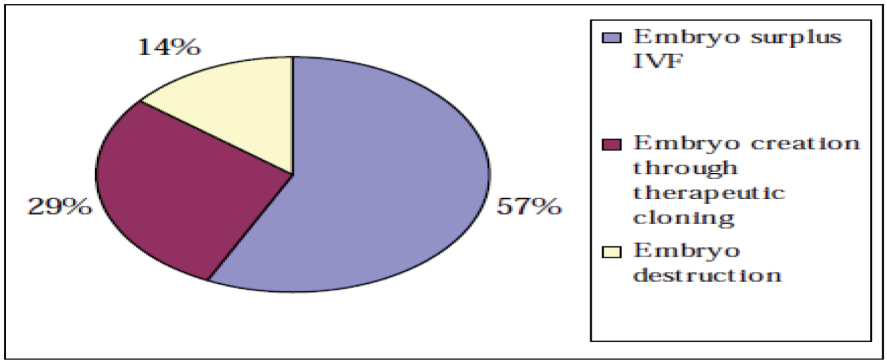

Figure 4: Preference for raw materials in Indian stem cell sector

of human resources. Separate questions were asked concerning human resources. The response pointed to the fact that in most of the institutes only 1-5 scientists were engaged in the stem cell research. The number of students as well as technical staff varied between 1-5, except in one firm the number of technical staff was found ranging 5-10 in number.

There is a lack of enabling technologies to support the sector. One of the entrepreneur opined that the lack of enabling technologies are most important barriers for the stem cell sector in India. Lack of venture capital was also identified as one of the important barriers in the commericialisation. The country needs strict legislation as so many contentious issues are involved with the stem cells field. Some scientists and entrepreneur feels that there should be a clear cut IPR regime. Ethical issues did not figure as critical barriers in the development

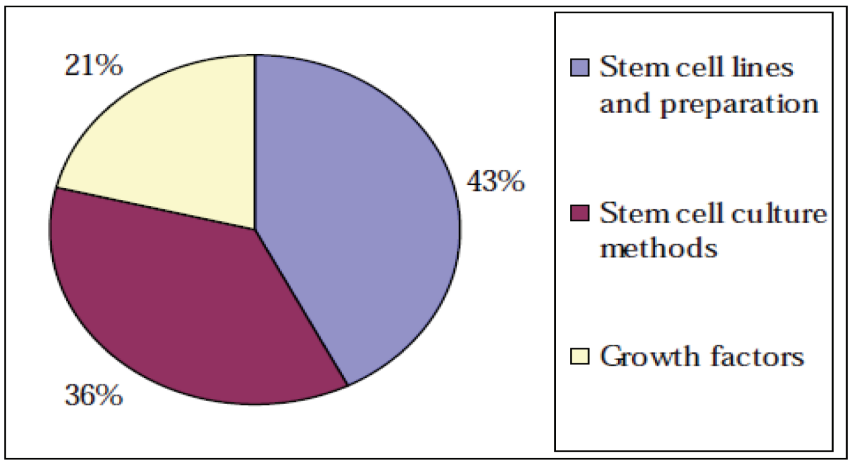

Figure 5: Potential for Patenting

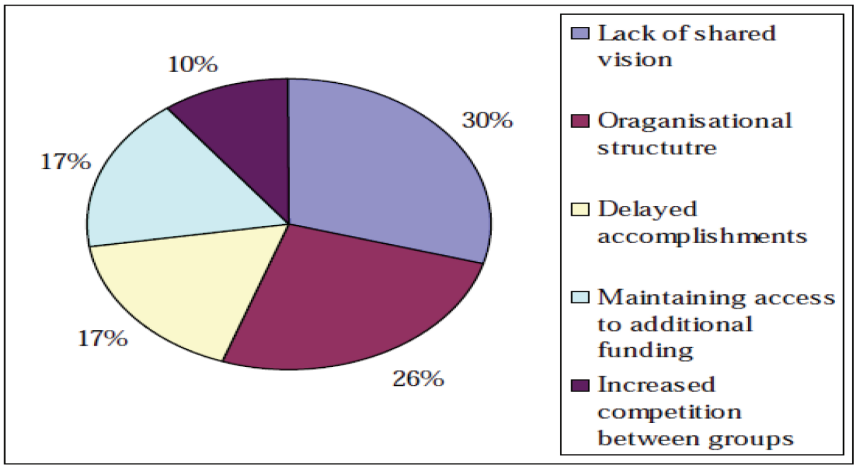

Figure 6: Challenges of Collaboration

of stem cell research. Some of them expressed that "India lacks coherent national policy and has affected the development of the sector".

Regarding government funding is concerned, there is a general opinion that India lacks adequate government funding and there is a need of more funding.

Potential of Indian stem cell sector

Large patient pool in India is ranked as the most favourable condition. Skilled clinicians are also seen as the strength of India. Scientists on an average opined that there is a strong government support and favourable regulation in India. On the issues of availability of raw materials for the research, there is no consensus. Some of them treated it as potential but some of them feel that it is not so much influential. The unaddressed ethical issues are not given so much importance as far as potential is concerned.

The question was also asked about a possibility of India being a global player in the stem cell sector. Some of them feel that in the next 5 years India would be the global player while others are of the opinion that it is possible in the next 10 or 15 years. Other responses also included "No idea". Thus, no consensus seemed to emerge on this issue.

CONCLUSION

It is observed that though the Indian stem cell innovation system is in nascent stage, there are clear indications of rapid growth and the co-evolution of technology and institutions is yet to emerge. The preceding analysis has identified the following features of the pathways to the futures of the Indian stem cell innovation system.

A. The public research laboratories and hospitals have emerged as the dominant actors in this sector and the university system plays a moderate role.

Only a few private firms are engaged in research and are largely engaged in cord blood banking rather than the adult and embryonic stem cells research. As far as hospitals are concerned, both private and government hospitals are conducting research offering stem cell therapies to the patients. However, there are concerns over these therapies in the absence of peer review.

B. Though there are conscious attempts by the Government of India to introduce promotional and regulatory policies, it seems that the institutions have lagged behind technology. The stem cell sector in India is jointly governed by DBT, ICMR and DCGI. Because of multiple agencies, administration would be not very smooth and hassle free. In this context, perhaps India needs a single apex body for governing the stem cell science. Now the fully functional NAC-SCRT could be seen as a step forward in this direction (Sinha, 2011). It is pertinent to note here that the DBT had constituted many committees for governing the development of stem cells in the country. Out of these only a few committees have become functional.

C. Stem cell sector is technology intensive; the sector needs strong knowledge and technology base. Keeping this in view, government seems to be active in enhancing knowledge base in this field. It has opened exclusive stem cell research centre. The DBT through its city cluster programme has attempted to establish linkages among the frontier research centres of the respective cities. In the city cluster programme a local company is also included which could be a public–private linkages.

D. These linkages encourage knowledge flow among different players in the sector. However, the study finds that lack of shared vision and organisational structure act as barriers in establishing strong linkages.

E. The DBT-ICMR guidelines are considered to be relatively permissive compared to other countries. It largely permits research on human embryonic stem cells, therapeutic cloning as well as chimeras studies. On the other hand, it prohibited reproductive cloning and some other research on embryos. However, these guidelines are not stringent and legally binding. There are possibilities of violation and violator can't be punished. The study finds that absence of effective legislation is one of the barriers in the development of stem cell research in India. It affects the international collaborations and commercial linkages.

F. Adult stem cells and cord blood banking turned out to be a dominant area of research in India rather than the embryonic stem cell research. As the adult stem cells have lesser capacity of differentiation than embryonic stem cells, the commercial value is not so high. The work in this area is not getting apace as it requires more focussed R&D.

G. There are noticeable efforts to build up human resource base as reflected

in various university programmes at different levels. An interesting point to be noted is that there are private firms that are collaborating with the Indian as well foreign universities for introducing doctoral programmes. This is perhaps a good indication of creating knowledge and technology base.

H. Linkages are important for the sectoral growth. On examination of linkages, it was found that, firms, research laboratories, and hospitals have developed linkages with each other along with international collaboration.

I. A large patient pool with genetic diversity and skilled clinicians in India is an additional strength.

J. There are many barriers to commercialisation of stem cell research in India such as lack of enabling technologies; lack of venture capitals and relatively inadequate funding. These constraints have posed serious challenges.

K. In the context of increasing global patent thicketing, India might have to opt for some alternative patent strategies such as patent pooling, Open Source Licensing- Open Source Drug Discovery or compulsory licensing.

Finally, it seems that given the nature of complex technologies involved, there is a greater need felt for R&D and training collaboration and hence linkages of various types are taking place. For shaping futures for a balanced growth of this sector, the institutions in India will have to be geared towards greater coordination, promotion of greater knowledge flows at national as well international levels.

BIOGRAPHY

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