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BIONETWORKING: BETWEEN GUIDELINES AND PRACTICE IN STEM CELL THERAPY ENTERPRISE IN INDIA

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Abstract

Many stem cell therapies, even though largely unproven, are widely viewed as promising to global healthcare provision. India is a leading proponent of the practice of making this therapy available as a last resort to patients from around the world, who are prepared to risk their remaining health and financial resources in exchange for hope. Stem cell therapy service centers, labeled as ‘rogue’ or ‘maverick’ by some, are vigorously promoting such therapies as ‘safe’ modes of treatment in the guise of ‘experimental’ therapy. This has been carried on in India even since its promulgation of the Guidelines for Stem Cell Research and Therapy in 2007. This article is based on a multi-site ethnographic study carried out at several locations in India between September and December 2008. It raises two questions: why the use of unproven therapies is becoming common practice in jurisdictions in which regulatory apparatus is in place; and, how these service providers are succeeding in sustaining and proliferating such therapeutic practices. By employing the concept of bionetworking, we have tried to describe the gap between regulation and implementation. This article divides service providers into three categories - public sector, private sector and individual practitioner - on the basis of their institutional embeddedness. It explores how service providers are able to exploit the gray areas of regulatory systems to their own entrepreneurial ends. The article highlights how local actors engaged in stem cell therapy draw on international norms of bioethics but adopt them according to various underlying rationales, shaped by local patterns of governance, institutional development and policy-making.

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1. Introduction

It is widely thought that stem cell research has great medical promise.¹ Many healthcare service centres and clinics around the world have, however, begun to use stem cells as therapies before such promise has been medically and scientifically validated. Such centres and clinics are labelled as ‘rogue,’² ‘maverick,’³ or ‘trading on hope and desperation,’⁴ because they offer unproven stem cell-based therapies to people who are desperate⁵ or who have a debilitating disease and have given up on conventional medicine.⁶

There is a general global consensus in the stem cell community that international regulation and oversight of unproven treatments is urgently needed.⁷ Yet, in many jurisdictions, such as India, in which such therapies are available, regulations are already in place.⁸ This raises two questions: (i) why are there questionable medical practices in locations in which regulatory apparatus is in place?; and, (ii) how or through what mechanisms are these centres/clinics able to successfully sustain and expand the enterprise of stem cell therapy. In this article, by using the concept of *bionetworking*,⁹ we try to describe the gap between regulation and implementation. Using empirical evidence, we discuss the institutional circumstances that allow service providers to circumvent regulation. Bionetworking, in the context of our study, denotes a form of connecting up with key individuals involved in research and healthcare organisations who take advantage of the unequal socio-economic and regulatory contexts in which research takes place and healthcare is provided. Bionetworking explains the strategy that service providers use in the recruitment of patients. Service providers differ on the basis of their institutional embedding. Thus, in order to gain better insight into the growing enterprise of stem cell research and therapy in India, we categorise providers according to whether they belong to the

¹ S Kiatpongsan and D Sipp, “Offshore stem cell treatments” (2008) available at <http://www.nature.com/stemcells/2008/0812/081203/full/stemcells.2008.151.html> (accessed 10 Jul 2010).

² B Jones “New guidelines drawn up in fight against rogue stem cell clinics” (2008) available at http://www.bionews.org.uk/page_13604.asp (accessed 10 Jul 2010).

³ A Bharadwaj and P Glasner *Local Cells, Global Science – The Rise of Embryonic Stem Cell Research in India* (Routledge: London and New York, 2009).

⁴ J Qui, “Trading on hope” (2009) 7 *Nature Biotechnology* 790-792.

⁵ O Lindvall and I Hyun, “Medical innovation versus stem cell tourism” (2009) 324 *Science* 1664-1665.

⁶ Qui, see note 4 above.

⁷ *Ibid.*

⁸ For example, countries like China and India that are viewed as most preferred destinations for stem cell research collaborations and clinical practice leading to stem cell tourism. See Lindvall & Hyun, see note 5 above, and Qui, see note 4 above.

⁹ PK Patra and M Sleeboom-Faulkner, “Bionetworking: experimental stem cell therapy and patient recruitment in India” (2009) 16 *Anthropology and Medicine* 147-163.

public, private or independent sectors.^{10,11} We then analyse the exploitation by service providers of the ambiguities within existing regulations, and the vital role that patients play in their collusion against regulation.

Data for this study was collected using qualitative anthropological fieldwork methods, including participant observations, case studies and semi-structured interviews at various locations in India, from September to December 2008. Hospitals and research centres, from both public and private sectors, involved in stem cell research and therapy were randomly selected as study sites in a stratified manner. Though we had no insight into the precise practices and patient recruitment methods that were employed, the healthcare institutes were carefully selected on the basis of their reputation as leading SCT service providing centres, using patient narratives, media reports and web-searches. Interviewees include, among many others, three premier national level public hospitals from New Delhi and Mumbai, and three private sector stem cell research centres from Chennai and Bangalore. The informants included: three practitioners or clinicians involved in research or clinical uses of regenerative medicine in cities such as Delhi, Kolkata and Cuttack; ten patients who have received or are receiving stem cell therapy using embryonic, umbilical and adult stem cells; and the relatives of the said patients.

2. Stem Cell Research and Therapy in India

Stem cell research and therapy in India are rapidly growing fields. Currently, there are over 40 institutions and hospitals involved in stem cell research.¹² Both the government and private industry have invested heavily in research institutes studying stem cells.¹³ In private industry, Reliance Life Science, Mumbai, for instance, has characterised ten stem cell lines, including two neuronal cell lines, dopamine producing neurons and neurons for patients of stroke.¹⁴ Government policies in India are supportive of stem cell science and, keeping in view its potential therapeutic application, both basic and translational research are being promoted by the government in various institutions, hospitals and industry. The government has so far identified 55 programmes and supported various aspects of stem cell research. These aspects include: generation of human embryonic stem cell lines; differentiation of

¹⁰ PK Patra and M Sleeboom-Faulkner, "Stem Cell Therapies in India: Bio-networking Strategies and Patient Recruitment", unpublished paper presented at the Cesagen conference on *Mapping the Genomic Era: Measurements and Meanings* at University of Cardiff, 7-9 October 2009, UK.

¹¹ M Sleeboom-Faulkner and PK Patra, "Experimental Stem Cell Therapy in Japan and India: Bionetworking, Biohierarchies and Boundary Objects" unpublished paper presented at the international conference *The Cultural Politics of the Life Sciences in Asia – opportunities, risks and the changing body*, organized by the International Institute for Asian Studies, 10-11 April 2009, Leiden, The Netherlands.

¹² S Dey, "Selling Stem Cells" available at <http://www.expresspharmaonline.com/20071215/market01.shtml> (accessed 1 April 2010).

¹³ M Sleeboom-Faulkner and PK Patra "The Bioethical Vacuum: National Policies on Human Embryonic Stem Cell Research in India and China" (2008) 5 *Journal of International Biotechnology Law* 221-234.

¹⁴ A Sharma "Stem Cell Research in India: Emerging Scenario and Policy Concerns" (2006) 8 *Asian Biotechnology and Development Review* 43-53.

pancreatic progenitor cells to insulin secreting cells; isolation of multi potential adult progenitor cells from bone marrow and their clonal expansion; use of banana lectins for stem cell preservation; hematopoietic stem cells (HSC) for haplo-identical HSC transplantation; use of limbal stem cells for ocular surface disorders, isolation and characterisation of mesenchymal and liver stem cells; in vitro differentiation of human embryonic stem cells to neural and non-neural lineages; cardiac stem cells; embryonic stem cells etc.¹⁵

Public-private partnerships (PPPs) between government institutions and private enterprise are an important form of collaboration in the field of stem cell research and therapy. There are many such initiatives in India among academic institutes, hospitals and industry. PPPs have a wide role in the formation of a network that helps stem cell science and technology achieve a strategic advantage through public funding. Challenges identified by the government of India in this regard include: availability of human resources with the desired expertise; adequate infrastructure; an interdisciplinary network of researchers and clinicians for theme based research; appropriate regulatory mechanisms; well defined basic research leading to clinical/translational research; and focused centers and institutions.¹⁶

3. Stem Cell Based Therapies and Clinical Trials in India

Regenerative therapies using stem cells (we will concentrate on adult stem cells which are generally used) has attracted great interest in India as a treatment modality. There are high expectations that stem cell transplantation will provide the answer to a large number of acute and chronic disease conditions for which modern and conventional medicines have produced few effective treatments.¹⁷ These stem cell transplants take place mainly in private sector research-cum-hospital set ups, though some public hospitals have also ventured into this field. While the evidence in support of the efficacy of adult stem cells in curing a wide range of disease conditions is questionable, many Indian health care centres have been carrying out such therapies without official approval,^{18,19} and under the ambiguous guise of experimental therapy. Some physicians interpret the term experimental therapy as a research protocol that falls between animal model test and phase I-II of clinical trials, while others view it as another name for phase I and II clinical trials, or as ‘proof of concept’ studies. There is purportedly a clinic in New Delhi, Nu Tech Mediworld, which is providing therapies using transplants of embryonic stem cells derived from a single stem cell line developed at the clinic’s own research facilities.^{20,21} It claims to have cured or

¹⁵ Government of India, “The National Portal of India” (2009) available at http://india.gov.in/sector/science/stem_cell_biology.php (accessed 1 April 2010).

¹⁶ *Ibid.*

¹⁷ MD Nair, “Stem Cells Research: New Vistas in Regenerative Medicine” (2006), available at <http://www.pharmabiz.com/article/detnews.asp?articleid=32758§ionid=50> (accessed 10 Jul 2010).

¹⁸ S Pandya “Stem Cell Transplantation in India: Tall Claims, Questionable Ethics” (2008) 5 *Indian Journal of Medical Ethics* 15-17.

¹⁹ Nair, see note 17 above.

²⁰ G Shroff *Human Embryonic Stem Cells – A Revolution in Therapeutics*. (New Delhi: Nu Tech Mediworld, 2005).

improved the conditions of hundreds of patients with Alzheimer's disease, Parkinson's disease and spinal cord injuries from foreign countries, as well as various parts of India.^{22,23}

A recent report in *Nature*²⁴ announced that on 22 April 2009 The Drug Controller of India (DCGI) approved the first 'true' clinical trials designed to test stem cell products. A Bangalore based private research institute, Stempeutics Research Private Limited, had however already launched a combined phase I and phase II trial to evaluate the benefits of its stem cell products for people who have experienced myocardial infarction and individuals with critical limb ischemia (CLI). The report also quotes a member of the government panel that made the recommendations to DCGI, saying "[t]hese are the only two stem cell trials officially approved to date."

Interestingly, the premier medical institute of India, the All India Institute of Medical Sciences (AIIMS), reportedly started a stem cell clinical trial as early as 2003.²⁵ As a nodal agency, AIIMS conducted a multi-centric clinical trial of stem cell therapy – organised at five centres across India - for diseases including myocardial infarction, cardiomyopathy, muscular dystrophy, cerebral palsy, diabetes, retinal pigmentosa, spinal cord injury, and ALS. These trials started in 2003, and by 2006 more than 750 patients had, according to one newspaper report,²⁶ undergone clinical trials. An autologous adult stem cell treatment conducted at AIIMS between 2005 and 2009 on 85 patients suffering from Dilated Cardiomyopathy (DCM) is reported to have "met with reasonable success," and "half of the patients had responded to the treatment."²⁷ Public sector hospitals, such as Sion hospital in Mumbai, have also claimed to have provided stem cell therapy to patients suffering from multiple sclerosis.²⁸

4. Stem Cell Regulation in India

Given the rapid growth of biotech research in India and the putative future benefits of stem cell science, it has been necessary to use regulatory means to address the interests of the scientific community, healthcare professionals and patients.²⁹ In 2002,

²¹ Bharadwaj and Glasner, see note 3 above.

²² Patra and Sleeboom-Faulkner, see note 13 above.

²³ Bharadwaj and Glasner, see note 3 above.

²⁴ K Jayaram, "India's First True Stem Cell Trials" (2009) 27 *Nature Biotechnology* 498-498.

²⁵ The Hindustan Times, "Stem Cell Trials to Start at AIIMS" (13 November 2006); *Stem Cell Research Blog*, "Stem Cell Research in Heart Disease and other Ailments at all India Institute of Medical Sciences", available at <http://stemcell.taragana.net/archive/stem-cell-research-in-heart-disease-and-other-ailments-at-all-india-institute-of-medical-sciences/> (accessed 10 Jul 2010).

²⁶ The Hindustan Times, see note 25 above.

²⁷ The Indian Express "50% Success Rate in Stem Cell Therapy on Heart Patients: AIIMS Docs" (2010), available at <http://www.indianexpress.com/news/50-success-rate-in-stem-cell-therapy-on-heart-patients-aiims-doc/576335/> (accessed 10 Jul 2010).

²⁸ Times of India "Treatment was Carried Out for First Time at Sion Hospital" (2009), available at <http://timesofindia.indiatimes.com/city/mumbai/Treatment-was-carried-out-for-first-time-at-Sion-Hospital/articleshow/4586266.cms> (accessed 10 Jul 2010).

²⁹ S Basu "Regulating Stem Cell Research in India: Wedding the Public to the Policy" (2006) 90 *Current Science* 1476-1479.

the Indian Council of Medical Research (ICMR), under the remit of the ministry of health, announced a policy that permitted therapeutic cloning and encouraged stem cell research. During the previous year, however, the Department of Biotechnology (DBT), in the ministry of science, had also issued guidelines, and some clinics had exploited the difference between the two sets of guidelines by starting clinical treatments.³⁰

As a result of an increase in applications for funding, media reports of unethical practices in biomedical research, and government efforts to promote stem cell research, the DBT and ICMR decided in 2005 to jointly devise the *Guidelines for Stem Cell Research and Therapy*³¹, released in November 2007. The guidelines permit research pertaining to adult and umbilical cord blood stem cells, subject to approval by Institutional Committees,³² without indicating which stem cell therapies, aside from bone marrow transplants, that are to be approved for routine medical practice. There have nevertheless been many cases of violation by practitioners at both public and private sector healthcare institutions,³³ and failures in oversight on the part of the regulatory bodies.³⁴ In their current form, the present regulations (DBT-ICMR 2007) have no legislative power and impose no statutory sanctions, and it is this that has led to the large-scale violation by clinicians and medical practitioners who work to profit from the ‘gray areas’ in the regulation. As a result, a new bill, the *Biomedical Research on Human Participants: Promotion and Regulation Bill 2007* has, according to Visamohan Katoch, the director general of ICMR, been submitted for consideration by the Parliament. He says that if it is approved the Bill “would be a significant step forward”, in that it would grant ICMR the legislative power to regulate clinical research and medical practice.³⁵

5. Service Providers: Public Sector, Private Sector and Individual Practitioners

This section shows that the institutional embedding of stem cell therapy provisions in India is varied and is facilitated by bionetworks according to institutional set-up. There are three kinds of providers of stem cell therapy: public sector, private sector and independent practitioners. The overview of these in this section describes the emerging enterprise of stem cell therapy with its diverse funding sources, collaborative activities, motivational factors and strategies for survival and growth in Indian contexts.

³⁰ KS Jayaraman, “Indian Regulations Fail to Monitor Growing Stem-Cell Use in Clinics” (2005) 434 *Nature* 259-259.

³¹ DBT-ICMR (Department of Biotechnology and Indian Council of Medical Research) “Guidance for Stem Cell Research and Policy” (2007), available at http://www.icmr.nic.in/stem_cell/stem_cell_guidelines.pdf (accessed 21 Apr 2010).

³² Research pertaining to reproductive cloning, introducing animal embryos in human, etc has been categorised as prohibited (DBT-ICMR 2007).

³³ M Sleeboom-Faulkner and PK Patra, “The Bioethical Vacuum: National Policies on Human Embryonic Stem Cell Research in India and China” (2008) 5 *Journal of International Biotechnology Law* 221-234.

³⁴ Pandya, see note 18 above.

³⁵ Qiu, see note 4 above.

5.1 *The Public Sector*

Though there are many public sector hospitals and research institutes involved in stem cell research and clinical application, there is no reliable data on the scope of their activities. The government of India has taken proactive policy measures to turn stem cell research and its applications into a frontline field, engaging in major capacity building efforts to create an inter-connected, well-managed stem cell research industry in the country. The Department of Biotechnology, a national policy-making body, has set up a separate taskforce for stem cell research and regenerative medicine, engaging eminent scientists and clinicians to deal with stem cell proposals. The task force considers new proposals and monitors the progress of ongoing projects of basic and translational research in the areas of both embryonic and adult stem cells.³⁶ Based on empirical findings, we discuss two stem cell research centres that are involved with stem cell related research and /or clinical trials.

5.1.1 *All India Institute of Medical Sciences (AIIMS), New Delhi*

Contrary to the claim made by senior ICMR officials that “...the ICMR has not received any clinical trials or research proposals in stem cells and we cannot consider claims being made presently for cure or therapy” (interview dated 26 November 2008), the All India Institute of Medical Sciences is organising a large-scale clinical trial as the nodal agency. Dr SM, who is in charge of the stem cell department, commented that:

We have already completed clinical trials on around 750 patients using autologous adult stem cells, all at AIIMS and other coordinating centres in the country. This is for a variety of disease conditions that include; myocardial infarction, limb ischemia, cymbal stem cells for eye and many others. Being a premier public medical institute, we strictly follow the ICMR guidelines and are careful about our collaborations.

The main stated motivation of public institutions lies in meeting the needs of patients and saving funds. AIIMS, according to Dr SM, tries to illustrate this:

See, there are so many patients who come to AIIMS for cure [*sic*] for so many diseases for which the state need [*sic*] to spend a lot from the public fund. But, if stem cell therapies, with all safeguards, can be the answer, then imagine how useful it would be for the patients, and for the state! We could save so much! Moreover, with India developing so rapidly, you will have increasing disease burdens that perhaps only stem cell therapy can answer...It's all about healthcare needs.

Though it is clear that providing healthcare for all patients is the reported aim of the institute, problems have been reported pertaining to whether AIIMS has acted in accordance with ICMR guidelines.

³⁶ S Dey, see note 12 above.

5.1.2 Tata Memorial Hospital and KEM Hospital, Mumbai

Tata Memorial Hospital and KEM hospital are two public-sector hospitals based in Mumbai. The Tata Memorial Hospital provides adult autologous stem cell therapy to paediatric and adult patients and engages with basic research on mesenchymal stem cells, especially for cancer-related diseases. Patient recruitment for stem cell therapy is generally made on a referral basis or on the basis of medical conditions assessed by the treating doctors. As Dr M from Tata said:

We admit patients mainly who come as a referral case with a steady medical follow-up procedure. Of course, it is true that the vast majority of our patients are central and state government employees and bank employees, but there are many poor patients too who are treated here.

Due to the hype around stem cell therapy in the newspapers lately, more and more public hospitals are keen to conduct clinical trials on stem cell-based treatments. As Dr LR, head of stem cell department at KEM Hospital Mumbai said:

There are many private hospitals and clinics in and around Mumbai that provide stem cell therapies. But as a public sector hospital we are a bit conservative, or you may say we are cautious. It is because; since we are a public body we are bound to abide by the regulations set by the state. We are finished with the animal model. Now, in 15 days time we are planning to go for experimental therapy on human patients. The inclusion and exclusion criteria decisions will be taken by a medical committee of the hospital. For us, the medical conditions of the patients will decide the inclusion, but not his social status or financial background, as most of the medical expenses will be borne by the hospital.

It is clear, then, that there are bureaucratic procedures in place that check bioethical aspects of trials and experimentation. Furthermore, hospitals are keen on keeping up a reputation of equal medical treatment for poor and rich. Scientists and doctors usually refer to the DBT's motivation for focusing on stem cell research, drawing legitimacy from official public policies. There are few incentives for public sector hospitals to engage in collaborative research with other hospitals and institutes. Treatment is highly subsidised by the state, and large numbers of in and out-patients visit overly busy medical staff for basic and specialised treatments. This leaves little leeway for collaborative initiative, and public-private research collaborations develop only gradually, due to the bureaucratic culture endemic to public institutions. Altogether, the driving force to engage in risky stem cell therapies is weak.

5.2 The Private Sector

The motivation behind investment into the infrastructural development in the private sector is based on a mixture of assessment and speculation and is mainly driven by commercial considerations. Assessment is based on the plethora of media reports of success stories of centres that are providing therapy. Speculation is based on the projected disease burden in various locations and the anticipated flow of "medical tourism" from national and global regions. The infrastructure for private sector stem cell research and therapy is developing rapidly. Many private sector hospitals are opening stem cell research wings, as a cover for commercial therapeutic service, or

are linked-up with larger client networks³⁷. Others are developing facilities in anticipation of a growing flow of desperate patients from the West in search of therapies that are not ‘standard’ in their own country. They also aim at wealthy patient groups in India, a rapidly growing target group.

Below, we discuss three examples of privately funded stem cell enterprises and hospitals, which serve to illustrate the structural features of their recruitment methods, corporate objectives and institutional embedding. These centres have developed in the cities of Chennai and Bangalore, which have witnessed tremendous growth in medical biotechnology and healthcare infrastructure over the last few years.

5.2.1 *MEMG*

Manipal Education and Medical Group (MEMG) is one of the largest commercial institutions in India working in diverse areas such as education, research and healthcare with a presence in over twenty countries. The group has a stem cell education wing called Manipal Institute for Regenerative Medicine (MIRM), which provides a master degree programme in stem cell science and creates manpower that will pursue further developments in basic research in the field. It also has a commercial wing called Stempeutics Research Pvt. Ltd, a Bangalore based Stem Cell Company with two branches in Bangalore and one in Malaysia. As announced by its president, Mr BN Manohar, in a press conference in India, the Drug-Controller General of India (DCGI) has cleared Stempeutics’ phase I and II clinical trials using stem cells to treat two conditions – acute myocardial infarction and clinical limb ischemia or immobilised limb. The company would use mesenchymal stem cells (MSCs) taken from the bone marrow (The Hindu 2009). In a personal interview with the first author, the President said:

For experimental therapy in stem cells we have tied up with around twenty corporate hospitals in India and we are trying our best to come out with therapeutic products by 2010 or 2011, which we will be able to market. Our motto is to make it ‘safe – effective – affordable’. We are a private company and we want to be the market leader of the Asian region and to make profit, but by ensuring that the products are safe, effective and affordable to all service classes. We understand the needs of the patients of our country (interview dated 16 November 2008).

This statement reflects the profit drive inherent to the private sector investment strategies for new medical biotechnology, and a strong interest in a reputation for safety and accessibility.

5.2.2 *LIRM*

The Lifeline Institute for Regenerative Medicine (LIRM) is part of the Lifeline Hospital Group, a private enterprise and one of the largest referral centres in Chennai. LIRM is emerging as a leading adult stem cell therapy centre in India. The co-coordinator of LIRM claims that the centre has provided therapy to 470 patients over

³⁷ PKPatra and M Sleeboom-Faulkner “‘Experimental’ and Patient Recruitment in India: Questionable Practices Through ‘Bionetworking’” (2009) 16 *Anthropology & Medicine* 147-163.

the last two years for a variety of disease conditions, including spinal cord injury, liver cirrhosis, cardiac infarction and Alzheimer's. LIRM receives patients from all over India and from over twenty other countries. As a mentor organisation of LIRM, the Lifeline Hospital Group systematically uses the 'hub and spokes' model to supply patients to its 'hub' or the super-specialised hospitals based in the southern part of Chennai (Patra and Sleeboom-Faulkner 2009).

The patients visiting LIRM have various backgrounds. Domestic patients may be divided into those who receive reimbursement of the cost of their after-treatment medical care through employment in the public sector or large private enterprise, and patients from the upper economic strata of society who can afford to pay their own medical expenses. Patients from abroad are usually referred through the large patient networks of Lifeline Hospital Group to clinics and doctors inside or outside of India. Patients from abroad fall into two groups. One comprises patients from developing countries, such as Pakistan, Sri Lanka, and countries in the Middle East, in which technological infrastructure related to the clinical application of stem cells is not available. The other is a group of medical tourists from developed countries such as the USA, Canada, Australia and some western European nations, in which the therapies and associated technologies are present but are not made available because of stringent regulations. When asked about the main motivations of LIRM's stem cell department, a researcher at the department replied:

Our main motivation is to provide alternative and up-to-date therapy modules to our needy patients. For diseases like spinal cord injury, myocardial infarction and diabetic ulcer, stem cell therapy seems to be the best option, and since we receive most patients from these types of disease, we want to focus on them. Our aim is to be the market leader in the country.

Although LIRM advertises its concern with all needy patients, in practice it focuses on patients who can afford to pay for relatively high-cost treatment, be it out of their own pocket or through insurance coverage. Attracting patients is openly regarded as a lucrative business.

5.2.3 *NCRM*

The Nichi-In Centre for Regenerative Medicine (NCRM) is an Indo-Japanese joint venture based in Chennai with an office in Tokyo. The activities of NCRM in India cover various areas of pursuit: first, it tries to perform R&D at lower cost than would be possible in Japan and applies for Indian patents for these basically unaltered, but now tested technologies; second, it stores various types of stem cells, and aims to establish the world's first corneal endothelium stem cell bank (CESBANK) with external funding; third, it finds users of Japanese technologies, whose fees they reinvest in the enterprise. NCRM also uses show-case patients to advertise the effectiveness of their experimental therapies in advertisements for stem cell tourism in newspapers and on the web. This is intended to attract patients and new collaborations, both in India and in other parts of Asia, such as in Malaysia, Singapore, Indonesia and Brunei, where for example the Nichi-In-Asia Centre for Regenerative Medicine has been set up to provide cancer immunotherapy. In India NCRM benefits from the government policy in support of public-private partnership efforts for which the Department of Biotechnology has initiated a new scheme called

Small Business Innovation Research Initiative (SBIRI) (Express Pharma 2006). The main motivation of NCRM is, as explained by its Director:

Keeping in mind the steady increase in number [sic] of patients for regenerative diseases and the cost of medical attention, it is imperative that in the long run stem cells are going to be the answer as an effective plus cost effective treatment module. As a private centre we recognise this and are working hard to achieve this.

Thus, NCRM regards its network activities, including those with the Indian government and Japanese scientists as an important source of funding and patient recruitment.

Though the three centres differ both structurally and functionally, in their approach to stem cell research and therapy, they share certain common features: their stem cell enterprises are funded mainly by private sector bodies with very little or no funding from the state or central governments; they work on building robust networks and strategies in terms of patient recruitment and healthcare manpower management; the core group of stem cell research and therapy wings are managed or spearheaded by powerful individuals. Their networks are devised in such way as to attract patients and physicians from local, national and global spheres.

5.3 Individual Practitioners (INDEPENDENT SECTOR)

Medical practitioners offering stem cell therapy in India present a complex subject for analysis. We studied three individual practitioners, based in the cities of New Delhi, Kolkata and Cuttack who provide adult and embryonic stem cell therapies.

5.3.1 Dr PM

Dr PM is a medical doctor and expert in biochemistry based at one of the leading publicly funded medical colleges and hospitals in Cuttack, Orissa. Dr PM claims to provide autologous stem cell therapies using bone marrow for medical conditions such as diabetic foot ulcer and Duchene muscular dystrophy (DMD). He acknowledges that most of his patients are well off and come from the neighbouring state of Andhra Pradesh, although some come from the state of Orissa. They suffer from DMD, attributed to the traditional consanguineous marriage pattern they follow. Dr PM uses a private clinic to provide the therapy, as the Institutional Review Board of the medical college and hospital with which he is affiliated did not give him permission for the clinical application. The college did, however approve of him carrying out laboratory research on stem cells. PM said:

Since ours is a government hospital, the committee is very strict about ICMR guidelines. They cannot approve my study for clinical trials within this hospital. Even though they know that what I am doing is medically and ethically correct. But they are waiting for other frontline hospitals like AIIMS to practice these therapies first. Perhaps then they will say yes. Once it is practiced at a big place, then they will have no problem in approving me. This made me provide this therapy out of this medical college purview.

Thus, due to the need of the government hospital to follow ICMR guidelines, Dr PM decided to operate independently in a private clinic. Although not particularly lucrative, the practice forms a testing ground for the research he does in the college.

5.3.2 *Dr NB*

Dr NB is a medical surgeon and gynaecologist based at one of the public hospitals in Kolkata. He claims to provide therapies for medical conditions such as motor neuron disease, Parkinson's disease, cardiac myopathy, restrictive lung disease and advanced rheumatoid arthritis through stem cells derived from placental umbilical cord blood, amniotic fluid and foetal tissues. He also claims that he has been working on stem cell research at this public hospital since 1999, and has published many articles in peer-reviewed journals and has academic collaboration with prestigious universities in the United States. Many doctors in the same hospital accuse him of being engaged in fraudulent activities. When asked about his motivation, objectives and his detractors, he said:

It is very difficult to work in India. People around you are so jealous. People here are not ready to work hard, innovate or help the poor... I am just using discarded body materials, and I use them in a scientific manner to treat poor patients with state of the art technology. Most of my patients are poor patients from the state of West Bengal.

The former head of the hospital, Dr BP, denied that the hospital is using stem cell treatment and said:

Dr NB adopted fraudulent methods. The hospital does not have the approval from either the state government or the ICMR. His claims need to be properly verified by competent authorities.

Albeit with difficulty, at least some public hospitals make efforts to ward off illegitimate practices. The unruly behaviour of politically well-connected practitioners, however, is hard to stem.

5.3.3 *Dr GS*

Dr GS is an infertility expert based in New Delhi and she provides embryonic stem cell therapy to patients from India and abroad for a variety of medical conditions, including spinal cord injury, diabetes, multiple sclerosis, Parkinson's disease and cardiac conditions. She has gained considerable fame among patients and their relatives, and notoriety among state policy-makers. When asked about her work and the disparate attention that she receives, she said:

In my book, what I am doing is ethical. Those who cannot do it, they only complain. I follow the best medical standard in the world. I have one embryonic stem cell line that I found by using a surplus embryo with proper consent. I provide therapies using embryonic stem cells from that cell line. I can provide therapies for all kinds of 'untreatable diseases' that do not have any cure through conventional therapies. I am getting patients from all over the world and they are happy with my state of the art medical services and hospitality. That is the great achievement for me and the best motivation to march ahead.

Clearly, policy-makers, patients and scientists disagree about what kind of stem cell therapy services should be provided to the public. The therapy is inherently controversial. Independent private practices, however, seem able to offer the stem cell therapies unchecked.

6. Discussions and Conclusion

As both the promise of breakthrough treatments for scores of medical conditions and the availability of unregulated commercial “therapies” have grown, so too have the concerns of global research community.³⁸ Many scientists believe that international as well as national oversights are urgently needed (see ISSCR). Many countries, including India, have taken regulatory measures in the form of guidelines to oversee such malpractices and to smooth the way for medical research. Considering the widespread violation and exploitation, however, such actions seem inadequate. Many factors impede the appropriate regulation of stem cell clinics, including sluggish legal systems, political lobbying on the part of companies and advocates, overburdened regulators, uncertainties existing over the legal status of cell therapies and a sense of unwillingness to restrict the autonomy of patients seeking urgent care.³⁹ Apart from the inadequacies in the existing regulatory structure, which have been dealt with in the DBT-ICMR-2007 guidelines, the actual practice of stem cell therapy is shaped by its degree of institutional embeddedness. With regard to the institutional embedding of service providers, a distinction should be made between public sector, private sector and individual practitioners. We have tried to explicate the structural and functional issues in stem cell enterprise in India through the concept of ‘bionetworking.’

Regulation plays a crucial role in making bionetworking a lucrative success. Bionetworking makes use of the gaps existing in regulation and of the differences between the national regulatory systems in various countries. Though regulatory gaps within India are gradually closing, the implementation of regulation itself remains problematic and advantageous to bionetworking physicians who provide experimental stem cell therapies to desperate patients. In its current form, the guideline is soft law, presently awaiting approval by the government before it can become law. Though the DBT-ICMR 2007 guidelines permit basic, translational and clinical research on stem cell science under certain conditions, private hospitals indiscriminately provide service facilities for therapies in various stages of development, both as experimental therapy and as clinical trials. The DBT-ICMR clearly stipulates that all institutions and investigators, both public and private, engaged in human stem cell research must be registered (Clause 4.1), and must obtain prior approval and ethical clearances at the institutional and national levels (Clause 4.5). Nevertheless, the DBT-ICMR is unable to provide a clear overview of the clinical studies that are being carried out, or where and how they are being evaluated. In a personal communication, one official at the stem cell division of ICMR confirmed that:

³⁸ S Kiatpongsan and D Sipp, see note 1 above; *Ibid*.

³⁹ D Sipp “The Rocky Road to Regulation” *Nature Reports Stem Cells* (2009) <http://www.nature.com/stemcells/2009/0909/090923/full/stemcells.2009.125.html> (accessed 10 Jul 2010)

Only one private hospital in India has approval from the ICMR to carry out clinical trials using stem cells and there is another large clinical study going on across India involving five centres and AIIMS as its nodal agency. Besides, no other centre in India has approval to carry out clinical trial [*sic*] using stem cells. All other claims are false (an official at ICMR, interview dated November 2008).

Interactions with stem cell therapy service providers in India reveal wide displeasure about the non-existence of the proposed NAC-SCRT. Some argue that instead of multi-centre regulatory bodies for clinical trial approval, such as ICMR and DCGI, there should be one central authority that can ensure expediency and transparency in the system.

In short, the lack of transparency of guidelines and a lack of means to supervise experimental stem cell therapies allow bionetworking to thrive. Bionetworking, then, involves recruitment of patients to undergo therapies for the sake of new research or money, while being aware of regulatory matters and identifying loopholes. A dose of scientific savvy is also important.

Another issue concerns the use that service providers make of the terminological ambiguity surrounding stem cell therapy activities in India. The DBT-ICMR (2007) guidelines say the following about stem cell trials:

13.1 As of date, there is no approved indication for stem cell therapy as a part of routine medical practice, other than Bone Marrow Transplantation (BMT). Accordingly, *all stem cell therapy* other than BMT (for accepted indications) *shall be treated as experimental*. It should be conducted only as clinical trial after approval of the IC-SCRT/IEC and DCGI (for marketable products). *All experimental trials shall be registered with the NAC-SCRT*. [emphasis added]

The crux of the matter is in the language, especially in the two sentences under clause 13.1 which stipulates that “stem cell therapy other than BMT shall be treated as experimental” and that “[a]ll experimental trials shall be registered with the NAC-SCRT.” Many service providers refer to the registration as ‘presumed’ approval by the ICMR. The fact that the NAC-SCRT is not yet in existence is taken to mean that all types of stem cell therapeutic services can be done with intra-institutional review board clearances, such as those of the IRB and IC-SCRT.

The motivation of service providers appears to be dependent on various factors such as institutional setup, corporate goals and sources of funding. Public sector service providers receive state funding and view themselves as representing official government policy on scientific and technological enterprises. They regard the emergence and scope of stem cell research and therapy as a social enterprise that has potential to transform the economic and healthcare needs of the nation. For the private-sector service providers that invest enormously in infrastructure and collaborations it remains a commercial enterprise. Independent medical practitioners consider it to be an opportunity for earning money, experience and fame, while targeting the growing middle class of patients searching for better healthcare outside the public healthcare system. We analysed the varied motivations of service providers and the wide-ranging implications of stem cell enterprise in India in a global regulatory and therapeutic context. We have illustrated how local actors engaged in

stem cell therapy draw on international norms of bioethics but adopt them according to various underlying rationalities shaped by local (Indian) patterns of governance, institutional development and policy-making.

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