Bionetworking: Experimental stem cell therapy and patient recruitment in India

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Abstract

Over the last three to four years, an increasing number of private and public sector tertiary level hospitals and research centres in India have been using stem cell therapy, especially adult stem cell therapy, in the guise of experimental therapy for a variety of medical conditions. The promotion and growth of this experimental field across local and national borders traverses regulatory, ethical, social and financial boundaries. In this complex context, the article examines how health care centres in India negotiate bio-medical and health care circumstances in promoting a therapy that raises questionable medical, technical and ethical issues.

The process of promoting experimental stem cell therapy is explained here by employing the concept of bionetworking and illustrated by two case studies of hospital groups. The case studies show how through bionetworking a centre creates and maintains novel networks of mutual exchanges with other collaborative bodies situated in local, national and global echelons.

Drawing on a three-month period of fieldwork and interviews in various locations in India, this article shows that: (1) Questionable stem cell therapy is promoted through bionetworks that resonate across local, national and global constellations; (2) Regulatory gaps facilitate the growth of such therapeutic practices; (3) The experimental stem cell therapies augment the health care divide in Indian society; (4) The weakening Indian state facilitates commercialization of health, indirectly supporting the bionetworking practices of therapy providers.
Introduction

The enterprise of clinical stem cell science applications constitutes a complex social, medical, economic, regulatory and scientific venture that resonates across local and national borders. The provision of stem cell therapy is increasingly market driven, involving a struggle among players at various institutional levels, including the state, public and private healthcare providers, and regulatory bodies (Salter et al. 2007). In recent years, India is emerging as a global player in this field. Regenerative therapies using stem cells, usually adult stem cells from various sources, has attracted great interest as a treatment modality. High expectations are raised about stem cell transplantation as the answer to a large number of acute and chronic disease conditions for which modern and conventional medicines have little to offer (Nair 2006). These stem cell transplants mainly take place in private sector research-cum-hospital set ups, though some public hospitals have also ventured into this field.

Although the evidence of the usefulness 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 due official approval (Pandya 2008, Nair 2006) and under the ambiguous guise of experimental therapy. Some physicians interpret the term experimental therapy as a research protocol that falls in-between animal model test and phase I-II of clinical trials, while others view it as another name for phase I and II clinical trial, or as ‘proof of concept’ studies. This article examines how healthcare centres in India promote such experimental therapies, advertising their activities as bona fide stem cell science research, while profiting from questionable experimental stem cell applications. The article identifies the constituent factors involved in this enterprise and shows how they are brought together through the activation of links we term bionetworking.

Bionetworking is a form of connecting up with key-individuals involved in research and healthcare organisations that takes advantage of the unequal social contexts in which research takes place and healthcare is provided. It thrives under conditions of health inequality and forms part of what Petryna and colleagues call the remake of the global geography of human experimentation (Petryna 2007). Bionetworks constitute a plurality of actors forming biotechnical ventures (Waldby and Mitchell 2007) that work across geographical space, forming what Sunder Rajan calls ‘biocapital’ (Sundar Rajan 2007). To sustain itself, a biotech enterprise makes
use of capital to provide the therapy and its infrastructure. These costs depend on the institutional and legal structure within which these companies operate. The production costs of experimental therapy provided in India can be relatively low, while investment into the therapy’s infrastructure, such as legal permissions, hospital facilities, quality certificates, advertising and intellectual property rights, can be kept to a minimum through bionetworking activities. Bionetworking operates across local, national and global levels, promoting and sustaining a bio-political and bio-economic enterprise in the face of incapacitated state power and differences in health provision, access and purchasing power. It proceeds from the manipulation of complex inter-relations and lopsided interdependencies between stakeholder groups, such as patients and their relatives, researchers and physicians, regulators and the media.

The concept of bionetworking, then, emphasises the activities of individuals acting upon their observation of existing and potentially lucrative exchanges involving biomaterials, healthcare services, research in the life science and newly developed therapies. Bionetworking involves the managerial activities that combine elements of political economy and political subjectivity. On the one hand, the bionetworker makes use of the differences and inequalities detected between healthcare systems, regulatory systems, standards of wealth, and the capacity for conducting science research and development. On the other hand, it takes part in the creation and manipulation of existing subjectivities concerning life values and human existence in different national, class and health environments. In the case we explore in this article, we focus on the exchanges around the provision of experimental stem cell therapies to patients from India and the West.

Bionetworking, compared to the concept of global assemblages, which refers to global projects refracted through particular localities (Collier & Ong 2005), refers to one of the forms in which these practices take shape at different localities by means of calculated delineation between the legal, the ethical and the lucrative. These regimes, though professed by international organisations to be of international relevance and significance (e.g., the Hinxton report, and guidelines proposed by the International Society for Stem Cell Research [ISSCR]), in practice are characterised by various extents of bioethical dislocation (Sleeboom-Faulkner 2008) in that they reflect the views of different peoples in uneven ways. In cases of radical bioethical dislocation, the regulatory regime, including its implementation and execution, caters little for the vulnerabilities of the population involved, who in other countries are
relatively protected. Instead, space opens up for bionetworking, in which individual actors activate their scientific and informational networks across borders to pray on the potential surplus value to be made from scientific, regulatory, wealth and health differences. Bionetworking activities cover networking performed in organ trade (see Scheper Hughes 2005). However, they do not necessarily involve illegal activities. And although bionetworking is commercially motivated, it proceeds from therapeutic subjectivities: imagined, moulded, and calculated aspects of potential patients’ biocitizenship (Petryna 2002; Rose and Novas 2005). In this case, consisting of the subjective estimations and thought associations concerning patients’ financial capacity, their attachment to life, their degree of Westernisation, and the healthcare amenities though to be available in their home country.

This article is based on data collected by the first author during three months of fieldwork between September and December 2008 at two leading centres of India’s private sector initiatives in stem cell science and regenerative medicine: the X Institute for Regenerative Medicine (XIRM) based in Chennai and the Y Group of Hospitals in Bangalore. Data were collected from a wide range of interviews, primary and secondary sources gathered at these centres, and at other locations.

The layout of the article is as follows. The next section explains the relevance of bionetworking to patient recruitment for experimental stem cell therapy in India. The next section describes the two main field sites showing the infrastructure in which bionetworking thrives, followed by an examining of the role of patients, stem cell therapy providers and regulation in the recruitment of patients. Finally, four factors are identified that are relevant to the creation and promotion of bionetworking as a tool for patient recruitment and pushing experimental stem cell therapy.

Background: Stem cell research and therapy in India

In recent years stem cells have become central to global healthcare provision. In support of this enterprise, companies have come about that coordinate the provision and the need for therapies and, in the cases discussed here, experimental therapies. This coordination requires collaboration between physicians, patients, hospitals and public institutions. Where such collaboration is problematic, the bionetworks of individual physicians and healthcare providers become crucial in bringing together
patient and therapy. Bionetworking, as is shown in this paper, involves the strategic combination of resources from both private industry and the public.

Stem cell research and therapy in India are rapidly growing fields. Currently, there are over 40 institutions and hospitals that are involved in stem cell research (Dey 2007). Both the government and private industry have invested heavily in research institutes studying stem cells (Sleeboom-Faulkner and Patra 2008). In private industry, Reliance Life Science, Mumbai, for instance, has characterized ten stem cell lines, including two neuronal cell lines, dopamine producing neurons and neurons for patients of stroke (Sharma 2006).

Government policies on stem cell science in India have initiated stem cell programmes with the aim of promoting both basic and translational research in view of its potential application (Sharma 2006). Public-private partnerships are a form of collaboration between government institutions and private enterprise, also important in stem cell research. A public-private partnership signifies an atmosphere of renewed vigour, flow of capital and strengthening of capabilities by joining forces. There are many such initiatives in India among academic institutes, hospitals and industries in the field of stem cell research and therapy. As one well-known stem cell entrepreneur in India, Dr A, puts it, ‘Public-private partnership is important especially in a country like India wherein government funds co-operate with private industry, so that we can find cost-effective remedies’ (Khan 2007). This public-private partnership is not just limited to technological exchange or capital flow. It has a wider role: a role in the formation of a network that helps the stem cell science and technology achieve strategic advantage using public funding.

Stem cell therapies in India
Currently, stem cell applications are undertaken in several institutes in India for a variety of disease conditions such as spinal cord injury, muscular dystrophy, liver cirrhosis, diabetes, Parkinson’s disease, Ischemic heart disorder, and retinal pigmimtosa. The sources of stem cells vary from centre to centre. They usually derive from bone marrow, cornea, liver, peripheral blood, umbilical cord, fetal stem cells, and embryonic stem cells of animal origin (Shroff 2005), but here we only discuss adult stem cell therapies. In general all human stem cell research and therapies require official registration and ethical clearing. Experimental stem cell therapy and research are mainly provided by private hospitals, among which only a few are public, such as
AIIMS (All India Institute of Medical Sciences). As the nodal agency, AIIMS reported conducting a multi-centric clinical trial, using 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 more than 750 patients have already undergone the trials (The Hindustan Times 2006).²

Clinical applications of stem cells in treating ‘untreatable’ diseases take place mainly at private sector hospitals. Such hospitals use autologous adult stem cells (where cells are removed, stored, and later given back to the same person), which are claimed to be safe and ethical therapy modules. Two issues concern us here: the questionable scientific basis, medical efficacy and regulatory permissions for using adult autologous stem cell therapies, and the way adult stem cell therapy is being promoted ambiguously as experimental therapy in many service providing centres. As interviews with scientists indicate, there is a widespread belief that adult autologous stem cell therapy, unlike embryonic stem cell therapy, is free from ethical problems and has a great therapeutic potential (Khan 2007). But, as shown by scientific literature (Strauer and Kornowski 2003; Passier et al. 2008), more basic research is needed on its efficacy and side-effects before such claims would be accepted in more strictly monitored environments. In this context, the use of the concept of experimental research is premature.

Two case-studies: Institutional complexities

The two main fieldwork sites described here constitute the main source of data used for this article. The description of the two settings is meant to give an impression of the complexity of the institutional structures in which stem cell research takes place. The manifold links between health institutions and the diversity of collaborative forms between public and private elements of these healthcare centres make for opaque organisational structures. This opaqueness forms an important feature of bionetworking strategies.

Setting-1, Chennai: the X Institute for Regenerative Medicine (XIRM)
The medical centre named XIRM, in Chennai (Madras), capital of the state of Tamil Nadu, is emerging as one of the healthcare hubs in India. Many of its corporate
medical centres have started to focus on biomedical education, research and translational research. These centres provide ‘super-specialty medical facilities,’ and are popular sites for global clinical trials. In Chennai, there are 14 or more institutes working on basic research and clinical applications of stem cells (Som 2007).

The X Group of Hospitals – a private enterprise and one of the largest referral centres in Chennai - has increased its strength twenty-fold (from 25 beds in 1997 to 500 beds in 2008) since its establishment in 1997. A 2006 report describes how the X Group has acquired 15 clinics in 13 healthcare locations across the state of Tamil Nadu through their ‘hub and spokes model’. Each of the clinics has one or two consultants depending on the size of the clinic, a pharmacy, a laboratory with ECG, and X-ray facilities (Rangarajan 2006). The X Institute for Regenerative Medicine (XIRM) is a part of the X Group of Hospitals, and focuses on stem research and therapy. XIRM claims to provide adult stem cell therapy for several medical conditions, including spinal cord injury, liver cirrhosis, Alzheimer, cardiac infarction, and cerebral palsy. XIRM also claims to receive collaborative inputs from international centres such as the Biotechnology Department of Temple University and the Kennedy Kreiger Institute – both in USA, Nottingham University in the UK, and the Indian Institute of Technology, Madras and the University of Madras in India (International SC Summit, IIT-M proceeding, 2008).

Prior to the formation of XIRM in January 2007, X Hospital had collaborations with Z Centre for Regenerative Medicine (ZCRM), in the city of Chennai. ZCRM provided technical services, such as stem cell isolation and processing. ZCRM is an Indo-Japan joint venture claiming to use technical know-how from Dr. T of the ABC Institute in Japan for the treatment of diseases using adult autologous stem cell therapy. But in the second year after the establishment of XIRM, the X Group became self-sufficient in upgrading its stem cell research facilities. After it started conducting stem cell isolation, processing and clinical administration independently, the technical tie-up with ZCRM came to an abrupt end.

The co-coordinator of XIRM claims that the centre has provided therapy to 470 patients over the last two years for a variety of disease conditions that include spinal cord injury, liver cirrhosis, cardiac infarction and Alzheimer Disease. XIRM receives patients from 20 to 25 different countries, including Australia, New Zealand, USA, Japan, Pakistan and Sri Lanka. Patients from foreign countries are charged 15 –
20% more than are the Indian patients, reportedly because they require extra care during the treatment period.

Embedded in the infrastructure of the fast expanding medical sector of this city, the X Group’s network of hospitals grows applying the ‘hub and spokes model’, creating fruitful links with other research hubs, conquering new methods, and recruiting new patients from locations close by and faraway. As a result, distinctions pertaining to the private and public, such as public university and private enterprise, and pertaining to the Indian and foreign, such as home grown and global knowledge and Indian and foreign healthcare provision are increasingly blurred.

Setting-2, Bangalore: the Y Group of Hospitals

The Y medical institute, part of the Y Group of Hospitals in Bangalore, is considered to be a leading centre in stem cell research and therapy in India. Bangalore, capital of the state of Karnataka, has transformed itself over the last decade from ‘Garden City’ to India’s Silicon Valley. Apart from IT, Bangalore is home to leading biotech companies, such as Biocon, and numerous start-ups. It houses some of the world’s most advanced Research & Development Centres, such as the Indian Institute of Science, the National Centre for Biological Sciences, the Jawaharlal Nehru Centre for Advanced Scientific Research, the University of Agricultural Sciences, the Central Food Technological Research Institute, and the Institute of Bio-informatics and Biotechnology (Vijay 2007).

The Y Institute of Regenerative Medicine (YIRM) is part of Y University located in Bangalore under the Y Education Group – a leading education provider in India’s private sector. YIRM inaugurated itself in August 2007 to become a leading centre in stem cell research and education in India. Under the same Y Group, a commercial entity called Stemline\textsuperscript{4} Research Private Limited (SRPL) grew into a leading stem cell company in the field of regenerative medicine. Stemline claims to be the only Good Medical Practice (GMP) compliant stem cell research facility in the private sector in India, vetted by the Indian Council of Medical Research. Stemline advertises itself in its policy programme as committed to the delivery of ‘Bench to Bedside’ therapy. In collaboration with approximately 20 corporate hospitals in India, Stemline is conducting experimental stem cell therapies as a ‘proof of concept’ using bone marrow derived mesenchymal stem cells in patients suffering from various diseases, such as Parkinson’s disease, spinal cord injury, critical limb ischemia,
avascular necrosis, motor neuron disease, end stage liver disease, psoriasis, vitiligo and myocardial infarction. Stemline also has a branch in Malaysia, which aims to promote stem cell activity locally and focus on cutting edge research, therapeutics and therapy in the field of regenerative medicine. A news report published in October 2008 in India, announced the launch of therapy facilities at a centre in Kolkata and hospitals in the state of Kerala and the establishment of tie-ups with 30 to 40 hospitals in India within 18 months to conduct stem cell therapy.

Similar to the X Group, the Y Group ties together private and public research facilities and national and international efforts in its activities to promote stem cell therapies. The next section shows how through bionetworking this growing field of stem cell therapy takes advantage of the contrasting health needs of different societies, to pick the fruits of both corporate and private research, and to negotiate gaps in national regulation.

**Bionetworking**

This section shows how demands for scientific quality elsewhere in the world are at the same time exploited and neglected to offer low quality treatment to unsuspecting or hopeful patients from abroad and at home. Stem cell researchers and therapists can take advantage of the fact that in regulated affluent societies great efforts and capital are regarded as essential for establishing conditions for Good Clinical Practice (GCP) and evidence-based therapies. This has created a niche for the provision of relatively inexpensive therapies that have not been acknowledged internationally. Below we describe the roles of patients, providers and regulation in the recruitment and provision of stem cell therapies, before relating their inter-relational dynamics to the broader concept of bionetworking.

*Patients and their relatives in recruitment networks*

Desperate patients and their relatives, especially after having tried conventional therapies, are easy targets for this novel and non-standard therapy. Therapy providers in the settings of the X and Y Groups recruit patients by giving them the impression that stem cell therapy can help patients with varying disease conditions and keep known information on the therapy to a minimum. There are various issues at stake here. One is the moral and medical justification of intervention for terminally ill and
incurable patients. Another is the issue of providing stem cell therapy to patients whose medical conditions do not warrant it. There are also issues of taking proper informed consent, involving the explanation of medical procedures and risk-benefit analysis (Kiatponsan and Sipp 2008; Pandya 2008).

X hospital (XIRM) receives patients from all over India and also from 20 to 25 other countries. Indian patients chose this hospital on the basis of what they hear through wider media publicity and through referral hospitals. XIRM is part of the X group, which uses the ‘hub and spokes’ model to supply patients to its ‘hub’ or the super-specialized hospitals based in the southern part of Chennai. In general, the patients who come to XIRM have different backgrounds. Domestic patients are drawn from two groups: patients who receive reimbursement for their after-treatment medical bills through their job in the public sector or in large private enterprises, or patients from the upper economic strata of society who can afford to pay for the medical expenses out of their own pocket. Patients from abroad usually are referred through large networks that X general hospitals have with clinics and doctors based inside and outside India. The patients coming from abroad divide into two groups. One group consists of patients from developing countries, such as Pakistan, Sri Lanka, and countries in the Middle East, where stem cell therapy and related technological infrastructure are not available. The other group of patients, medical tourists, come from developed countries where the therapies and the associated technologies are present but are not made available because of stringent regulations.

Even though service providers claim that they provide therapies to poor patients, a look at recruitment procedures, the medical expenses and other related costs makes this hard to believe. It is important to note that keeping up the business of stem cell therapy is not easy, due to the considerable investment required into capital and manpower. As a coordinator at XIRM puts it,

It is not easy to get patients who can pay such big amounts, so there is always pressure on us... There is always pressure on us to meet the target number of patients per month. After all we have to take care of our salary as well as the investment in state of the art infrastructural cost.
The need for the high-end technology-based infrastructure, the novelty of the therapy and financial situation of the patients induce service providers to develop special recruitment networks.

There is no single procedure that these centres follow in recruiting patients. The various social and geographical backgrounds of patients disallow this. Furthermore, it is hard to gain access to patients under treatment, as patient confidentiality provides protection to both patients and provider. Patients are recruited actively, but largely not openly, which makes it challenging to gather trustworthy data on recruitment methods. However, participant observation at one of the centres, discussion with centre officials, and communication with patients outside the centres gave some insights into how patients are recruited.

On the third day of the first author’s visit to the stem cell department’s coordinating office of XIRM, a telephone call came for the coordinator, Mr. S.R, during conversation. This is the coordinator’s side of the conversation:

**Telephone conversation-1**

From where are you calling? Oh! Kerala…

(....)

No, we are not providing the therapy for kidney related problems right now. But, research is going on, and very soon the results will be out and….  

(....)

Yah! Yah! You can just keep on track; just keep on track in newspapers.

(....)

Yes, yes, usually the results will be declared through newspapers.

(....)

Yes, you can contact me after ……… say 15 days.

(....)

Yes, just listen. I am almost sure that the ongoing study will be positive and we will be able to provide the therapy. Yes, the research is going on at our hospital. We have advanced research facilities and we are also watching the results of studies at other places... But, I cannot say for certain. Yah! Yah! Please call me after two weeks.
Yes, you have to come with all your past medical reports and our experts will examine you and then decide if you can take the therapy or not. No, no. It is not painful. We have some experts who will administer it. Don’t worry about that.

See that aspect we cannot tell right now, it depends how much you need, the quality of cells and all that. But, since you will be the first case, we will charge very nominal. But, please call me after two weeks.

OK. Thank you. Hear you after two weeks. Bye.

On the same day, another incident took place, which yielded more knowledge about this stem cell centre’s recruitment procedure. A man came in searching for the Stem Cell Coordinator of XIRM, Mr. S. R. He looked worried and tired. The man was from Rajasthan, some 1500 kilometers from this centre, and he wanted to know more about stem cell therapy for his younger brother who has suffered from spinal cord injury for the last three years. The discussion between the Coordinator and the man went like this:

**Conversation-1**

**The Man:** Hello. I am… I am from Rajasthan and I want to know about what kind of therapy you are providing at this centre.

**Coordinator:** I see. We provide stem cell therapy for many untreatable diseases, but.. What is your problem?

**The Man:** No, my younger brother met with an accident some three/four years back and is suffering from spinal cord injury.

**Coordinator:** Yes, we do provide therapy for spinal cord injury, and I tell you, most of our patients are here for spinal cord injury. We have expertise on that. Since, you said, your brother’s accident history is only three years, I think it will be very receptive to the therapy. It is an ideal case for intervention. I tell you…
**The Man:** He has injury at C-5 and C-6 positions of his spine. We have already been to many places including Dr. G’s clinic in Delhi, where he has taken embryonic stem cells for six months, but there is not much difference. We have been to a doctor in Ahmadabad and one in Jaipur. I have also talked to people at Y Hospital in Bangalore…..

**Coordinator:** What did they say?

**The Man:** They also said their therapy will be receptive to my brother’s condition, but they are charging a lot of money.

**Coordinator:** How much they are charging?

**The Man:** Yah…. It's a lot, we cannot give that much, and we have already spent a lot at Dr. G’s clinic in Delhi…..

**Coordinator:** See, we charge the minimum in the market. Our results are the best. Of course if you want, you can talk to our medical team.

**The Man:** But, I want to know, how do you insert the stem cells. Is it at the injury site, or, I heard something like opening the spine…..

**Coordinator:** Yah… see, it all depends on your brother’s condition. Our experts will decide, whether to inject it at the injury site or to open the spine and inject. But, we are the least invasive in our techniques and methods, see we are the best.

**The Man:** What will be the price?

**Coordinator:** See, first you decide and then we talk about that. That is not the big issue. The thing is that you will get the best treatment. We charge something around 2.5 lakhs (around $5500). But, I will talk to the management, and will make some concession for you, since you have already spent a lot of money at other centres. It will be on humanitarian ground. Another good thing about our centre is that we just give the stem cells in one or two doses, or maximum three doses, not for so many times as the other centres are doing. They are just looting people. We are very clear about that. If it works, it will work in one or two times, or else, it does not work.
The Man: What is the success rate?

Coordinator: See, it varies from condition to condition, since your brother’s injury is relatively fresh, he will have better success rate. This is what I think. But, you know, it all depends on God! But, at our centre we have nearly 75% success rate for many patients.

These conversations between relatives of patients and the representative of the service provider give us an idea about the sense of urgency on both sides. Urged to recruit patients, the coordinator wittingly or unwittingly takes advantage of the dilemma in which patients and their relatives find themselves, placing their money on hope offered and a chance of survival. Speculation on the health, schooling, and financial capacity of the subject connect the biological needs of patients and the financial sustenance of coordinators in the business of bionetworking.

Service providers: Physicians and coordinators

In our analysis, service providers are physicians, including individual practitioners associated in hospitals, who provide stem cell therapy in India. Although there is a great variety in the kind of hospitals that offer stem cell therapies, there is a pattern showing systematic links between large well-known hospitals and small underground hospitals that engage in underground collaborations. Bionetworking plays a crucial role in the coordination of their activities.

The provided reasons for engaging in stem cell therapy vary. Physicians who provide it as ‘supportive’ therapy along with their conventional treatment modules, express the belief that stem cells provide better results. Other independent physicians connected with researchers and physicians in the country and abroad work in tandem on stem cell research. Circumstantial evidence and participant observation at some field sites in India show that some work as facilitators for clinical trials and experimental stem cell therapies. Although some physicians in smaller towns/cities provide experimental stem cell therapy to earn quick money, others insist that their treatment works and defend the moral correctness of helping patients by providing them with experimental stem cell therapy.

It is quite a daunting task to record how many centres or hospitals in India provide stem cell therapy as a regular medical practice, as many of these operate
underground, though there are also many centres that provide stem cell therapy openly. There is a general pattern, however, in which big private hospitals or health care centres function as a ‘hub’ and are known to the world, while small, less obtrusive hospitals, the ‘spokes’, are not. Every other day one hears media reports about breakthroughs reported by physicians in stem cell therapies for old ‘untreatable’ or new diseases made in both public and private sector hospitals. The individual statements of physicians, however, cannot be understood separately from the nature of the clinics that they work for or lead, many of which are ‘spokes’ connected to the hub of a large network.

The clinics providing experimental stem cell therapy have distinct characteristics. First, they are usually individually driven and network-based. The stem cell division of the centre revolves around a key figure or an influential individual physician who has a wider network across local, national and global levels. As the therapies are over-hyped and their clinical applications do not require highly skilful medical expertise, these centres manage with a few physicians and paramedical staff. Second, mutual interests are promoted through public-private partnerships. Since research and development (R&D) in the field of science and technology in India until recently was monopolized by the public sector, whose reputation is superior to private enterprises and which receives considerable public funding, emerging private clinics and hospitals are attracted to the public sector for social recognition and acceptance. Thus, in the field of stem cell therapy, private hospitals (hubs) enter into collaboration with reputed public institutions to gaining public recognition. One example is the recently held First International Stem Cell Summit at Chennai in joint collaboration between a premier public sector technological institute and XIRM, which also collaborate on other aspects of stem cell research. But as private funding for R&D has lately increased in the private sector, public sector centres are also motivated to collaborate with private sector enterprises.

The regulation of stem cell therapy
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 closed, the implementation of regulation itself remains
problematic and advantageous to bionetworking physicians who provide experimental stem cell therapies to desperate patients.

Considering the rapid growth of biotech research in India and the alleged promises of stem cell science, it became incumbent to regulate this area accommodating the interests of the scientific community, healthcare professionals and patients (Basu 2006). In 2002, the Indian Council of Medical Research, institutionally located under the health ministry, announced a policy that permitted therapeutic cloning and encouraged stem cell research. But, the previous year the Department of Biotechnology (DBT), under the science ministry, had also issued guidelines, and some clinics had exploited the difference between the two sets of guidelines, starting clinical treatments (Jayaraman 2005). With an increasing number of funding applications to the ICMR and the DBT, media reporting of unethical practices in biomedical research, and India’s growing thrust on stem cell research, the DBT and ICMR in 2005 decided to jointly devise guidelines, which were released as the *Guidelines for Stem Cell Research and Therapy* in November 2007 (DBT-ICMR 2007). The guidelines permit research pertaining to adult and umbilical cord blood stem cells if approved by Institutional Committees.5

The guidelines are not free from shortcomings, expressed in the comments by the legal critic, Basu: ‘The extent of ambiguity and subjectivity prevalent in the Draft ICMR Guidelines can be gauged from the phrase “Any violation of guidelines would be strictly dealt with”’ (Basu 2006, 1478). In its current form, the guideline is a mere soft law, presently awaiting approval by the government before it can become law. Though the central guidelines (DBT-ICMR 2007) permit basic, translational and clinical research on stem cell science under certain conditions, the X and Y Hospital hubs provide service facilities for therapies in various stages of development indiscriminately as experimental therapy or clinical trials. The DBT-ICMR clearly stipulates that all institutions and investigators engaged in human stem cell research, both public and private, should be registered (Clause 4.1) and require prior approval and ethical clearance at multi-level authorities both at the institutional level as well as at the national level (Clause 4.5). Nevertheless, no one in the DBT-ICMR has a clear overview of what clinical studies are being carried out where and how they are being evaluated. In a personal communication, one official at the stem cell division of ICMR confirmed that:
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 using stem cells. All other claims are false (official at ICMR).

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, includes recruiting patients to undergo therapies for the sake of new research or money, and being aware of regulatory matters, finding loopholes. A dosage of scientific savvy is also important.

**Discussion**

Bionetworking is the key to understanding how some healthcare centres are able to propagate experimental therapies. It is rooted in a social structure that builds on a political economy of hope (Rose and Novas 2005); it grows on hype and is nurtured through technological, economic and national competition. In examining the interrelationships between various stakeholders, above, the roles of individual players in patient recruitment have been described. This section explains how the interrelationships and inter-dependencies between stakeholders co-produce a complex set of networks at local, national and global levels sustaining the enterprise of experimental stem cell therapy.

Several factors are relevant to the creation and promotion of bionetworking as a tool for patient recruitment. The first factor concerns its global nature. All stakeholders discussed have significant roles at local, national and global levels. Patients are drawn into the therapy module from all three levels. Those who come from local and national territories represent a different set of social, economic and regulatory characteristics than those from across national boundaries. Local patients
have mixed social backgrounds and are drawn into the networks of recruitment through the referral systems based on the ‘hub-and-spokes’ model. The local patients are drawn mostly from the upper-middle and upper economic strata of Indian society. The patients who travel across India from other provinces usually are from upper economic strata, including from business families, high position public servants and private sector executives. Recruits from abroad are either desperate patients from developing countries where stem cell technology and therapies are not available or from affluent societies where stem cell technologies and clinical services are either not available due to regulatory restrictions or exorbitantly expensive. This situation raises two critical concerns. First, such global bionetworking furthers the already existing healthcare divide between the rich and poor in Indian society; and, second, it raises questions about the ethical and political justification of denying patients stem cell therapy services at the country of their origin. In India, corporate hospitals and newly-developing private sector hospital groups are eying patients from developed countries, such as the uninsured part of the population in the United States. Such patient groups are attracted to low cost service providing countries, and Indian super-specialty private hospitals aim to tap these potential markets (RNCOS 2008; Dalal and Basu 2007).

A second factor concerns the desperation on the part of service providers. Engaging in ruthless recruitment procedures and selling questionable clinical stem cell applications constitute the so-called ‘from book-shelf to bedside-approach’. This approach refers to the wish to translate the theoretical understanding of a therapeutic mechanism directly into clinical application on human beings to either gain a quick profit or to lead world research. There is fierce competition between clinics, hospitals and health care centres to become a ‘global first’ or a ‘national first’ and have a technological and market edge over others. Together with sister-organizations and collaborative centres, providers explore new ways to link researchers and physicians, together with their patients, to their net. For instance, XIRM had formed a technical collaboration with ZCRM in Chennai to obtain products facilitating stem cell separation and growth in culture medium using imported Japanese technology. But, upon seeing the emerging market potential in this sector, XIRM developed its own stem cell facilities and built its own networks for therapeutic facilities, which XIRM has done across local, national and global levels without any support from ZCRM. Now XIRM collaborates with centres in the UK and the USA, having entered into
agreements on the transfer of technical know-how. In two years time, XIRM and ZCRM changed from collaborators to competitors. They now are competing for technological edge and are both desperate to capture the market in the same area. This desperation is a key factor in bionetworking.

A third issue concerns the use service providers make of the terminological ambiguity that surrounds 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 lies in the language used, especially in the two sentences under clause 13.1: ‘stem cell therapy other than BMT shall be treated as experimental’ and ‘All 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.

Furthermore, there are technical terms that many service providers use in order to escape public, media and regulator scrutiny. One of them, experimental therapy, as discussed, has meanings varying from supportive therapy to strictly regulated research. The unclear use of terminology confuses patients, and circumvents regulatory protocols. Moreover, the ambiguity and the difficulty of medical jargon can easily confuse the patients, and are used in ways violating regulatory protocols and contravening scientific codes of practice. Such terminology allows therapy providers to provide questionable therapies, impeding basic bioethical notions of informed consent and free choice.

Conclusion
Bionetworking exploits new relations of dependency and exchange, and new financial and health uncertainties stretching around the globe. It links together institutional complexities covering both private and public means, semi-underground activities in small hospitals and healthcare hubs, and comprises the initiatives of individual physicians in hospital and university researchers. It makes use of the ambiguity of formulations and the gaps in the regulation of stem cell research, its poor implementation, and the despair of patients both at home in India and abroad.

Providers of experimental stem cell therapies take advantage of the increased mobility of global groups of patients with little knowledge of the providers but with everything to lose. However, patients are not necessarily desperate or just desperate, but also hopeful and eager, intelligent and often knowledgeable, believers in newly developed therapies and regenerative medicine. Similarly, physicians, though looking out for lucrative opportunities, may be full of hope and dedicated to their research, believing that they act in the best interest of the health of their patients.

At the same time, however, bionetworking sustains stem cell research and therapy activities, not by providing therapy to any severely diseased patients from any regional, cultural and class backgrounds. Rather, bionetworking involves weighing off the effectiveness of the speculated value of material and therapeutic services against estimations of the financial capacity, will to live, healthcare possibilities, the understanding, and the ‘cultural’ needs of the potential patient pool available in different countries and locales. Of particular relevance here are the spaces that open up as a result of differences in the availability of healthcare and access to it. Along these lines bionetworking values and understands subjects as human beings.

In India, bionetworking activities have consequences for healthcare distribution. Investment in experimental stem cell therapies means that Indian healthcare resources, including public ones, are indirectly spent on affluent foreigners, rather than on a population deprived of basic healthcare. As the price of stem cell therapies in India is driven up, middle class Indian patients pay increasingly high bills, which may mean bankruptcy for them. As for the part of the population that cannot afford stem cell therapy, only the possibility of entering the most risky experimental trials remains. As investment spent on these experimental therapies could have been channelled into recognised therapies, these sums can be regarded as diverted from bona fide hospital healthcare provision and research.
Providers cut through the webs of protection spun around patients by national healthcare systems and insurance companies, giving increasingly independent and active patients a last chance to stretch their lives and to spend their money. It is only a very thin line that constitutes the difference between providing therapies for financial gain and for scientific research purposes. The ambiguity of public-private stakes, the speculation and the part-underground nature of bionetworking activities, however, make suspect any pronouncement on the reliability of stem cell therapies by individual scientists with (even remote) links to these networks.

Notes

1. We have used pseudonyms, such as X, Y, Z and ABC for names of individuals, clinics, hospitals and places to avoid identification of individuals and to divert attention away from hospital and company names, as we aim to examine social phenomena rather than particular people and companies.

2. This data was shared during a personal communication with Dr. Sujata Mohanty, Asst. Professor, ORBO and Stem Cell facility, All India Institute of Medical Sciences, New Delhi, with PKP on 26 November 2008.


4. Another pseudonym for a stem cell company attached to the Y Group of Hospitals and has branch office in Malaysia.

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

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