



Stem cell science in India: emerging economies and the politics of globalization

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The globalization of stem cell science is increasingly being shaped by the emerging economies of the Asia/Pacific region. Undaunted and unhampered by the more established views of the commercialization of science, countries such as India are constructing models of innovation, policies and patterns of investment that challenge such orthodoxies. This report examines the position of India within the globalization of stem cell science, its adjustments to the developing knowledge market in this field and its particular contribution to the likely future of this promising bioeconomy.

On January 29, 2007, the first annual conference of the newly launched Stem Cell Research Forum of India took place in Bangalore, India, a clear indicator of Indian interest and intent in this rapidly evolving field [101]. It followed the earlier announcement in January 2005 by the Indian Council of Medical Research (ICMR) and the Department of Biotechnology (DBT) of plans for a national stem cell initiative that would prioritize research funding, focus on clinical applications and promote 'stem cell city clusters' [102]. The National Task Force on Stem Cell Research was established in April 2005 to take these plans forward [103].

As in some other countries, Indian government and industry is beginning to think through the steps required if India is to establish an advantageous position in the fast developing global stem cell market. The unprecedented 25% increase in its 2005 R&D budget, coupled with the rapidly expanding activities of the DBT, show the extent of India's ambition with regard to its science as a whole. In the case of stem cell science, what policies, interventions and resources are necessary to support the development in India of this promising area of regenerative medicine and how and when should they be introduced? In the UK, the response to these questions is embodied in the report and recommendations of the UK Stem Cell Initiative (Patton Report) of November 2005, which sets out a 10-year strategy for the development of stem cell research, therapy and technology dealing with state investment, the organization of science, venture capital, public-private alliances and regulatory issues, such as those connected with intellectual property rights (IPR) and human embryo research [1]. As yet, India has not produced such a strategy.

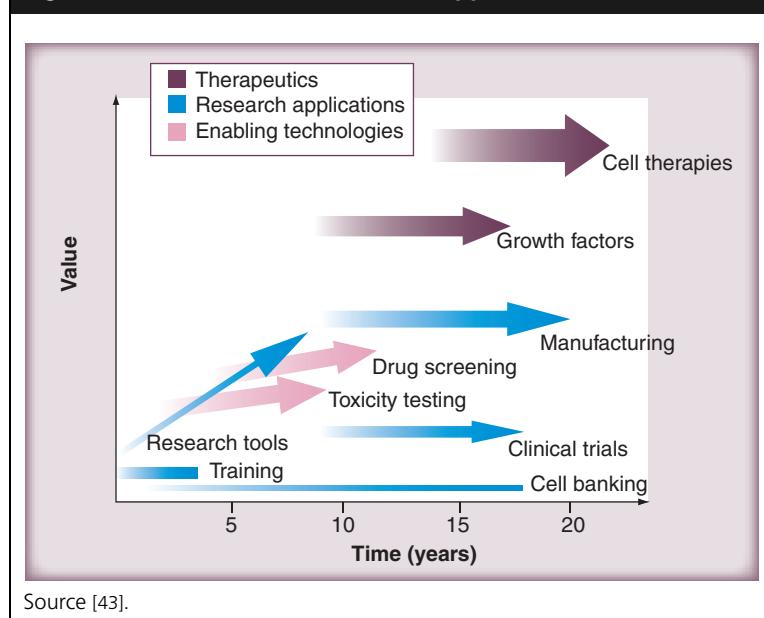
Should it decide that strategic state intervention is required, its approach is likely to diverge in several respects from that of the UK. Unlike the UK, India is an emerging rather than a developed economy. Its science, tax regimes, regulation, supporting industries and financial markets are at a different stage of evolution and it brings its own unique characteristics and considerations to the fluid politics of stem cell globalization. Its response to the commercial opportunities offered by stem cell science, its view of what constitutes an appropriate model of innovation in this field and its interpretation of its political interests will therefore be distinctive. Given this context, this article analyzes the current position of India as a player in the global stem cell knowledge market, the significance of its status as an emerging economy and the issues it will need to address if it is to compete effectively. India is already making policy choices that directly and indirectly impact on its ability to support this new form of health biotechnology, aware of the crucial role the state can play in technological development [2].

Political choices, commercial models & global opportunities

In reflecting on the forms of intervention to adopt in this field, any state must recognize that the journey to commercialization will be complex and arduous [104]. Depending on the model of commercialization adopted, the state can choose to intervene in any or all of the stages of innovation, from the basic science, through translational research and clinical experimentation to the production of cell-based therapies. As Figure 1 indicates, there is more than one route through the innovation process and choices will need to be made

Keywords: economics,
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Figure 1. Timescale for commercial opportunities.

Source [43].

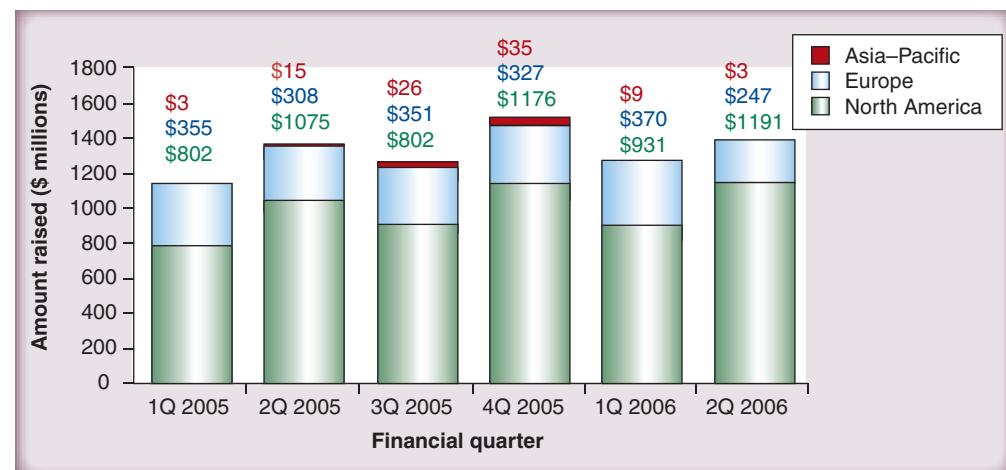
regarding which is the most viable. The lengthy interval between the early-stage research and the promised therapeutic product (commonly estimated to be between 15 and 20 years), means either a sustained and costly state commitment to this one scientific field among many (for any state a risky political choice in the high pressure arena of science policy) or a combination of state and market involvement in clearly demarcated arenas of commercial activity where both the risk and the product are identifiable.

For example, in the short to medium term, cell lines from human embryonic stem cells (hESCs) could be used as disease models to explore the pathology of a disease, as drug screening assays to demonstrate efficacy and as the means for the toxicity testing of candidate drugs. Such intervening usages in the overall commercial model would generate an early cash flow to nurture the development of the field (in September, 2006, the Roslin Cells Center in Scotland launched a public–private initiative that brings together the Roslin Institute, Scottish Enterprise, Edinburgh University and the Scottish National Blood Transfusion Service to develop human stem cell lines that will be sold worldwide for drug testing and medicines development. Interestingly, the Center is described as ‘the first step in a supply chain to support the development of the wider stem cell sector in Scotland, providing cells that can be used by academics, NHS Scotland and commercial companies’ [105]).

If state intervention is to be selective, this then raises the question of how the choices are to be made. One key factor is the resources immediately to hand that can support stem cell development. These can include intellectual resources (as in the Scottish case), a ready supply of the raw materials required for early-stage research (e.g., human oocytes and embryos), the physical resources of a large and diverse population to support the translational clinical research, the political resources of sound regulatory structures capable of maintaining scientific and public confidence and the financial resources of a viable venture capital or pharmaceutical sector. If such resources are already within the jurisdiction of a state, then clearly it would be unwise to neglect them.

If they are not, then a state can choose whether to acquire them and, if so, how. Since a positive decision in favor of resource acquisition involves a move into the international market, it is at this point that interaction with the forces of globalization inevitably takes place. For example, Singapore has decisively entered the international scientific labor market with policies expressly designed to attract stem cell scientists from the USA and the UK through financial support and a liberal regulatory regime [106]. These policies exploit the relatively high global mobility among this group (according to one survey, stem cell principal investigators [PIs] are 5.3-times more likely to receive at least one international job offer than PIs in other biomedical fields [3]).

For emerging economies, the ability to attract pharmaceutical companies in support of biotech innovation is much less problematic than it used to be as what has been termed ‘the second wave of globalization’ is now taking effect in the biomedical as well as the IT industry [107]. Propelled by the search for lower scientific and clinical labor costs in the context of a perceived crisis in their profits, multinational pharmas are increasingly outsourcing their R&D operations to developing countries [4,5]. In April 2006, pharma companies were performing 838 ongoing trials in the USA, 158 in the UK, 81 in Russia, 49 in India and 31 in China. The prediction is that pharma companies will double their clinical research activities in developing nations over the next 3 years [108]. At the same time, pharmas are attracted by the often lavish tax concessions accorded to foreign companies making Foreign Direct Investment (FDI) in emerging economies, such as India and China,

Figure 2. Global biotech venture capital investment.

For more than a year, venture capital has held close to US\$1.4 billion, with approximately three-quarters going to North America.

Source [109].

and, given the large populations of these countries, by their value as potential markets for drug companies [6].

The interest of multinational pharmaceuticals in emerging economies is also strongly influenced by the global loss of their quasimonopoly on leading-edge science and discovery. By 2002, small biotechs had become a critical part of pharmaceutical innovation and growth, accounting for 70% of the drugs approved over the previous 6 years. None of the top ten best-selling biotech products had been developed by a pharmaceutical company, although six are marketed through big pharma [7]. With their own drug pipelines drying up, pharma are driven by a global search for the intellectual property (IP) of potential products that can be acquired from small biotechs during the various phases of clinical trials through mergers and acquisitions or through joint ventures.

Amongst emerging economies, India has the unique advantage of its recent successes in the global software and IT services market [8]. In this respect, India offers one of the very few examples of an emerging economy that has managed both to attract FDI in the area of high-tech software development, while successfully inserting itself as a competitive presence in the very heart of Silicon Valley. It remains to be seen whether it will be able to replicate this experience in the area of pharmaceutical and new health technologies.

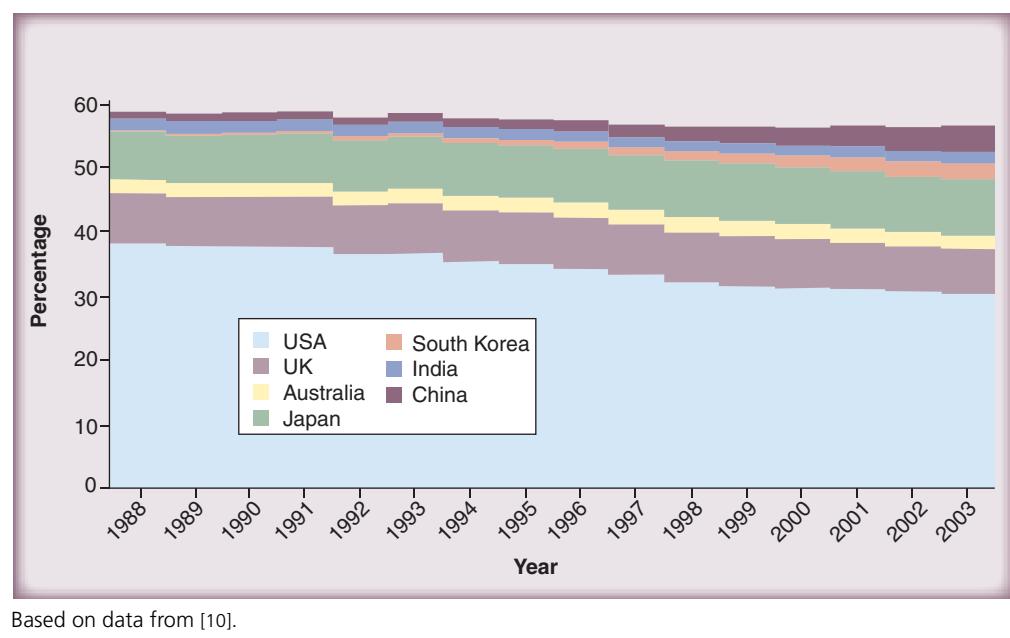
Where emerging economies are much less advantageously placed, it is their access to the global financial markets that are essential to

enable early-stage biotech companies to take forward the results of basic stem cell research. Although private investors and individual venture capital companies (VCs) can help biotech startups 'it has been the long-term capital flowing from the likes of the New York Stock Exchange (NYSE), the American Stock Exchange (AMEX) and, most importantly, the NASDAQ stock market that has played the pivotal role in making the USA biotech industry by far the largest in both market values and product sales' [9]. Bearing in mind that 40% of all USA venture investing is in the life sciences, in 2005, private biotechs raised US\$7 billion in USA capital, up from US\$5 billion in 2004, of which US\$3.5 billion was by venture capitalists [9]. In contrast to this, VC investment in Asia was minuscule and barely registers when placed in the global context (Figure 2). Apart from Japan, Asian stock markets do not have the liquidity and volume necessary to attract Western VCs or biotech firms on any scale. Emerging economies in this region therefore have to recognize that they face a funding gap in the life sciences innovation process and decide what policy options might address this if their commercial model of stem cell science is to be viable.

India's global position

If, as an emerging economy, India is to become a significant player in the future stem cell market, it will need to be clear about its current strengths and weaknesses with regard to those areas of globalization likely to impact on the stem cell commercialization process.

Figure 3. Share of global science and technology publications, 1988–2003.



Based on data from [10].

Science

Science is an international activity aggregated from national components that remain fairly stable over time. Here, we examine a selection of these components to assess India's global position in the international scientific community relative both to developed countries and to other emergent economies in the Asian region with an interest in stem cell science.

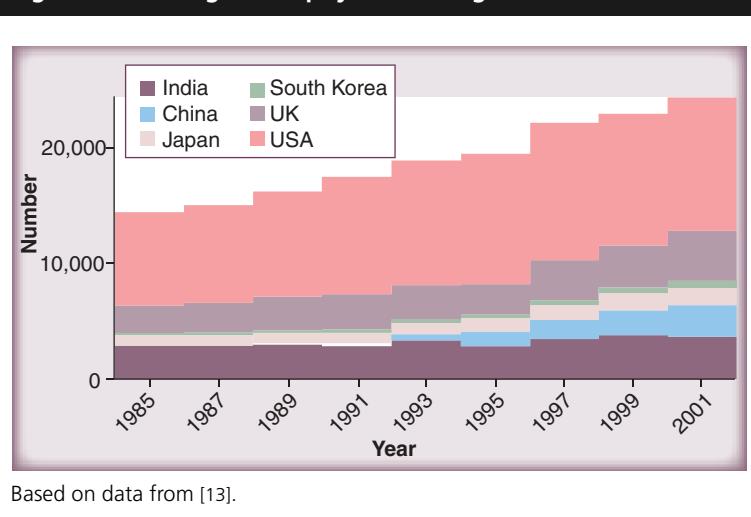
A country's proportion of the global output of science and technology publications measured over time provides an indication of its control of important intellectual resources necessary for the first stages of the commercialization process. In the Indian case, between 1988 and 2003, this proportion has remained static at 2% (Figure 3). This compares unfavorably with China (a dramatic rise from 1 to 4% – more than a doubling of the articles published) and South Korea (a rise from 0 to 2%). Thus, although the USA's share in this period has declined from 38 to 30%, it is not India that has benefited.

A similar relative weakness with regard to India's Asian competitors is apparent in the data on the number of doctoral degrees in the field of physical/biological science awarded between 1983 and 2001 (Figure 4). Although India has a higher absolute number (3727) than either South Korea or China, the rate of increase in PhD production is much higher in the case of the latter and, indeed, China may have now overtaken India. To an extent, this may be because the lack

of training opportunities in Indian universities in the life science encourages postgraduate students to leave India to complete their PhDs abroad [11]. At the Indian Institute of Science, 90% of those who finish PhDs choose to go abroad – an indicator of India's difficulty in sustaining the important middle tier of postdocs required for successful scientific teams and laboratories [12].

In assessing the significance of these figures, it has to be remembered that scientific training, as with other aspects of science, is an international as well as domestic activity. If we now examine the ability of Indian students to access the largest sector of the international graduate education market, the USA, we find that India dominates other Asian countries in terms of both absolute numbers of graduate students and the rate of increase in these numbers (Figure 5). Between 1987 and 2004, while the number of Indian graduate students in the USA has quadrupled from 15,600 to 63,000, Chinese students have increased at a much lower rate from 20,400 to 50,800.

However, these figures do not necessarily translate into a global advantage for Indian science since most of these graduates choose to remain in the USA once they have gained their degrees. Between 1992 and 2003, the proportion of Indian graduates with science and engineering doctorates and biological/agricultural doctorates who had 'definite plans' or 'plans' to stay in the USA was consistently approximately

Figure 4. PhD degrees in physical/biological sciences.

Based on data from [13].

90% (Table 1). The net effect of this brain drain is that in 2003, there were 448,700 Indian-born residents in the USA with degrees in science and engineering or related subjects, although only 41,300 (9%) of these had doctoral degrees. In comparison, the equivalent numbers of Chinese-born residents in the USA was 294,800, of whom 62,500 (21%) had doctoral degrees [15].

Given these data, it is to an extent surprising that if we employ a more interactive measure of India's global scientific position, the geographic scope of its international collaborations, a picture nonetheless emerges of India as marginally ahead of its Asian emerging economy rivals. Based on 2003 data, the USA had the broadest

network of international collaboration with US-based researchers co-authoring articles with researchers from 172 other countries. The UK followed with co-authored articles with researchers from 158 other countries. Among low- and middle-income countries, India ranked first, with 107 co-authoring countries, ahead of China (102) [17].

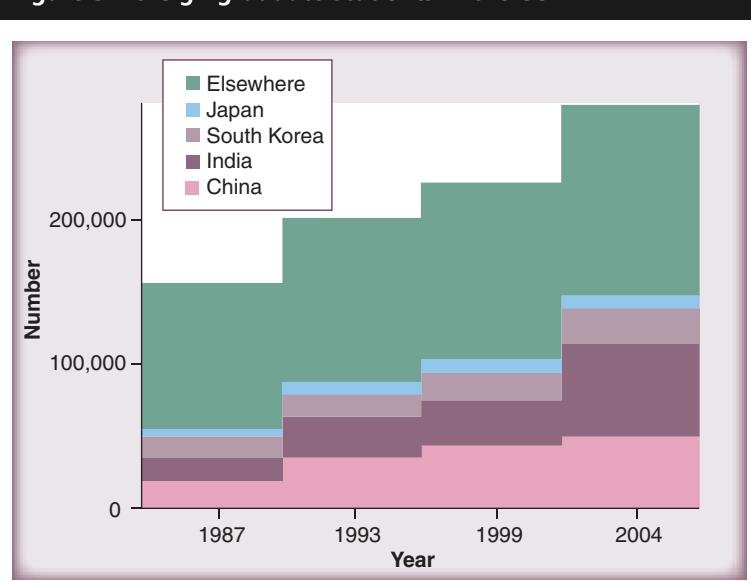
Intellectual property

Although the ability to train, recruit and retain a scientific workforce with international publications and networks is an initial measure of a nation's capacity to compete in the global knowledge economy, the significance of this measure has to be weighed alongside a country's ability to exploit the knowledge produced through trading in the national and international markets of IP. If the IP issue is neglected, a state will find it difficult to move from the knowledge base to the subsequent stages of commercialization. A crude but valuable indicator of inventive activity is the use of the patent system in terms of patent filings by residents and nonresidents (Figure 6).

Although India has increased the number of its patent filings by 365% between 1995 and 2004, its patenting activity is very small when compared with South Korea and China (the latter also has a larger rate of increase of 557%). Nor is it yet a significant global player in terms of its filing of patents in the patent offices of other countries – a useful indicator of a country's ability to penetrate the knowledge economies of other states. In 2004, India filed just 2400 patents in other countries, compared with 30,900 nonresident filings by South Korea and 137,800 by Japan [19] (China is also weak in this respect with only 3100 nonresident filings.) This pattern is particularly evident in filings with the USA Patent and Trademark Office (USPTO) and indicative of India's inability to access what, at present, is the home to the engine of biotechnology innovation (Figure 7). When assessed in terms of the efficiency of the translation of R&D investment into patent filings, India also falls well behind its Asian competitors. In 2004, its resident patent filings per million dollars of R&D expenditure was 0.23 (30th in the world), compared with 0.78 for China (12th) and 4.60 for South Korea (1st) [20].

Biotechs

In order for the fruits of stem cell science to be translated from proof of principle to a potential therapeutic product that is economically viable,

Figure 5. Foreign graduate students in the USA.

Based on data from [14].

Table 1. Plans of Indian recipients of US science and engineering doctorates to stay in USA, by field, 1992–2003.

Year	All science and engineering fields		Biological/agricultural sciences	
	Number (%)	Definite plans/plans	Number (%)	No plans
1992–1995	3708 (88)	506 (12)	714 (92)	58 (8)
1996–1999	4308 (90)	473 (12)	923 (91)	87 (9)
2000–2003	2889 (89)	350 (11)	762 (91)	76 (9)

Data include permanent and temporary residents. Recipients who plan to stay report plan to locate in the USA; those with definite plans report postdoctoral research appointment or definite employment plans in the USA. Based on data from [16].

the early-stage involvement of the biotechnology sector is necessary. India has a rapidly developing biotech sector currently estimated at US\$1.3 billion, which has been growing at a rate of 35–37% per annum and is expected to increase to US\$3.5 billion by 2008. In terms of numbers of companies, within the Asia–Pacific region, India is placed third behind Australia and China/Hong Kong [22].

Within the biotechnology sector, healthcare constitutes an increasing proportion of the total number of firms rising from 24 to 35% between 2001 and 2003 (Table 2). It is also the sector in which the number of large firms has grown by the largest amount (88%) in this period, signifying the rapid entry of transnational corporations. When assessed in terms of workforce, the growth of the healthcare sector is even more marked, with healthcare employees constituting 53% (85,600) of the total biotech workforce in 2003 compared with 20% for agriculture, the next largest sector [111]. In terms of the important question of international links, it is the healthcare sector that has formed the majority of alliances with foreign companies: 70 alliances (54%) out of a total of 129 [112].

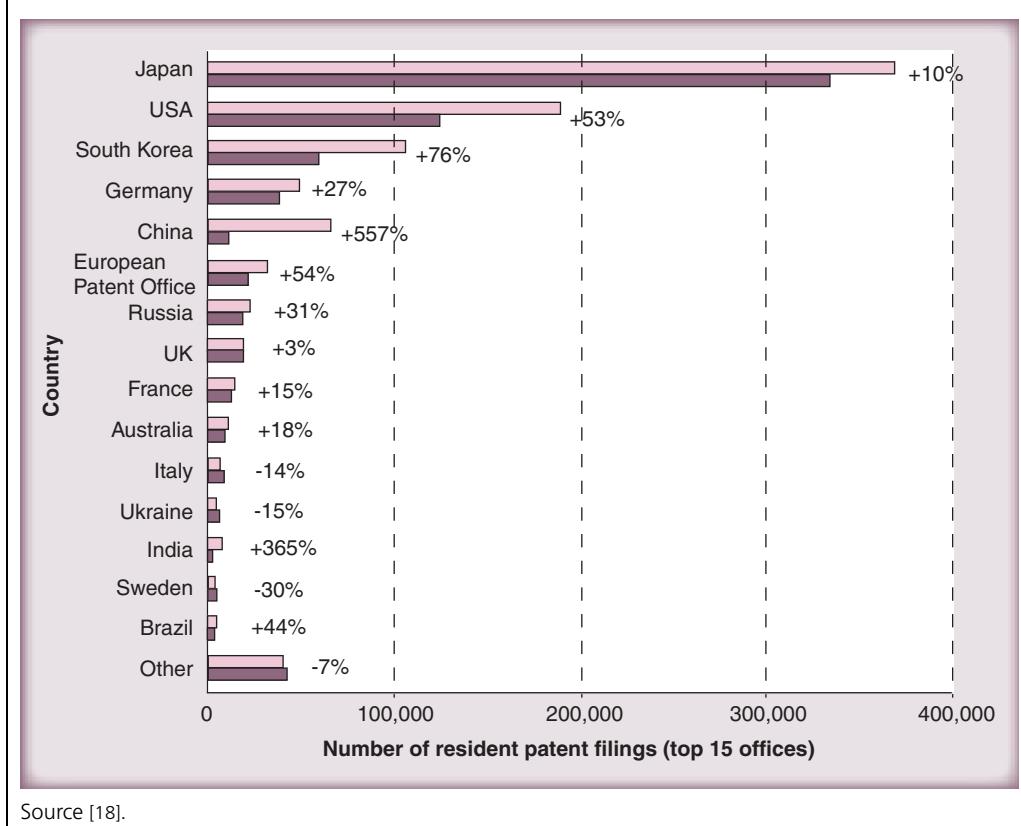
Pharmaceuticals

Once proof of principle has been established, experimental trials conducted and biotech companies involved to take the early-stage work forward, a strong pharmaceutical involvement is an essential component in the commercial development of the stem cell field. In this respect, India has the advantage of an established pharma industry that, over the past two decades has, along with IT, become a major part of its high tech sector (Table 3).

Originally established as a vehicle for producing generic drugs at low cost for a domestic market through the use of reverse-engineering skills, India's pharma industry has expanded rapidly

and, with overall sales of US\$8 billion and exports of \$2.7 billion, is now establishing a global presence (Table 4). In the view of Ernst and Young, Indian pharma companies are in transition from international companies with successful export strategies to multinational companies (MNCs) with a significant presence in multiple foreign markets [24].

Here again, a number of regulatory and human resource problems must be addressed if India is to successfully make the transition towards a global presence in the pharmaceutical market. Although its large scientific labor force is frequently cited in its favor, Ernst and Young's 2006 report nevertheless cites high staff turnover and a lack of adequately trained clinical research staff as an abiding problem [24]. It is likely that state investment in graduate clinical research training, as well as some kind of incentive scheme for returnees, will be needed in order for these market failures to be overcome. Moreover, it appears that India, much more so than its competitor China, suffers from a number of weaknesses in essential infrastructure – India lacks specialized patent offices and IP courts and, although it has a Drug Controller General responsible for clearing all clinical trials, it is widely thought to be understaffed, insufficiently standardized and too closely aligned with the interests of the domestic pharmaceutical industry [25]. As yet, there is no centralized database listing all the clinical trials taking place in India. However, there is evidence that the Indian government has already undertaken several initiatives to address these problems. Plans are underway to create an independent drug regulatory authority along the lines of the US FDA over the next 2 years, with the long-term aim of securing reciprocal approval rights. In this way, a drug approval in India will automatically grant approval in the lucrative North American market [114].

Figure 6. Patent filings by residents.

Source [18].

At the same time, the establishment of a patent product regime in early 2005 looks to have reassured foreign-based MNCs that they can safely re-enter the Indian market from which they had withdrawn because of the historic absence of IP protection for their branded products. Their interest in the Indian market is sharpened by the growth of the Indian middle class, which is fuelling an increase in Western style chronic diseases and hence a demand for the drugs that can treat them [26].

Foreign MNCs are also increasing their R&D investment in India, which, between 1994 and 2002, rose from US\$5 to 80 million. However, these data need to be seen in the context of a parallel rise for China from US\$5 to 646 million and for South Korea from US\$17 to 167 million (Figure 8).

As an emerging economy, India has a mix of strengths and weaknesses when assessed in terms of certain basic infrastructure requirements relating to its global competitiveness in the stem cell field. Its science base is developing but at a slower rate than that of its major Asia competitors, its scientific workforce suffers from a brain drain to the USA and its approach to, and use of,

its science IP is, in global terms, still relatively unsophisticated. However, both India's healthcare biotech and pharmaceutical industries are established and rapidly expanding – the latter on a global scale.

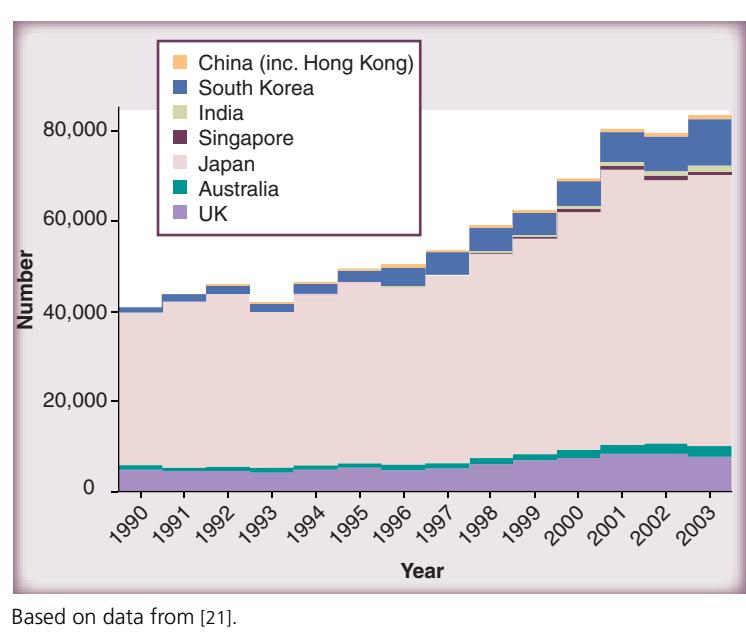
Policy interventions

Given this global position and given that India is aware of the potential of stem cell science, what steps is it taking to improve its prospects in this part of the global knowledge economy? To what extent is India sensitive to the difficulties of commercialization in this field and to the novel forms of state support that may be needed?

Organization & funding of R&D

India's commitment to biotechnology was first formally recognized with the creation of the National Biotechnology Board (NBTB) in 1982, with the brief to create a research infrastructure and identify priority needs as a platform for long-term expansion of the healthcare and agricultural sectors [115]. This was succeeded in 1986 by the DBT, part of the Ministry of Science and Technology, that funds research, manages and oversees projects

Figure 7. USA patent applications by origin of first-named inventor, 1990–2003.



Based on data from [21].

through 16 task forces in specialized areas of biotechnology and acts as a link between the public sector and private industry [116]. Recognition of the significance accorded to biotechnology policy is apparent in the DBT's rapidly increasing budget over the past 5 years (Figure 9). Decidedly ambitious, the DBT's latest plan announced its intention to create a biotechnology industry that would generate US\$5 billion in revenues per year and one million jobs by 2010 [28]. To date, the DBT has supported more than 30 programs of stem cell research, including limbal, hematopoietic, neural, liver, cardiac, human corneal and embryonic stem cells and the establishment of stem cell lines [117].

The DBT's new strategy for the development of India's stem cell science has the following features:

- The promotion of research for therapeutic applications using adult and embryonic stem cells as well as other more readily available sources, such as bone marrow, peripheral blood and umbilical cord blood;
- A focus on basic research and the study of factors that generate stem cells and how stem cell proliferation can be stopped;
- The biology of stem cells;
- The expansion of hematopoietic stem cells without differentiation and gene transduction, gene regulation and plasticity of stem cells;
- The establishment of centers of excellence to increase productivity in stem cell research. Interdisciplinary proposals are being developed with the involvement of basic researchers, clinicians and industry;
- The expansion of stem cell research in India [117].

City cluster stem cell programs are planned for Delhi, Vellore, Hyderabad, Pune and Bangalore. At present, seven hESC lines are held at the Reliance Life Sciences Laboratory in Mumbai and three at the National Center for Biological Sciences in Bangalore [118].

Two other government agencies with responsibilities that include the stem cell field are the ICMR, part of the Ministry of Health, and the Council of Scientific and Industrial Research (CSIR). The ICMR is responsible for formulating, coordinating and promoting biomedical research in response to national health priorities. It has a supporting network of 21 national research institutes and centers as well as six regional medical research centers. Meanwhile, the CSIR is a broadly based agency with an infrastructure of laboratories, institutes and centers for technology transfer.

India's awareness of the need to expand its R&D base is evident in the 25% increase in its 2005 research budget allocation – the highest rise in Asia and comparing favorably with that of

Table 2. Biotechnology firms in India by sector.

Sector	2001		2003	
	n	%	n	%
Agriculture	85	48.3	132	32.9
Healthcare	43	24.4	142	35.4
Environment	4	2.3	16	4.0
Industrial biotech			42	10.5
Others	44	25.0	69	17.2
Total	176	100	401	100

Source [113].

Table 3. The Indian pharma market in 2005.

	Amount
Overall sales by India-based operations (foreign and domestic)	US\$8 billion
Domestic sales	US\$5 billion
Exports	US\$2.7 billion
Outsourcing services	US\$300 million
India market by 2010 (estimate)	US\$8 billion
Indian market by 2015 (estimate)	US\$12 billion

Source [26].

China (16%) and South Korea (10%). Furthermore, India is moving towards creating its own version of the USA National Science Foundation, with a proposed annual budget of US\$250 million [29]. R&D allocations are generally made within the country's National Five-Year Plans and changes in the pattern of these allocations can be taken to reflect shifts of national priorities. In this respect, it is interesting to note that in the most recent Tenth Five-Year Plan there has been a shift in focus from agricultural to medical biotechnology. From only 13% of the total budget in the Ninth Five-Year Plan, the proportion allocated to medical biotechnology has increased to 36%. This priority change includes an emphasis on the clinical application of stem cells and the commercialization of the tissue culture program [119].

While public expenditure on medical R&D is increasing, so also is that of the private sector. Stimulated by the change in the patenting regime (see below), India's large pharmaceutical companies, such as Dr Reddy's Laboratory, Ranbaxy Laboratories and Wockhardt Ltd, are increasing their R&D allocations in their search for innovative drugs. In 2003, average R&D expenditure as a percentage of sales stood at 4.4% compared with 3.8% in 2002. It is estimated that this percentage may have surged to 12% in 2005–2006 [120].

Table 4. Indian high-tech industry production, by industry (USA 1997 \$ millions).

	1980	2003
Pharmaceuticals	1217	6488
Medical, precision and optical instruments	258	1620
Aircraft	68	322
Office and computing machinery	21	2963
Communication equipment	109	6199

Source [23].

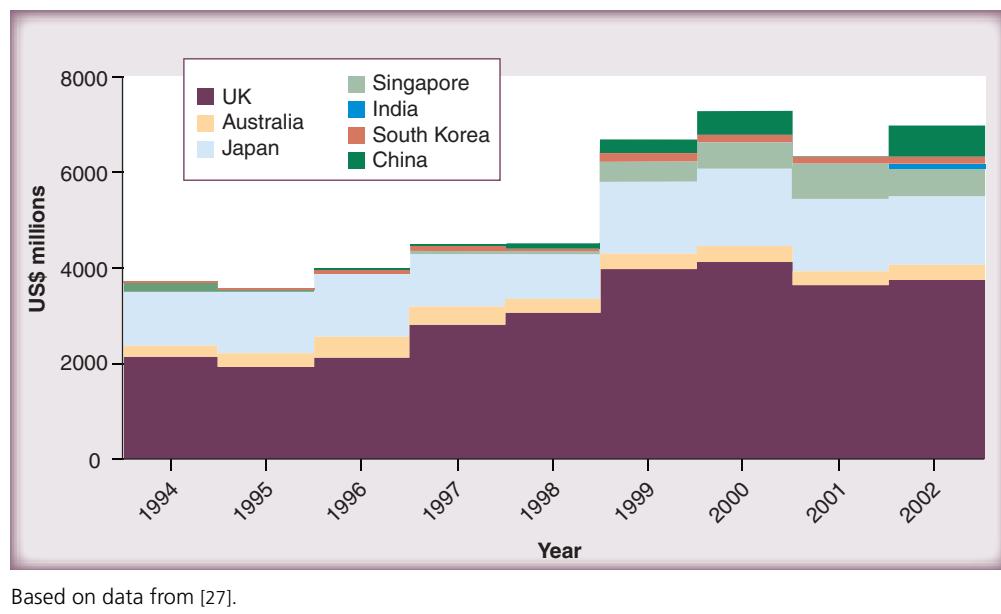
Stimulating the biotech market: IP & VC

As an emerging economy, India lacks a stock market with sufficient volume and liquidity to attract substantial international venture capital investment in support of the early-stage and high-risk health biotechnology companies in the stem cell field. Nor is the protection of IP (a necessary condition of venture capitalist interest) as yet an established feature of biotechnology commerce in India. However, recent legislation makes it clear that the Indian government recognizes the important contribution of IP reform to its global competitiveness.

In April 2005, the Patents (Amendments) Act 2005 implemented India's 1995 accession to the World Trade Organization's Trade Related Aspects of Intellectual Property Rights (TRIPS) agreement. In amending India's Patent Act of 1970, the new Act removes the previous encouragement for process patenting, makes reverse engineering of copycat drugs illegal and encourages novel product development capable of accessing global markets. Its effects are likely to be several. First, small biotechs will become more aware of the ways in which patenting can be used to realize the market value of their early-stage translational research. Second, the domestic pharmaceutical companies will be obliged to shift from process innovation and generic manufacture to product innovation [30]. This, in turn, will encourage both their search for alliances and mergers with the small biotechs with innovative product potential and, as we have seen, pharmaceutical investment in R&D. Finally, the introduction of exclusive marketing rights as a result of the implementation of TRIPS means that foreign pharmaceutical companies will once again begin to view India as an attractive location for strategic investment, particular in the current climate of cost reductions and outsourcing [31] (a 2005 survey of pharma senior executives found that 62% considered patent infringement a problem in India, lower than China [70%], but still too high for comfort [32]). Although it will take time for India to build the appropriate patenting infrastructure, such as specialized IP courts and more patent offices that are computerized and digitally linked, the broad patenting policy direction is now established.

With regard to stem cell science in particular, Section 3 of the 2005 Patent Act lists biotechnological inventions that are not considered patentable. These include any living entity of artificial origin, such as: transgenic animals or plants; biological materials, such as

Figure 8. R&D performed by foreign affiliates of USA multinational companies.



organs, tissues, cells, viruses, and the process of preparing them; and processes for cloning human beings or animals [121].

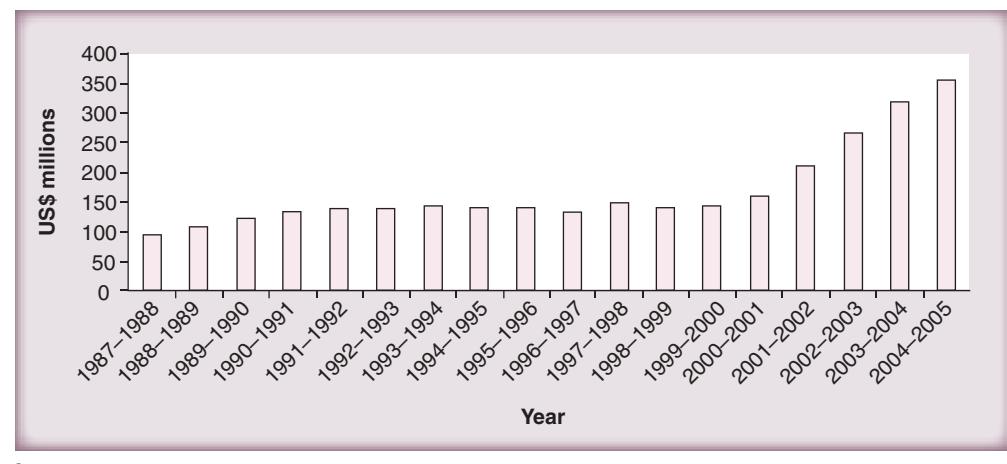
With a patenting policy being implemented, a logical policy partner is national support for the facilitation of the VC function and the market stimulation of new technologies, such as biotechnology. In 1999, the Indian government established the Technology Development Board to support and finance promising new ventures. By 2003, it had promoted 103 projects valued at a total of US\$1.7 billion in biotechnology areas that included health and medicine. At the same time, India has introduced guidelines to facilitate the emergence of venture capital funds (VCFs). In 1996, the Securities and Exchange Board of India (SEBI) framed the SEBI (Venture Capital Funds) Regulations. While only eight domestic VCFs were registered with SEBI during 1996–1998, by 2003–2004 more than 70 additional funds were registered, the majority located in four major clusters – Bangalore, Hyderabad, Pune and Mumbai and Chennai – where growth in the biotech industry is very fast [33]. Overseas VCFs were given tax-exemption privileges in 1995. By 2000, figures from the Indian Venture Capital Association show that the combined total for domestic and overseas venture capital investment was approximately US\$2.6 billion [122].

A parallel policy initiative in facilitating the early-stage commercialization of biotechnology is the Biotech Consortium India Limited

(BCIL). Established in 1990 by the ICMR's Department of Biotechnology, the BCIL is designed to act 'as a public limited company, with the objective of providing the linkages amongst research institutions, industry, government and funding institutions, to facilitate accelerated commercialization of biotechnology' [123]. Given the limited VCF presence in the early 1990s, the BCIL 'was to fulfill the same functions as the venture capital companies in the USA – i.e., promote the creation of firms by providing venture capital and other forms of assistance for scientists to set up firms' – an interesting form of state intervention to counteract market failure [124].

State Governments in India also play an important role in shaping the market environment of stem cell science. Building on their considerable experience with IT innovation, most States have strategies to attract biotechnology industry through policies such as tax concessions, cheap credit, subsidized industrial infrastructure and state support for technology incubators [120].

In the private sector, a significant player in India's emerging VC market and an indicator of India's growing domestic capacity in this field is Industrial Credit and Investment Corporation of India (ICICI) Venture. A subsidiary of ICICI Bank, India's second largest bank, ICICI Venture has aggregate funds under management in excess of US\$2 billion and focuses on sectors where it

Figure 9. Budgetary allocations to the DBT 1987–1988 to 2004–2005.

Source [120].

views Indian companies as having a global competitive advantage: IT, life sciences and service sectors. It is currently forming a dedicated incubator fund for supporting start-ups in the area of biotechnology and life sciences [125]. ICICI is also happy to work with State Governments. In collaboration with Andhra Pradesh, the company is designing a joint initiative for a Knowledge Park near Hyderabad for the promotion of life sciences.

Governance & trust

Emerging economies inevitably search for modes of commercialization that can accelerate them beyond the gravity of the developed world's globalization dynamic. It is in their interest to move fast enough to establish their own counter dynamic that can act to redefine aspects of the globalization process. However, as the case of South Korea's Professor Hwang and stem cell science vividly illustrates, if this is at the expense of scientific and ethical standards there may be a high price to pay. Scientific and public trust in a country's science may be undermined at national and international level. And if trust goes, so does market confidence.

The maintenance of trust through the appropriate governance of a new field of biotechnology therefore constitutes an essential part of the model of commercialization for an emerging, as much as a developed, economy. In stem cell science in India, there are three areas of governance where political issues that can impact on public and scientific trust have already arisen: the supply of oocytes and embryos required for hESC research, the conduct of hESC research and clinical experimentation with stem cells.

India's *in vitro* fertilization clinics are an established source of embryos for research to which foreign scientists come for supplies [126]. However, in the wake of the setting up of the ESC line research at Reliance Life Sciences Laboratory and the National Center of Biological Sciences in 2001 and its associated publicity, the government announced a 'crack-down' on the trade to counter the international view of India as 'an embryo surplus' nation [127]. Given the medical profession's entrenched resistance to the regulation of *in vitro* fertilization, an area of their work that, in India, is both sparsely monitored and highly lucrative, the government's proposals are unlikely to be implemented diligently [34]. If they are not, there is no reason to suppose that there will be much public conflict on this issue. Where debate has occurred, both supporters and opponents have been able to draw on the same Hindu conceptual terrains of Vedic and Upanishadic philosophy suggesting a less-than-straightforward connection between religious values and political position. In addition, the cultural intricacies, stigmas and taboos surrounding infertility in Indian culture seem more likely to promote a self-protective silence on the moral status of the human embryo rather than an open discussion [35].

Moreover, as stem cell therapies move into the later stages of development, the field will be confronted with many of the problems that currently plague the conduct of pharmaceutical trials in general. As India becomes a global center for clinical trials, both for its own industry and contract research organizations working on behalf of foreign companies, the question of

ethical oversight becomes increasingly difficult to ignore. It is significant that the current guidelines for human subject experimentation were established after an incident in 1999, prompting the government to order a review of safety and ethical standards. The *Ethical Guidelines for Biomedical Research on Human Subjects* were published by the ICMR in 2000. However, their recommendations are nonbinding and scandals continue to emerge [36]. At the same time, the Drugs Controller General has issued binding regulations on *Good Clinical Practices for Clinical Research in India* (2001), based on the World Health Organization's standards, and it is reported that programs to train clinicians in GCP are proliferating around the country [128].

The formation and implementation of policy on the regulation of stem cell research itself is heir to the problem of bureaucratic competition: resolvable but continuing. Of the two agencies that fund stem cell research and could therefore assume responsibility for its licensing and monitoring, DBT forms part of the Ministry of Science and Technology and ICMR part of the Ministry of Health. Significantly, the DBT and the ICMR each issued guidelines – the DBT in 2001 and the ICMR in 2002 – without consulting one another [37]. It was not until 2005 that they came together to draft a joint document and, in 2006, produced their *Guidelines for Stem Cell Research and Therapy* [129].

The guidelines propose a system of review and monitoring of the field, based on a National Apex Committee (NAC) for Stem Cell Research and Therapy and, at the institutional level, Institutional Committees for Stem Cell Research and Therapy. All research, including clinical trials, would require the prior approval of, and be registered with, the NAC. Prohibited areas of research include reproductive cloning, implantation of a human embryo into the uterus after *in vitro* manipulation and transfer of human blastocysts generated by somatic cell nuclear transfer (SCNT) into a human or nonhuman uterus. Studies of chimeras and the creation of a zygote by *in vitro* fertilization or SCNT with the specific aim of deriving a hESC line are restricted but not prohibited. At present, these guidelines have been sent for consultation to the USA National Institute for Science and the USA Department of Health and Human Services. Precisely when, how and with what legislative backing they will be implemented is not known.

In this situation of uncertainty, Indian stem cell scientists feel free to consult their own consciences and make their own decisions. Even if the stem cell guidelines are still in draft form, medical scientists can, if they so wish, abide by the principles of the ICMR's *Ethical Research for Biomedical Research on Human Subjects* published in 2000 [130]. Unfortunately, a 2005 survey by the ICMR showed that in the absence of any powers of enforcement, only a minority choose to do so: 40 (22%) of India's 179 institutional ethics committees followed the principles laid down in this document [38]. As stem cell science moves from the laboratory to the clinic and the experimental treatment of patients, it does so in a governance vacuum [39]. As a result, scientists such as Geeta Shroff can publicize her treatment of 100 clinical cases of spinal injuries, paralysis, tuberculosis, neuromuscular dystrophy and multiples sclerosis conducted without ICMR approval and receive simultaneous praise from the Indian Health Secretary and condemnation from Western stem cell scientists [40,131].

Although in the short term the absence of effective regulation may not limit (indeed in some respects it may facilitate) the clinical experimentation phase of stem cell science commercialization, in the longer term it will prove a disadvantage. To be a global player in the stem cell field, India must engage with the international scientific, financial and industrial communities and, sensitive to the need for public trust, these communities will increasingly require adherence to international ethical standards in the conduct of stem cell research and development.

Conclusions

To assume that there is but one model for the commercialization of a new science is to ignore the dynamic nature of globalization and the possibilities it generates. In their review of the opportunities for biotech companies in India and China, Goodall and colleagues remark on the possibility that India and China are opening up a new model of biotech development: 'Call it the 'modular model', a kind of decentralized R&D system where different aspects of R&D are distributed globally and conducted almost autonomously in different locations' [41]. As the emerging economies begin to make their own distinctive contribution to globalization in the health biotech field, so the Western-centric assumptions regarding the

components and sequence of commercialization from basic science to therapeutic product may need to be rethought.

In the India case, we can already see challenges emerging to those assumptions as India becomes aware of its strengths, its potential points of global leverage and the means for compensating (or finding a means for trading against) its weaknesses. At present, India's basic stem cell science is weak and reflects the country's general difficulty of retaining and recruiting high-quality scientists (both overseas-based Indian scientists and foreigners), despite the priority shift towards a proportionally greater investment by the state in medical biotechnology R&D. Yet, in terms of research materials, India has both a plentiful supply of the oocytes and embryos necessary for hESC research and a large and diverse population to support the expanding presence of a domestic and multi-national pharma industry. India may find it feasible to provide Western scientists access to its research materials in exchange for access to some of the scientific knowledge generated as a result.

Until recently, investment in early-stage research was inhibited by the porous patenting regime in India and the consequent inability of investors to assure the gains that might be made from IP. However, the 2005 reform of the patenting system, coupled with the active

state encouragement of, and investment in, the VC function of the biotech market, has engineered a more promising state of affairs. Domestic Indian private VC is now being targeted at its life sciences market and its health biotech sector and associated international alliances are growing rapidly. This raises the question of whether USA VC and NASDAQ membership, the traditional engines of the global health biotech industry, are still necessary conditions of global success in this field.

A more lasting constraint may be the limitations of India's governance of its basic stem cell science, clinical experimentation and drug trials. The not infrequent negative publicity on these issues may not seriously dent public trust within India itself but is likely to be highly relevant to any potential international collaborators – be these scientists or industrialists – who see themselves as accountable to other constituencies [42,132]. The Western outsourcing of R&D may have its cost attractions, but the Hwang affair demonstrates the risks that must be borne if the protective mantle of appropriate governance is not in place.

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