State strategies and speculative innovation in regenerative medicine: the global politics of uncertain futures

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Introduction
The vast but uncertain value of the global market promised by the science of regenerative medicine places governments in a difficult position. Should states choose to embrace the knowledge economy of regenerative medicine as part of their future there is no accepted model for its support and development that can immediately be employed, no known package of innovation policies that will guarantee a country advantage in the global competition. Governments therefore immediately enter a political terrain which, if not uncharted, is at best poorly mapped. But should states instead choose to ignore the promise of regenerative medicine science they may then find themselves portrayed as irresponsible in their neglect of their populations’ future economic health. Furthermore, if other countries subsequently profit from an early commitment to the regenerative medicine field, less perspicacious governments may find that it is too late to catch up.

It is difficult for governments to claim that state intervention is unnecessary and that the market will take care of the development process. As with other areas of novel health biotechnology, the why of state involvement in regenerative medicine is clear. Without it, the lengthy gestation from the basic science to the eventual therapy (usually calculated as between 10 and 15 years) becomes commercially unlikely if not untenable, particularly in the early stages where the theoretical route from bench to bedside is often obscure. Given such large uncertainties, private investors are reluctant to commit resources unless government is prepared to take up at least some of the inevitable risk associated with basic science. For despite its theoretical promise, the research may not produce results that are commercially viable.

The uncertainty of the development path of regenerative medicine science is compounded by its complexity. Its evolution is dependent on social, cultural, economic and political factors that render the construction of a state strategy an essentially speculative exercise. But it is nonetheless a bounded exercise. Although the precise way forward may be unclear, there exists a range of possible policy interventions in the national and international knowledge production process that states must consider if they are to enable scientific progress towards a market outcome that benefits their national economy. Such interventions will include both national policies to support their domestic knowledge economy and moves calculated to protect or enhance a state’s position in those arenas of international governance that impact on new health technologies.

For emerging economies such as China and India, the issue of what, if any, state strategy to adopt towards regenerative medicine is particularly acute. Unlike the European and North American states, they have until recently had little experience at the frontiers of health technology innovation and lack elements of the necessary supporting infrastructure that the former states take for granted. Yet at the same time both China and India are keenly aware of the potential value of the new field and the importance of not ‘missing the boat’. They have every incentive, therefore, to adopt a proactive approach to the science-market relationship that acknowledges their own strengths, exploits the needs of the more developed economies in this field, and builds
alliances based on a commonality of emerging economy interest. Their strategies on regenerative medicine are likely to be different in kind from those of their Western competitors.

In developing a perspective on the position of China and India in the global competition for state advantage in regenerative medicine, I begin with a discussion of how the ‘opportunity’ of the field is conceptualised. What understandings are there of the future value of regenerative medicine science, the demand for its therapeutic products and its potential global market? Secondly, in analysing the response to this opportunity, how can we best theorise the role of the state in promoting what I term ‘speculative innovation’ as the basis for commercialisation in such an uncertain scientific field. To what extent do the concepts of ‘the competition state’ and ‘the developmental state’ provide an appropriate theoretical platform for this exercise? Finally, using a number of key indicators suggested by this analysis, I briefly explore the strategic capacity of China and India to compete for position in the regenerative medicine future.

Future value
Regenerative medicine is an emerging multidisciplinary field involving tissue engineering, biology, biochemistry, medicine, and physics that aims to restore, maintain or enhance cell, tissue and organ function.\textsuperscript{1} The promise is that its applications will be both diagnostic and therapeutic. For diagnostic purposes, cells cultured in vitro are being developed for the pharmaceutical industry as alternative methods for testing drug efficacy and toxicity. For therapeutic purposes, the intention is to regenerate damaged tissues and organs \textit{in vivo} through reparative techniques that stimulate previously irreparable organs into healing themselves. In addition, regenerative medicine promises to allow scientists to grow tissues and organs \textit{in vitro} and implant them in cases where the body cannot be prompted to heal itself. Its future value lies in its claimed capacity to produce therapies for a broad range of diseases and conditions including diabetes, heart disease, renal failure, osteoporosis, and spinal cord injuries for which there is at present only partial treatment or none at all.\textsuperscript{2} Almost none of its promise has yet been realised.

In a political sense this does not matter because, as with many scientific ventures, regenerative medicine is concerned with the political capture of future imaginations, be these of publics, patients or politicians. Embedded in these imaginations are hopes and expectations of what the future might bring and, if the faith is sufficiently strong, a commitment to support the allocation of the resources required to enable that imagined future to become reality.\textsuperscript{3,4,5} In power terms, it is its political sustainability that is important, not whether the belief subsequently turns out to be true. Recent examples such as transgenics, reproductive science and bioinformatics reveal the competitive nature of this enterprise and the importance of not allowing a rival area of science to capture the imaginative high ground. For if public support is gained then the authenticity of the future market becomes more tangible; if political support, then the winning of scarce scientific resources becomes more likely. At the same time, scientific advocates must beware of over-hyping their future products since this may overstretch the imaginary envelope and cause both its collapse and that of its associated anticipated future values. To be politically effective, advocates must be seen to act responsibly, rationally and with due discretion.
Regenerative medicine is unusual because it incorporates a wide range of both scientific disciplines necessary for its advancement and disease groups to which it will apply. The breadth of the disease groups is important because it indicates not only the range of patient organisations that will lend their support to the advancement of the new science, but, more significantly, the size of the value of the potential market that regenerative medicine will create. It enables regenerative medicine to expand its future territory to include the economic as well as the scientific imagination and with it to capture the interest of such significant players in the innovation process as state actors and venture capitalists (VCs).

In the promotion of the economic imagination of regenerative medicine, statistics are frequently employed in attempts to demonstrate the rationality and hence the legitimacy of the projected market future. In terms of future patient population demand, the United States National Academies of Science report *Stem Cells and the Future of Regenerative Medicine* estimates that in the US the market for stem cell–based therapies, an important sub-division of regenerative medicine, includes more than a hundred million patients with conditions such as cardiovascular disease, autoimmune diseases, diabetes, cancer, neurodegenerative diseases, and burns. In terms of financial value, one source ‘conservatively estimates’ the worldwide market for regenerative medicine to be $US500 billion by 2010, while another announces that the European market is expected to reach $15 billion by the same year – though precisely how these figures are calculated is not revealed. Forecasts by consultancy firms on the stem cell market include a US market of $3.6 billion and a world market of $8 billion by the same year. Others are less optimistic, predicting a world market of $100 million by 2010 rising to $2 billion by 2015. Although the market forecasting of regenerative medicine can be seen to be a highly variable exercise dependent on what diseases, technologies, and types of firm are included, it is nonetheless sufficiently prevalent to help establish the impression of an achievable future reality even though the precise nature of this reality may be elusive. It is also an exercise usually detached from any consideration of the impact on patient demand for the new health technologies of factors such as the mode of health care funding, cost constraints, ethical considerations, regulatory frameworks or policies aiming at the protection of domestic pharmaceutical industry.

Closely allied to the carrot of future economic benefits is the stick of the opportunities to be lost by states that are too limited in their political imagination. The assumption is one of a finite reservoir of future value in regenerative medicine that only those states with the appropriate foresight and commitment will be able to access. For the developed countries of the West, this means ensuring that their traditional hegemony in the health biotechnology field is not lost. Thus the 2006 US report on regenerative medicine starkly warned the nation that ‘the U.S. pre-eminence in the field of regenerative medicine is in jeopardy’. Similarly, the United Kingdom’s report on a ten year strategy for the development of stem cell research, therapy and technology (the ‘Pattison Report’) made clear its ambition ‘for the UK to consolidate its current position of strength in stem cell research and mature…..into one of the global leaders in stem cell therapy and technology’. The report was at pains to document in detail the investments being made by other countries in stem cell science. Most recently, the German government produced a study that whilst noting Germany’s leading
international position in regenerative medicine argued for urgent policy changes to facilitate the translation from the science to the therapeutic product.\(^{12}\)

Whilst the developed countries may be anxious that their dominance in the future markets of new health technologies is not eroded, developing countries are equally concerned that their ability to compete is not undermined by their own failure to anticipate and respond to these future opportunities. For them it is less a case of building on what they already have and more a question of what new kinds of innovation infrastructures they are best placed to construct, given their previously limited activity in regenerative medicine science. Their policy choices are both more generous and more demanding in scope.

Responding to regenerative medicine as a leading example of the promise of the new health biotechnology, states such as China, India, South Korea, and Singapore have all made an investment in regenerative medicine science. China’s annual investment in stem cell research was recently said to be between US$4 and 10 million with 300 researchers working in 30 separate institutions.\(^{13}\) However, these figures are set to increase dramatically. Estimates quoted in the UK’s Pattison Report suggest that over the next five years China’s Ministry of Science and Technology (MOST – the main source of public research funds) is expected to spend between RMB 500 million (US $63 million) and RMB 2 billion (US $0.25 billion), depending on how productive the science turns out to be.\(^{14}\) In January 2005 India’s Department of Biotechnology (DBT) and the Indian Council of Medical Research (ICMR) announced plans for a national stem cell initiative that would prioritise research funding, focus on clinical applications and promote ‘stem cell city clusters’\(^{15}\). Despite (or because of) the fallout from the Hwang affair,\(^{16}\) South Korea remains firmly committed to the aggressive expansion of stem cell research and in May 2006 allocated $454 million to the field over the next decade.\(^{17}\) Meanwhile, Singapore’s vast investment in its Biopolis complex ($8 billion committed through to 2010) continues to act as a magnet for Western regenerative medicine scientists.\(^{18}\)

The commitment of both developed and developing countries to the imagined future value and global opportunity of regenerative medicine is clearly present. How can we best analyse their capacity as states to translate this imagined future into a globally competitive reality through strategies that deal with the social, cultural and economic dimensions of innovation?

**States and speculative futures**

The theoretical roll call of types of states that are categorised as responding to the opportunities of the global knowledge based economy is long. They range from the competition state (with variations such as the entrepreneurial, regulatory and managerial states) through the developmental state (with variations such as the post-developmental and democratic developmental states) to the more loosely framed enabling or facilitative state and the very loosely framed adaptive or flexible state. Despite the conceptual promiscuity of the field and the confusing use of categories based on both functions and institutional characteristics, a picture emerges of states responding in a variety of ways to the problems and prospects of globalisation, and learning as they do so. What is significant is that some states learn faster than others and at a speed that reveals the static quality of some social science categories. This is particularly true of the globalisation of the life sciences where states confront an
essentially speculative future. In such a context, states characterised by rigid planning systems are unlikely to produce policies that serve the national interest.

**Competition states and commercialisation**

It was precisely to deal with the uncertainties accompanying the shift from Fordist to post-Fordist modes of mass production and consumption that the ‘competition state’ of the advanced economies of the West is seen to have developed. Rather than concerning themselves with government interventions to ensure full employment and respond to market failures states, states began to focus their attention instead on the neo-liberal supply-side policies that would give a sharp edge to their competitiveness in the global knowledge economy. Particularly in the case of the bio-industries, this meant a concentration not only on the infrastructures of innovation but also on ‘agglomeration and network economies and the mobilisation of social as well as economic sources of flexibility and entrepreneurialism’. To be effective, competition states needed to bring their social and cultural values into line with their entrepreneurial ambitions. Entrepreneurialism needed to be embedded: as a consequence the institutional reforms of the competition state eschewed rigid bureaucratic hierarchies and relied instead on new forms of network based governance.

Should they choose to respond to the demands and opportunities of the new knowledge economies, competition states can make the decision to intervene at any or several points in the process of knowledge production from the basic science through to the market product. Such decisions are highly political in the sense that they involve the allocation of scarce scientific resources, the acceptance of the risk involved in speculative science, the assumption that public support for the field selected can be maintained over time and, above all, the need to outmanoeuvre a state’s global competitors. When analysed in terms of the knowledge production process, each political intervention becomes a policy component which, if brought together in a sequence, would constitute a state strategy. In terms of components, this approach is similar to the conceptualisation of ‘a national innovation system’ defined by the World Bank as:

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a complex set of relationships among actors producing, disseminating, acquiring and applying various kinds of knowledge. Performance depends on how these actors relate to each other as elements of a collective system of knowledge acquisition, creation, and use. These actors are primarily private enterprises, universities and public research institutes – and the people in them. The linkages can take the form of joint research, personnel exchanges, cross-patenting, technology licensing, equipment purchases, and a variety of other channels.
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However, whereas the concept of a national innovation system is concerned with performance and economic efficiency, the 'state strategy' approach adopted here focuses on the murkier realm of the politics of national advantage (Figure 1). Performance and efficiency form part of this politics, but by no means the only part.
In deciding how to intervene and with what policies, the competition states of Europe and North America have moved away from the national sponsorship of particular firms and technologies and towards policies designed to foster ‘the conditions necessary for innovation’. The objective has become less one of specific structural change and more one of stimulating a dynamic that enables the knowledge production process to become self-sustaining. It has become part of the established policy orthodoxy that regional governments should initiate programmes to foster cluster developments in sectors such as biotechnology; that commercialisation can be facilitated through academic-industry collaborations and high profile, publicly funded R & D centres acting as magnets for venture capital investment; that networks of science and industry should be enabled; that regulation should be facilitative rather than restrictive; and that intellectual property rights (IPR) should favour the operation of the market. As with all orthodoxies, there is the expectation of policy convergence between states characterised by assumptions regarding ‘best practice’ in the field.

However, although competition states may agree on the list of policy components that support participation in the global knowledge economy, they differ considerably on the relative significance they attach to each component, the resources to be committed to individual policies and the interrelationship between the components. As always, political factors such as scarce resources, ideological preference, global and regional position and cultural constraint will influence what policy choices are made. As a result states have different strategies on the bioeconomy, or their strategies may be partial with some policy components present and others missing. For example, the study by Benner and Löfgren comparing the biotechnology sector in the three groupings of Finland and Sweden, the USA and the UK, and Australia concluded that, whereas there was some convergence in the area of public investment, there were differences in the approaches to market regulation, industrial support, venture capital and ethical restrictions. Differences, furthermore, that did not follow the dichotomy between ‘liberal’ and ‘coordinated’ models of capitalism.

The idea that there is a global wave of neoliberal policies sweeping uniformly and remorselessly across the political planet is therefore challenged by the evidence that competition states make distinctive choices about their involvement in the bioeconomy in general. In addition, the high level of uncertainty that characterises regenerative medicine science and its therapeutic applications means that competition states are also likely to have different views about the commercialisation of this particular field. There is no accepted commercial model for its development on which they can draw, no package of policy components that can be applied. Indeed, the technological novelty of the field challenges the skills and inventiveness of the business community as much as those of science. Both are aware of the value of the speculative future of regenerative medicine yet neither can be sure of how, or whether, it will be achieved or of what kind of science-market relationship is appropriate at what point in the commercialisation process.

In terms of its therapeutic outcome, the commercialisation of regenerative medicine is designed to achieve a ‘product in which human cells are administered to the body for
the purpose of replacing, repairing, regenerating or enhancing function of tissues’.

Such a broad definition of the cellular and tissue based products on which regenerative medicine is founded succeeds in spanning the two dominant business models of the health products field, pharmaceuticals and medical devices, and, in a theoretical sense, can be seen to result in a third hybrid business model that incorporates features of both (Figure 2 – 37). Whereas the pharmaceutical model recoups the high costs of its up-front investment and long development times (typically 15-20 years) through high gross margins and large markets, the medical devices model can tolerate lower gross margins and smaller, more focused markets because it has lower development costs. Unfortunately for its market appeal, the theoretical hybrid business model of cell-based products includes the negative characteristics of the other two models: high up-front investment, medium/long development times (10-15 years), low gross margins and markets focused on a range of separate diseases. In this pure form, it is therefore unlikely to move from theory to reality.

The decision making by states on whether to intervene to render the regenerative medicine business model more tenable is made more complicated by the fact that the model is not static but rapidly evolving. As Figure 3 shows, commercial opportunities are being identified in the regenerative medicine field that are driven by products other than the therapies themselves. 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 business model would generate an early cash flow to nurture the development of the field.

The need to adapt a business model to the characteristics of the new health technology markets that are situated between the basic research and the therapeutic product is not peculiar to regenerative medicine. Genomics companies have also recognised the importance of refocusing their research efforts: in their case, downstream within the drug innovation cycle. Employing proprietary technology or knowledge based assets protected by patent, research based genomics companies have formed alliances with pharma and biotech partners to generate the all important cash flow through licensing arrangements and/or subscription fees. Admittedly this strategy has been facilitated by pharma’s need to bolster drug pipelines through a focus on the upstream stages of the drug innovation cycle but genomics companies have still had to make their business models work. For states anxious to promote regenerative medicine, the experience of the closely related genomics sector shows that the mode of state intervention may need to be as adaptive as the business models they seek to support.
**The adaptable developmental state**

Like competition states, the states of the developing world are responding to the global opportunities of regenerative medicine through strategic interventions in the knowledge production process (Figure 1). However, the literature on developmental states suggests that they approach this task from a perspective shaped by a different historical experience of globalisation. Focusing in the main on South Korea, Taiwan, Japan, and to some extent Singapore, in the 1980s and early 1990s, the earlier work highlights the role of the developmental state in the promotion of rapid economic development through the targeting of particular industries with large global markets. The markets were already there. The political task was to penetrate them. To achieve this goal, the state protected their chosen industries using a range of policies such as import and credit controls, promoted them through state investment, guided private capital through incentive schemes, and measured their progress in terms of export achievements.  

Backed by a strong, professional and autonomous bureaucracy, the state sought to define the specific path of industrialisation through the “government of the market”. As with the competition state, there were substantial variations on the model of the developmental state. Nonetheless, given where they were starting from, the simple fact remains that the developmental states of the Asia Pacific had more in common with each other than with the competition states of Europe and North America.

In essence, their commonality is that they sought to challenge the control exercised by the developed world over the dynamic of globalisation. If they were to access the wealth of global markets, if they were to ‘catch up’ with Western countries, then the power of the state was required to make globalisation work for them. However, having caught up using the targeting of known markets as a primary policy objective, developmental states faced the problem of ‘keeping up’ in the context of future markets such as the life sciences that were either unknown or decidedly uncertain. At the same time, the forces of global economic integration and the liberalisation of capital markets appeared to threaten the advantages conferred by their policies of protection and promotion. Through the propagation of international economic governance measures such as the World Trade Organisation’s (WTO’s) Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS), Agreement on Trade Related Investment Measures (TRIMS) and General Agreement on Trade in Services (GATS), countries such as the UK and the US sought to diminish the developmental states’ room for manoeuvre by forcing them to adopt neo-liberal, fiscally conservative policies. It seems to have been assumed that greater liberalisation was in the interests of the developed countries because it exposed the weaker economies of the developing world to global market pressures. The Asian financial crisis of 1997-98 is often quoted as proof that this strategy was impacting on the developmental states.

However, the view of developmental states as global victims underestimates the capacity of all states to adapt their strategies in the light of both threats and opportunities in the international economy. Developmental states are no exception and, to varying degrees, have demonstrated their ability to evolve their apparatus of economic government. In reporting this phenomenon, observers have consequently been obliged to evolve a new nomenclature including ‘adaptive state’, ‘flexible state’, ‘post-industrial developmental state’, ‘transformative state’ and ‘catalytic state’ in their studies of Japan, South Korea and Taiwan.
As we have already seen, developmental states are as committed as competition states to the belief that health biotechnologies, and regenerative medicine in particular, are industries of the future. They are also aware that their traditional modes of direct state intervention do not suit the innovation requirements of what is an elusive science with a speculative future, an uncertain market and a difficult path to commercialisation. Knowledge based economies require more subtle forms of developmental support across the range of policy arenas summarised in Figure 1 in order to generate, as Wong observes of biotechnology in Taiwan, ‘the right mix of public policies aimed at facilitating technology innovation and knowledge-based interventionist strategies’. For example, ‘cutting edge technologies can no longer be borrowed; rather they must be created’ – which means a change in state direction and an investment in, or access to, basic science. In moving from borrowers to innovators, developmental states are obliged to review the extent of their autonomy and the style of the bureaucracy that implements their policies. Can they transform the autonomy of the developmental state into a more relevant bureaucratic form characterised, for example, by collaboration between administrative and business elites, or will bureaucratic change simply result in administrative confusion and inefficiency?

Perhaps unsurprisingly, the mode of state adaptation varies and is dependent on local political conditions, the regional context, and decisions regarding the strategic entry points on the biotechnology value chain of innovation that a state deems appropriate. In Singapore, the state retains tight control in its pursuit of economic prosperity through the promotion of the biomedical industry. It remains a single party state with a high level of state ownership that still prohibits public demonstrations, exercises a tight labour control scheme, and limits public debate. Yet at the same time its bureaucracy has adapted itself in order to ‘enable’ the emergence of its health technology economy by providing research facilities, funding, and a supportive regulatory climate responsive to international requirements. It may have moved towards a more liberal economy, but on the state’s terms. Contrast this with the situation in Taiwan where, in the promotion of biotechnology, the earlier cohesive bureaucracy has been replaced by a proliferation of government agencies characterised by overlapping and competing jurisdictions. Or again, South Korea where the growth of working class and bourgeoisie opposition combined with the divisions between the chaebol (family controlled corporate groups) and the state to reduce the traditional autonomy of the latter. Nonetheless, despite their considerable differences, all three developmental states have taken the view that their national innovation strategies on health biotechnology should form part of a larger, global enterprise. With the effects of the WTO’s initiatives on international economic governance feeding through the global system, developmental states are obliged to be proactive in their approach to globalisation regardless of their earlier leanings towards protectionism.

As relatively recent emerging economies, China and India bring a different perspective to the evolving nature of the developmental state. Unlike Singapore, South Korea, Taiwan and Japan, they did not experience the rapid economic growth of the 1980s and early 1990s. For China, the massive shift from a centrally planned to a market influence economy that commenced in 1978 required a seismic change in the role of the state that only gathered real momentum in the mid-1990s. Membership of the WTO and exposure to the pressures of global competition in the early 1990s
caused what Saich has described as ‘the internationalisation of the reform process’ and an intensification of demands for the state to move from a directive to a facilitative role. In practice, although the level of administrative intervention has diminished, the state has retained many of its old monopoly functions whilst simultaneously expanding its role into the new regulatory policy arenas needed for China to participate effectively in the global knowledge economy. Its infrastructure needs as a player in the global knowledge economy remain considerable and, as a developmental state, it is still in important respects playing ‘catch up’. India, meanwhile, is a revealing example of a country that initially took the traditional developmental state path characterised by direct state intervention and a top-down bureaucracy but, by the early 1990s, had clearly failed to meet its economic objectives. With impressive adaptability, the Indian state subsequently reconstructed itself as the enabling vehicle for a deregulated economy that has produced the explosive growth of the last 15 years.

State capacity and strategic speculation in the Asia Pacific region

The degree of adaptability of developmental states is a critical political factor in their response to the bioeconomic possibilities of regenerative medicine. Lacking the resources to compete for global advantage across the full range of policy components that shape the knowledge production process in this field (Figure 1), developmental states must necessarily be selective, choosing their points of policy intervention in the light of how they seek to position themselves in the global game. As the World Bank report China and the knowledge economy: seizing the 21st century observes, ‘developing countries do not have to reinvent the wheel: there are many ways for them to tap into and use the knowledge created in developed countries’. In this respect a state’s territorial jurisdiction of knowledge is less important than its strategic capacity for global access to the components of knowledge production.

Working within the context of the developmental states of the Asia Pacific and drawing on the policy components of Figure 1, in this section I review the extent to which China and India, the emerging giants of the region, have developed a capacity for state speculation in the global political market of regenerative medicine. This capacity is analysed in terms of the global significance of selected key indicators of the knowledge production process in China and India: scientific infrastructure (investment, workforce and outputs); patenting; and inward flows of foreign investment from pharma, other multi-national companies (MNCs) and venture capitalists. What do these indicators tell us about the ability of China and India to become global players in regenerative medicine?

Scientific infrastructure – investment, workforce and outputs

The commitment of China and India to regenerative medicine science documented earlier forms part of their broader intent to increase research spending to levels comparable with Western states. R & D investment is seen as an essential platform for effective global competitiveness in new technologies where access to basic scientific knowledge provides an initial market advantage. In China, R & D spending has more than doubled from 0.6 per cent of GDP in 1995 to just over 1.2 per cent in 2004. Predicted to spend over USD 136 billion in 2006, China will then overtake Japan as the second largest investor in R & D in the world after the United States.
India’s government R & D expenditure is much more modest but in 2005 dramatically rose by 25% to USD 4.5 billion. This was followed by an announcement in October 2006 by India’s Prime Minister Manmohan Singh that it would increase from 0.8 to 2 per cent of GDP in the next five years – a clear signal of global intent and, if achieved, of state adaptability.

Both nations have a large scientific workforce. According to OECD figures, China’s stands at 926,000 (the second largest worldwide) and India’s is also substantial. But perhaps more significant in terms of their future scientific capacity are the trends in their training and retention of scientists relevant to the regenerative medicine field. The data on the number of doctoral degrees in the physical and biological sciences awarded between 1983 and 2001 shows that 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 (Figure 4). To an extent this may be because the lack of training opportunities in Indian universities in the life sciences encourages postgraduate students to leave India to complete their PhDs abroad. At the Indian Institute of Science, 90% of those who finish PhDs choose to move overseas – an indicator of India’s difficulty in sustaining the important middle tier of postdocs required for successful scientific teams and laboratories, particularly in a highly competitive field such as regenerative medicine.

In assessing the significance of these figures, it has to be remembered that scientific training, like other aspects of science, is an international as well as a domestic activity and a source of future research networks as well as current knowledge. If we now examine the ability of Indian students to access the largest sector of the international graduate education market, the United States, 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 US has quadrupled from 15,600 to 63,000, Chinese students have increased at a lower rate from 20,400 to 50,800. However, if we focus the lens on the top end of the science and engineering market we find that here China predominates: in 2003, doctoral students from China gained 2501 (25 per cent) out of the total 9846 doctorates in this field awarded to foreign students in the US.
However, these figures do not necessarily translate into a global advantage for Indian or Chinese science since the majority of graduates choose to remain in the US 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 US was consistently around 90%.\(^{82}\) In China’s case, between 1998 and 2001 the actually stay rate of qualified science and engineering PhDs was 60 per cent. To put this in an Asia Pacific perspective, the equivalent figure for South Korean PhD students was below 30 per cent.\(^{83}\) Overall, China’s Ministry of Personnel estimates that about 580,000 students have gone abroad since the late 1970s with only about 160,000 (27%) returning. These figures are highly significant for the development of health biotechnology in China: of the nearly 300,000 Chinese students overseas in 2004, a third were involved in the biotechnology field.\(^{84}\)

The net effect of this brain drain is that in 2003 there were 448,700 Indian born residents in the US with degrees in science and engineering or related subjects though only 41,300 (9%) of these had doctoral degrees. In comparison, the equivalent numbers of Chinese born residents in the US was 294,800, 62,500 (21%) of whom had doctoral degrees.\(^{85}\)

The Chinese government in particular is well aware that if it is to develop its health biotechnology capacity to innovate then it must at least stem and preferably reverse this drain on its scientific workforce. Incentive measures include salaries that are competitive in the international domain (particularly for top scientists), government financing for scientists who wish to set up laboratories in China, support programmes and business incubators for entrepreneurs wishing to launch start-up companies, and a special fund to finance the Chinese side of international S & T collaboration projects (100 million RMB (US $12.5 million) initially but can be increased as necessary).\(^{86}\) Two recent examples of initiatives taken to promote the inward flow of international scientists in the health biotechnology field are the establishment of Beijing Life Sciences Research Institute (December 2005) and of the China National Academic Centre for Biotechnology (May 2006). An alternative strategy is for a state actively to build its capacity by attracting high quality scientists from the international labour market. For example, Singapore has decisively entered this market with policies expressly designed to attract stem cell scientists from the US and the UK through financial support and a liberal regulatory regime.\(^{87}\) These policies exploit the relatively high global mobility of scientific labour in regenerative medicine science. (One survey reports that stem cell principal investigators are 5.3 more times likely to receive at least one international job offer than PIs in other biomedical fields).\(^{88}\)

It is to an extent surprising that if we employ a more interactive measure of global scientific position, the geographic scope of international collaborations, a picture emerges of India as marginally ahead of its Asian emerging economy rivals. Based on 2003 data, the US 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. Amongst low and middle income countries, India ranked first with 107 co-authoring countries, ahead of China (102).\(^{89}\)
However, a country’s proportion of the global output of science and technology publications measured over time provides a surer indication of its control of important intellectual resources necessary for the first stages of the commercialisation process. In the Indian case, between 1988 and 2003 this proportion has remained static at 2% (Figure 6). This compares unfavourably 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 it is principally China and South Korea that have expanded their global knowledge base at the same time as the US share has declined from 38% to 30%.

**Figure 6**

*Patenting*

Intellectual property rights (IPR) are an essential component of a knowledge economy because they commodify the intangible capital of knowledge, generate value and facilitate trading (see eg 91 92). Without IPR, and in particular patent protection, emerging markets would find it difficult (or more difficult) to develop since the tangible product has yet to appear and economic value is embedded in the potential application of the knowledge. This problem is particularly acute in high-tech and research based Small to Medium Enterprises (SMEs) for whom their IPR is their main asset. The economic significance of patents is further enhanced by the need for new forms of knowledge to compete for attention in an increasingly global venture capital market with its own clear demands: investors, often institutional investors, make their decisions in the light of the patents held by companies. 93 94 95 For capitalisation of a new knowledge market to occur, then, investors need to be reassured that the value of the knowledge, as opposed to the value of the eventual product, is in the hands of the company concerned. Investors are likely to be particularly sensitive to the patenting issue in high risk areas such as the early stage development of health biotechnologies where the science is very new and the potential therapies very distant.

Patenting therefore provides a useful global indicator of a country’s innovation activity. What capacity does a state have 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 difficulty to move from the knowledge base to the subsequent stages of commercialisation. A crude but valuable indicator of inventive activity is the use of the patent system by a state as manifest in its resident and non-resident patent filings.

**Figure 7**

China (557 per cent) and India (365 per cent) have easily the highest rates of increase in the number of resident patent filings between 1995 and 2004 when compared to other nations but both lag behind South Korea; and India in particular started from a very low base (Figure 7). Importantly, neither is yet a significant global player in terms of non-resident filings 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, China managed only 3100 non resident filings and India 2400 compared with 30,900 by South Korea and 137,800 by Japan. 97 This pattern of weak penetration is particularly evident in filings with the USA Patent and Trademark Office (USPTO)
and indicative of both countries’ inability to access what, at present, is home to the engine of biotechnology innovation (Figure 8). When assessed in terms of the efficiency of the relationship between two components of innovation, R & D and patent filings, India 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). 

Figure 8

However, things may be changing. The most recent data from WIPO on its Patent Cooperation Treaty (PCT – through which one ‘international’ patent application can be sought simultaneously in all WIPO member countries) show applications received from the developing countries of north-east Asia in 2006 increased by 27.6 per cent over the previous year, far higher than the overall growth of 6.4 per cent. Commenting on these figures, the Deputy Director General of WIPO observed that they showed the changing geography of global innovation with developing country states capitalising on the tools of the intellectual property system for wealth creation. The largest filings in this group were from South Korea (5,935) and China (3,910) followed at a considerable distance by India (627) and Singapore (402).

Foreign investment
For emerging economies like China and India, the ability to attract pharmaceutical companies in support of regenerative medicine biotech innovation is much less problematic than it used to be as what has been termed ‘the second wave of globalisation’ is now taking effect in the biomedical as well as the IT industry. Propelled by the search for lower scientific and clinical labour costs in the context of a perceived crisis in their profits, multinational pharmas are increasingly outsourcing their R and D operations to developing countries. Between 1995 and 1999 the number of international human subjects involved in clinical trials grew one hundred fold from 4000 to 400,000 and the number of clinical trial investigators conducting multi-national drug research in low-income settings increased sixteen fold between 1995 and 2005.

In April 2006, pharma companies were performing 838 ongoing trials in the US, 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 three years.

The interest of multinational pharmaceuticals in emerging economies is also strongly influenced by the global loss of their quasi-monopoly 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 six years. None of the top ten best-selling biotech products had been developed by a pharmaceutical company, although six are marketed through big pharma. 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.
For their part, China and India are keen to exploit this need and to expand their biotech development capacity by attracting inward investment from the pharma industry. Employing tax incentives for Foreign Direct Investment (FDI), a non-threatening regulatory environment, and an emphasis on their large and diverse populations as both research subjects and potential markets for drug companies, both countries have sought the outsourcing attention of pharmaceuticals and contract research organisations (CROs). \(^{107}^{108}\) Guidance produced for pharmaceutical executives to inform their offshore decisions strongly suggests that this approach is successful. The Country Attractiveness Index for Clinical Trials, which ranks offshore locations in terms of patient availability, cost efficiency, relevant expertise, regulatory conditions and national infrastructure, puts China and India at the top of the table.\(^{109}\) Leading phar...SmithKline China (Beijing), Pfizer Pharmaceuticals (Beijing), Novartis Pharmaceutical (Beijing) and Merck China (Shanghai). In addition, China has more than 150 health biotechnology products in clinical trials and is increasing the number of health biotechnology patents by about 30% per year.\(^{110}\) India, meanwhile has its own well established pharmaceutical industry with overall sales in 2005 of US$ 8 billion and 20 per cent of the global market in generic drugs.\(^{111}\)

More generally, following the accession of both countries to the WTO and their agreement to the patent protection conditions of TRIPS, US based MNCs are increasing their R &D investment in China and India. Between 1994 and 2002 R & D MNC investments in China rose from US$ 5 to 646 million and in India from US$ 5 to 80 million (Figure 9). For South Korea the corresponding rise was from US$17 to 167 million. This investment is reflected in the rapid rise of multinational research centres with China now hosting 750 such centres and India 150. However, an important caveat is that if this investment is to provide increased developmental capacity there has to be engagement between the multinational centres and the local economy through spin-offs, labour mobility and partnerships with small companies and universities. In practice, this does not necessarily happen.\(^{112}\)

Where emerging economies like China and India are not yet advantageously placed is in their access to the global financial markets that are essential to enable early stage biotech companies to take forward the results of basic regenerative medicine research. Although private investors and individual venture capital companies (VCs) can help biotech startups it has been the long term capital flowing from 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 US biotech industry by far the largest in both market values and product sales. Bearing in mind that 40% of all US venture investing is in the life sciences, in 2005 private biotechs raised $7 billion in US capital, up from $5 billion in 2004, of which $3.5 billion was by venture capitalists.\(^{114}\) In contrast to this, VC investment in Asia was miniscule and barely registers when placed in the global context (Figure 10). Apart from Japan, Asian stock markets do not have the liquidity and volume necessary to attract Western VCs or biotech firms on any scale and the exit options for investors are limited. Emerging economies in this region therefore have a funding gap in the life sciences innovation process.
Both China and India recognise that this vulnerability must be addressed if they are to compete in the global knowledge economy of regenerative medicine and are seeking to evolve domestic alternatives to the conventional (US) model of venture capital and commercialisation. China has a number of venture capital firms that are publicly supported through national and local government. National government in particular is increasing its role in this area as witnessed by the recent loan by the China Development Bank to the Ministry of Science and Technology. In addition, there are corporate, university and foreign owned venture capital firms and hybrids formed by joint ventures between different types of firm. In the field of regenerative medicine, unconventional business models are emerging in response to the idiosyncrasies of the Chinese economy. For example, the Union Stem Cell and Gene Engineering Company Ltd (StemGene) was incorporated in February 2001 with two principal shareholders: the Institute of Haematology in Tianjin and the Shanghai Met Corp, an organisation involved in the import and export of textiles. Floated on the Shanghai Stock Exchange with a value of $30 million, it does not fund stem cell research directly but instead finances the building of a new hospital that will in turn generate revenue for the research.

The Indian government is also seeking ways of dealing with the paucity of Western venture capital flowing into India. In 1999 it established the Technology Development Board to support and finance promising new ventures. By 2003 this 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 8 domestic VCFs were registered with SEBI during 1996-98, by 2003-04 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. 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 about US $2.6 billion.

However, despite these state initiatives and despite the increase in the inward flow of VC funds, when placed in the context of the global VC industry, China and India still have a considerable distance to progress to overcome foreign investors’ reservations regarding their regulatory infrastructures and the exit opportunities afforded by their domestic markets. In addition, at present VC investment in these two countries tends to avoid the early stage, high risk phase of biotech development where the funds are most clearly needed.

Conclusions – Towards the opportunistic state
In deciding what strategy, if any, to adopt towards the knowledge economy of regenerative medicine, states have to confront a number of uncertainties. Although the political belief that there is a future value for regenerative medicine is global, the precise nature of that future when measured in terms of the path of the science, the
market demand, the cultural response, the commercialisation process and its associated business models is obscure. States must therefore make essentially speculative policy choices in their pursuit of the capacity to benefit from the regenerative medicine future. Depending on their assessment of how the knowledge production process is best supported, states may make policy interventions at any and many points in the several phases of regenerative medicine innovation from the basic science to the therapeutic product.

Given the speculative nature of the enterprise, the ability of states to diagnose the optimum points of intervention and then to formulate and implement the necessary supportive policies is dependent on both their available resources (eg funding, scientific workforce) and their adaptability. The extensive literature on competition states, developmental states and their many variants suggests that this quality is not peculiar to one type of state or another but is instead a product of their governmental traditions, domestic politics, and regional position. Even with their common infrastructures of scientific and industrial development, the competition states of the West differ widely in their response to the opportunities of the emerging knowledge economies. Equally, the developmental states of East Asia vary considerably in the adaptations made to the centralised bureaucracies which drove the earlier phase of their development. Then there are China and India, one an authoritarian single party state and the other a multi-party liberal democracy but both states adapting their government of science and innovation in order to compete effectively in the global knowledge economy.

It is a state’s ability to respond to global opportunities, rather than the coherence of its inward looking policies, that provides the key to its likely position in the regenerative medicine future. Knowledge economies are invariably global and this is reflected in the transnational movement of the scientific and financial capital that fuel them. More so than ever, no state can afford to be a political island. Increasingly it is the production of policies that facilitate an advantageous engagement with global forces that will determine a state’s effectiveness in innovative fields such as regenerative medicine, not the pursuit of protective policies that are bound to be undermined by the growing presence of international economic governance.

As adaptive states, neither China nor India is reticent in their policy support for new health technologies that may generate future value. The analysis of their performance with regard to three key policy components of the knowledge production process (scientific infrastructure, patenting and foreign investment) showed how they are making progress in all three areas with China on the whole moving faster. Both are seeking access to global resources to support their innovation strategies: such as to intellectual capital through scientific collaborations and to pharmaceutical investment through clinical trials facilitation. But in order to benefit from engagement with the global knowledge economy they must own the intellectual capital produced through a judicious use of national and international patenting systems. As yet, neither China nor India has registered the penetration of Western patents achieved by their Asia Pacific rivals Japan and South Korea – though China in particular is accelerating its efforts through WIPO’s Patent Cooperation Treaty. Exposure to the international knowledge economy also has its costs. The majority of Chinese and Indian scientists who access Western knowledge markets through their training in the United States are also captured by the allure of those markets and choose to remain there. An important
policy consideration for both states is how to make sure either that they return or, as in the case of the Non-Resident Indian community for example, they can be encouraged to provide a continuing source of global business expertise.

It is one of the signal lessons of globalisation that the permeability of state boundaries should where possible be turned to a state’s advantage. In their review of the opportunities for biotech companies in India and China, Goodall and colleagues remark on the possibility that China and India are opening up a new model of biotech development: ‘Call it the “modular model”, a kind of decentralised R & D system where different aspects of R & D are distributed globally and conducted almost autonomously in different locations’. 124 Because their innovation needs are different from those of the competition states of the West, China and India will inevitably push the dynamic of globalisation in directions that suit their interests and their particular strategies on the knowledge production process. In the case of regenerative medicine, there are already strong indications that both countries will play to their knowledge production strengths in terms of the availability of research materials (e.g. oocytes), a large and diverse pool of human subjects for clinical experimentation (clinical labour), and inexpensive scientific labour. In return they will want to obtain such advantages as access to the basic science in the field, a division of the patenting benefits, and a sustained supply of venture capital. At the same time we can expect that their strategies on the emerging governance of regenerative medicine through such mechanisms as TRIPS and international ethical guidelines will become considerably more proactive.

Notes


In September 2006 the Roslin Cells Centre 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 Centre 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’ (BBC News 2006).


73 OECD (2006). China will become world’s second highest investor in R & D by end of 2006 finds OECD. [2649_34273_37770522_1_1_1_1,00.html](http://2649_34273_37770522_1_1_1_1,00.html) Accessed 5th June 2007.


The China Development Bank is a ‘policy bank’ owned and operated by the national government.


Figure 1

States and the politics of the knowledge production process: policy components

1. The cultural acceptability of the aims, conduct and materials of the basic science and, in the event of cultural conflict, the regulation required to ensure compatibility with the dominant social values.
2. The training, retention and, if necessary, acquisition of the scientific labour necessary for the required knowledge production to take place.
3. Investment in, and organisation of, the science.
4. Ownership of the new intellectual property: the balance to be struck between the needs of the knowledge market, the freedom of science to access research results, and the cultural status of the new knowledge.
5. Stimulation of the market response through support for the venture capital function, public-private partnerships and pharma engagement.
6. The protection of citizens, consumer confidence and the integrity of the potential product through the regulation of the application and testing of the new knowledge on human subjects.

Figure 2

Cell based products: a hybrid business model

<table>
<thead>
<tr>
<th>Pharmaceuticals</th>
<th>Cell based products</th>
<th>Medical devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>• High up-front investment</td>
<td>• High up-front investment</td>
<td>• Lower up-front investment</td>
</tr>
<tr>
<td>• Long development times</td>
<td>• Medium/long development times</td>
<td>• Short development times</td>
</tr>
<tr>
<td>• High gross margins</td>
<td>• Low gross margins</td>
<td>• Low gross margins</td>
</tr>
<tr>
<td>• Large markets</td>
<td>• Focused markets</td>
<td>• Focused markets</td>
</tr>
</tbody>
</table>
Refining the commercial model
the total 9846 doctorates in this field awarded to foreign students in the US (67).
Figure 5 (81)

**Foreign graduate students in US**

- United States
- United Kingdom
- Australia
- Japan
- South Korea
- India
- China

Figure 6 (90)

**% share global S&T publications, 1988-2003**

- United States
- United Kingdom
- Australia
- Japan
- Singapore
- South Korea
- India
- China
Figure 7  Patent Filings by Residents 1995 to 2004 (96)

Source: WIPO Statistics Database
Figure 8 (99)

US patent applications by origin of first-named inventor, 1990-2003

Figure 9 (113)

R&D performed by foreign affiliates of US MNCs (US$millions)

Missing data: China 2001, India 2000 and 2001
Figure 10 (101) Global biotech venture capital investment