Regenerative medicine in Europe: global competition, international links and innovation governance

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Abstract
Leading EU nations with strong biotech sectors such as the UK and Germany are investing heavily in regenerative medicine (RM), seeking competitive advantage in this emerging sector. However, in the broader biopharmaceutical sector the European Union (EU) is outperformed by the US on all metrics, reflecting longstanding problems: limited venture capital finance, a fragmented patent system, and relatively weak relations between academia and industry. The current global downturn has exacerbated these difficulties. The crisis comes at a time when the European Union is reframing its approach to the governance of innovation and renewing its commitment to the goal of making Europe the leading player in the global knowledge economy. If the EU is to gain a competitive advantage in the RM sector then it must coordinate a complex multi-level governance framework which encompasses the European Union, member states and regional authorities. This article takes stock of Europe's current competitive position within the global bioeconomy, drawing on a variety of metrics in the three intersecting spheres of innovation governance: science, market and society. This data then provides a platform for reviewing the problems of innovation governance faced by the EU and the strategic choices that have to be confronted in the RM sector.

Introduction
The commercial regenerative medicine (RM) sector faces governance challenges that include a lack of proven business models, an immature science base and ethical controversy surrounding hESC research. The recent global downturn has exacerbated these difficulties: private finance has all but disappeared; leading companies are close to bankruptcy, and start-ups are struggling to raise funds. In the UK the government has responded by announcing £21.5M funding for the RM industry and partners [1]. But the present crisis extends considerably beyond RM alone, affecting much of the European biotech sector. A 2009 European Commission (EC) report showed the extent to which the global recession has impacted on access to VC finance in Europe: 75% of biopharma companies in Europe need capital within the next two years if they are to continue their current range of activities [2]. In response, in December 2009 EC staff met with representatives of the European biotech, pharmaceutical and venture capital industries to discuss how the crisis could be addressed.

The meeting came at a time when the European Union is reframing its approach to the governance of innovation [3]. Following the appointment of its first Commissioner for Innovation in November 2009 to coordinate innovation policy across the 12 DGs of the Commission, EC President Barroso will present the first EC Research and Innovation Plan to the Autumn 2010 summit of EU leaders [101]. The concern with innovation governance, and President Barroso's insistence that it be addressed explicitly, reflects the longstanding political aspiration of the Lisbon Strategy for the EU to become the "the most competitive knowledge-based economy in the world." [4]. At the heart of this ambition is the bioeconomy. Here the EU Life Sciences and Biotechnology Strategy (2002) framed the issue in terms of global competitiveness, warning that if Europe did not take governance action then it would, by default, weaken its competitive position, its research base and its capacity to drive policy on the complex social issues accompanying

some bioscience applications [5]. Rather depressingly, five years later a mid-term review of this strategy highlighted not only problems with access to private capital, but also two further difficulties for European biopharma: the EU's fragmented patent system, and relatively weak relations between academia and industry [6].

Such weaknesses are comparative disadvantages in an increasingly global bioeconomy characterised by an international trade in scientific labour and research materials, a global market for clinical research, and foreign direct investment in production and R&D facilities in Newly Industrialising Economies (NIEs). Success in the global bioeconomy requires astute innovation governance by both states and supra-national authorities in the domains of science, market and society: a viable R&D platform and organisation; market conditions favourable to commercialization; and regulatory regimes which address both risk and safety issues and the sensitivities of cultural values in order to maintain public (and consumer) trust in the field [7].

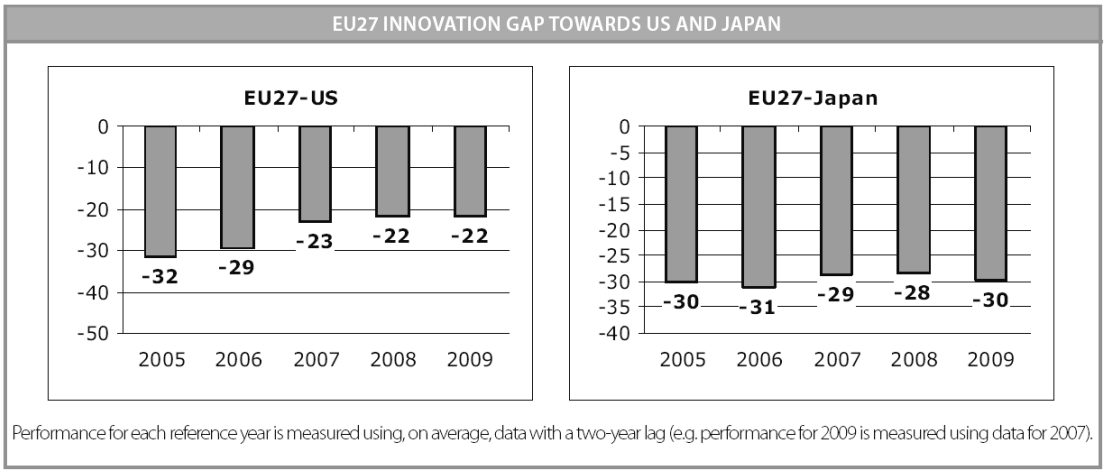
What are the prospects that the new Commissioner for Innovation will be able to implement a coordinated approach to both building effective international links amongst Member States (MS) and appropriate forms of innovation governance across the EU? The Framework Programmes for research funding provide a powerful lever for enhancing network collaborations between scientists (and industry) in different MS, but in other respects it may be questioned whether the Commission is the appropriate focus for governance solutions to the problems facing RM companies and other parts of the biopharma sector. In seeking to promote MS advantage in an increasingly global knowledge economy, the EU is constrained by the fact that it is a partial polity. Whilst more than simply a trade confederation, its powers are considerably less than those of a nation-state, and many of the traditional policy levers used to foster innovation, such as tax incentives for R&D, lie within the jurisdiction of Member States. Innovation policy has necessarily to work through a complex multi-level governance framework encompassing the European Union, the MS, and regional authorities within the MS. Indeed, the current trend towards regional devolution means that governance within the EU is becoming more complex, as exemplified by Scotland Act and the Governance of Wales Act in 1998. 74 regions in the EU have direct responsibility for the transposition of all, or part of, some EU directives and these regions have direct influence on EU policy through the Committee of the Regions. Energizing this complex multilevel framework is a necessary condition of European success in the RM sector.

Given this context, this article takes stock of Europe's current competitive position within the global bioeconomy and the international networks being developed by European scientists, drawing on a variety of metrics in the three intersecting spheres of innovation governance: science, market and society. This data then provides a platform for reviewing the problems of innovation governance faced by the new Commissioner and the strategic choices that have to be confronted in the RM sector.

A measure of the problem

Europe's competitive disadvantage in the global knowledge economy is made clear by data from the European Innovation Scoreboard which measures performance on metrics

such as R&D expenditure, patenting and the education level of the workforce. The overall innovation scores of both the United States and Japan consistently outperform the EU by a considerable margin, although since 2005 there has been a gradual closing of the gap, particularly with regard to the US (see figure 1) [8].
Figure 1: EU27 innovation gap towards US and Japan



Source: [8]

Europe thus faces twin challenges, from the West and the East, reflecting a broader dynamic as countries outside Europe and North America, particularly the NIEs of the Asia Pacific (AP) region, such as South Korea, Singapore and China, seek to capture an increasing share of the knowledge economy. This trend is illustrated by figures 2-4 which show that on three key metrics - spending on R&D, the number of researchers and patent applications – the EU and the US have a diminishing share of the total activity [9].

Figure 2: Global shares of researchers FTE

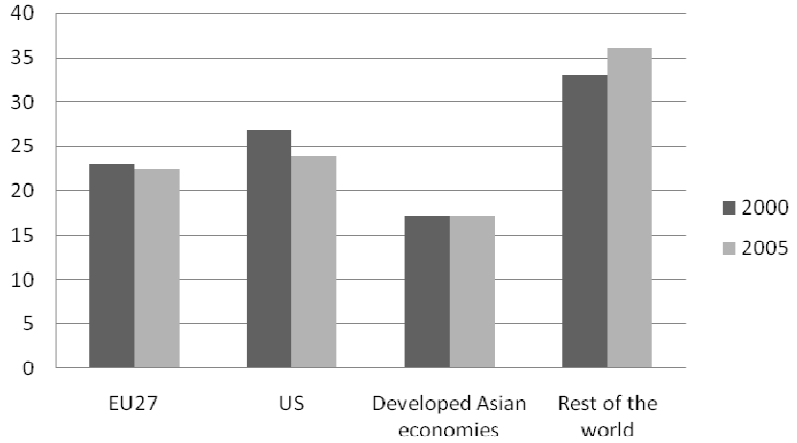


Figure 3: Global shares of gross domestic expenditure on R&D

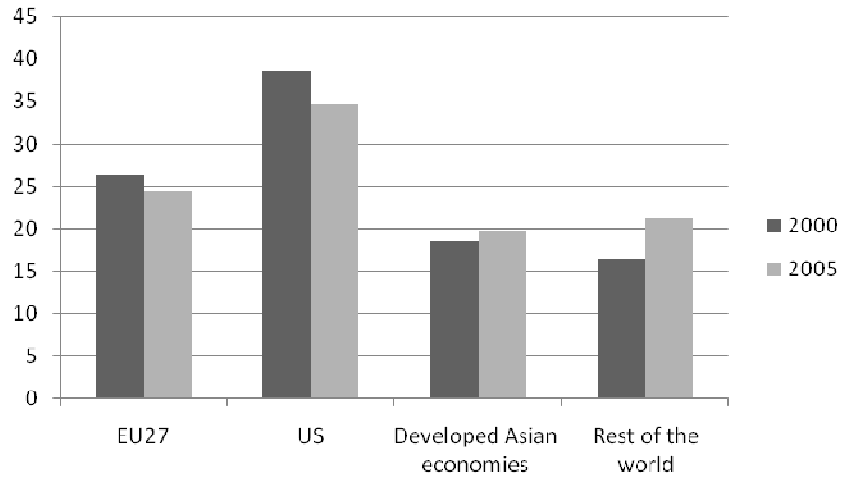
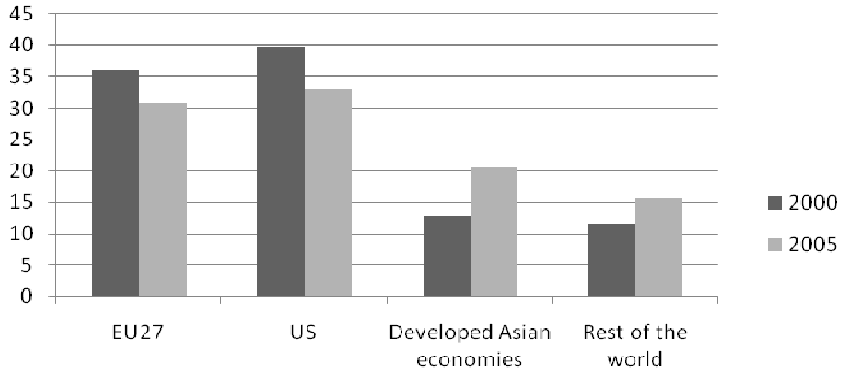


Figure 4: Global shares of patent applications



Source for figures 2-4: [9]
(Developed Asian economies: Japan, Korea, Singapore, Taiwan)

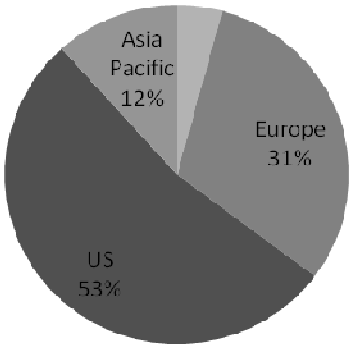
In general, then, it can be said that the trends in the relative innovation capacity of the EU are at odds with its global ambitions regarding the future knowledge economy. To what extent is this true of the bioeconomy and RM in particular and what are the governance issues that need to be addressed by the EU in the domains of science, the market and society?

Governing Science
Infrastructure support for the scientific research base can take a number of forms. Here we examine data relating to levels of investment in R&D, support for the development of clusters and the creation of a scientific labour force.

Public funding for R&D
Data compiled by the Global Forum for Health Research (GFHR) shows that US public expenditure on health R&D in 2005 was $35 billion, 53% of the total invested by high-income countries. Europe spent 20.4 billion or 31% of the total, and named Asia Pacific

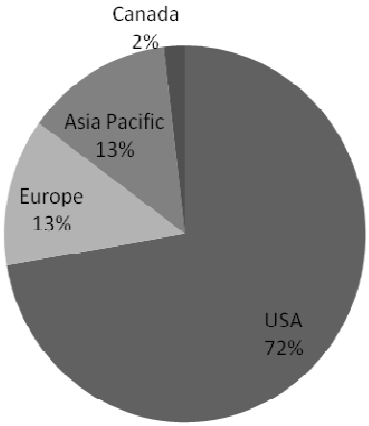
countries (Australia, Japan, Korea, New Zealand) account for 12% (Figure 5) [10]. The US dominance is no surprise, given that the NIH budget doubled between 1999 and 2003 [11]. However, five European countries had similar increases in health R&D between 1998 and 2005 [10]. Furthermore, the US has an even stronger lead in public investment on biotechnology R&D. The 2007 BioPolis report provided comparative data for 2005. Of a total public R&D investment of $32,077M for the countries and regions cited, the US spent 72% of this sum whilst Europe and the AP countries were responsible for just 13% each (Figure 6) [12].

Figure 5 Global shares of public funding of health R&D in high-income countries 2005



Source [10]
(Asia Pacific: Australia, Japan, Korea, New Zealand)

Figure 6 Global shares of public biotech R&D funding in 2005 in USA, Canada, Asia Pacific* and Europe



Source [12]
***Asia Pacific = China, Japan, Korea, Singapore**

Explaining this gap is difficult (not least because the biotech figure includes industrial and agricultural biotech) but the smaller gap between the EU and the US in health R&D would suggest that it is not simply a matter of capacity. Whatever the size of their budgets, research funders face difficult decisions about how to invest. The historic increase in the NIH budget has presumably afforded it the luxury of investing heavily in new areas like biotechnology whilst maintaining existing research programmes, whereas other states may face more difficult decisions about how to balance this with continued support for existing programmes of research. Such hard choices may not be faced by many of the NIEs in Asia Pacific who do not have to maintain Europe's level of embedded scientific infrastructure and historic commitments.

This may be a governance field where the EC has greater scope for action than its constituent member states, as most EC R&D expenditure is not tied up in maintaining existing capacity. At EU level further funding has been provided through the FP6 programme which ran from 2002 to 2007. According to the European Commission there were 111 FP6 programmes which involved components or partners using stem cells, and the funding for these programmes totaled 532M Euros [102] (appendix one, table one). Analysis of this data reveals the rich pattern of networks and alliances which these projects fostered - they involved 1,341 partners from 35 different countries. The most common partners were Germany, UK, France and Italy. The second group of countries were Netherlands, Spain, Switzerland, and Sweden (see appendix one, figure one). In terms of leadership of projects, Germany, France, UK, Netherlands and Belgium were the leading countries (see appendix one, figure two). In projects led by these member states the most frequent partner countries showed a high degree of overlap: Germany, France and UK were amongst the top five partner countries for this group of member states, Italy was in the top five for four of the countries and Sweden and the Netherlands were each in the top five for two of the member states (see appendix one, figures three to five). Although the vast majority of partners were from EU countries there was a small amount of partnering with non-EU states including Argentina, Australia, Brazil, Canada, China, Japan, Turkey and the USA. In addition to these EU-funded networks, individual member states are seeking to develop bilateral relationships with partners in a range of countries. For instance, the UK has held workshops with scientists in Germany and in Spain to further scientific cooperation, Germany has recently sent a delegation to India, Sweden has sent a delegation to the Bio conference in the US and the Karolinska Institute has recently established a collaborative agreement with STAR in Singapore. These developments indicate that EU scientists are beginning to look beyond Europe for scientific partners, but the increased funding available under FP7 makes it likely that the primary scientific alliances for EU scientists will continue to be within the EU.

Further funding is now being made available under the EU's FP7 programme. 50.52 billion Euros has been allocated for scientific research in FP7 (nearly double that allocated in FP6). However, EU funding for hESC has only been secured after protracted political negotiations. Five states member signed a 2005 'Declaration of Ethics' which sought to ban EU funding of hESC research: Austria, Germany, Italy, Malta, Poland, and Slovakia. A compromise was reached which renewed the arrangement made under FP6: funding is permitted for projects in member states where hESC is legally recognised.

However, the compromise also required a commitment by ministers that no funding will be given for work which will involve the destruction of human embryos. There is no specific data as to how much funding might be made available to RM researchers under FP7, but so far a total 187M Euros has been committed to 101 research projects including 49M Euros on 16 hESC projects [13].

However, when it comes to public R&D investments the EC's ability to make an impact on Europe's competitive standing is limited because its budget is just 5% of total EU public R&D expenditure [14]. Furthermore, the EC faces other types of governance challenges when allocating expenditure, in particular the need to ensure a politically acceptable division of spending across MS. The potential for this imperative to lead to policy failure has been highlighted in relation to the development of research clusters.

A cluster of problems

We have already noted the policy concerns about Europe's relatively poor industry-academia relations, a weakness which is considered central to what has been termed "the European paradox" – an excellent science base but limited capacity to capture the potential socio-economic benefits of its scientific discoveries [15]. Clusters facilitate technology transfer by bringing together scientists, entrepreneurs and investors. They are seen as an important tool in innovation governance, and one which has been crucial to the successful development of biotechnology [16]. National and regional governments in Europe have sought to foster the development of clusters by establishing incubators and science parks, providing R&D funding and other initiatives. However, as a form of innovation governance cluster policy is seen as failing in Europe. On the verge of a new announcement on cluster policy, the Commission criticised the limitations of current performance:

> Europe does not lack clusters, but persistent market fragmentation, weak industry-research linkages and insufficient cooperation within the EU mean that clusters in the EU do not always have the necessary critical mass and innovation capacity to sustainably face global competition and to be world-class [17].

The Science/Business Innovation Board, an independent expert group, has gone further arguing that a fundamental shift in policy is required:

> ... Europe's approach is small, timid and diffuse. The EU counts some 2,000 clusters, 70 different national cluster policies, and hundreds of regional programmes. We urge the EU to designate a few – and we mean just a few – existing clusters to benefit from a new legal status as special innovation zones. Europe's politicians cannot afford any longer the luxury of playing big spender to all regions great and small [103].

However, such clear priority setting on the basis of economic rationality collides with the politics that determine policy in the EU. So instead, the Commission is seeking to increase critical mass by promoting trans-national cluster collaboration, a governance choice which reflects the fact that much of the EC funding for cluster development comes

from the Cohesion Policy Fund, whose primary goal is support for poorer member states [16].

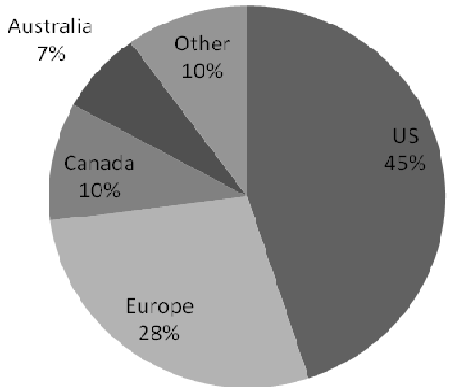
Human capital: building and retaining the skills base
A key measure of innovation capacity is the proportion of the population with science and engineering degrees and the proportion of the population employed in R&D. A recent UK report on the international mobility of pharmaceutical research indicated that one of the key factors influencing location of R&D programmes is access to "world leading scientists and ... an adequate stock of well-trained scientists to work on the programme." [18]. In this respect the US lags behind Europe on some measures. The proportion of science and engineering degrees relative to all new degrees is a measure on which the US is outperformed by 20 European countries (and five countries from the Asia Pacific region) [19]. The EU has produced more tertiary graduates and doctoral graduates than the US and Japan since 2000 and graduate growth rates are also higher. In 2005 the EU produced 100,000 doctoral graduates, nearly twice that of the US and nearly seven times that of Japan [9].

However, training skilled researchers is not enough, in a global labour market one must also retain them. In the US over 40% of doctorate holders and 25% of undergraduate degree holders in the S&E professions are foreign-born nationals, and up to 50% of postdocs are thought to be foreign-born [104]. The US relies heavily on a steady flow of scientific expertise from Europe to the US, a source of concern for EU policymakers:

In 2004, of the nearly 400,000 foreign researchers in the US an estimated 100,000 were born in the EU. This is a significant proportion of the total EU researchers' population of 1.3 million and these are also likely to be top performers in their fields [20].

This outward flow is to some extent balanced by migration to Europe. OECD data on the study destinations of foreign students shows that 22% travel to the US but that a greater proportion are choosing European countries (12% to the UK, 10% to Germany and 9% to France). The US share of foreign students dropped by nearly 5% between 2000 and 2005 [20 OECD 2008]. Furthermore there is significant migration to Europe by professional and technical migrants (see figure 7 [21]).

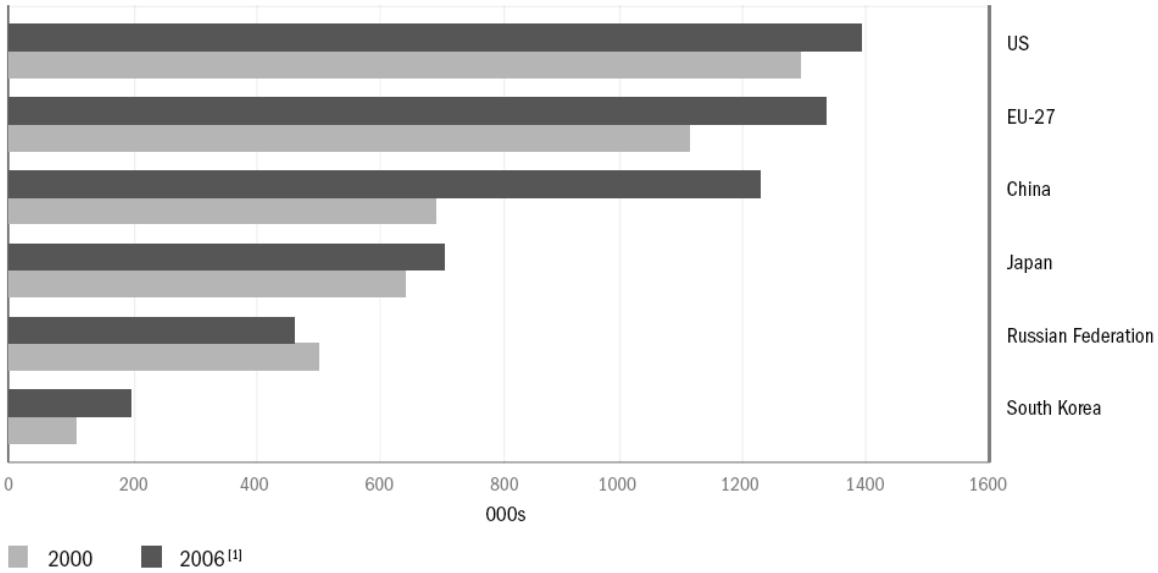
Figure 7 Share of employed professional and technical migrants to OECD countries, by country of residence, 2000 or 2001



Source [21]

One measure of the net effect of these flows of skilled labour is the number of R&D personnel (Figure 8). Whilst the US has the greatest number of R&D personnel, this lead is declining. Between 2000 and 2006 the number of researchers was growing twice as fast in the EU as it was in the US and Japan, although it was China and South Korea who exhibited the most dramatic increase, with annual growth rates of 9.9% and 10.8% respectively [9].

Figure 8 Number of researchers (FTE thousands) by world region, 2000 and 2006



Source [9]

The flow of scientific expertise from Europe to the US provides an example of the clear difference between creating value and capturing value which may also be applied to other aspects of the innovation process. Given the major difference in research funding between the two regions, it seems likely that this general trend will be difficult to reverse. However, the fact that, despite their relatively small populations, Canada and Australia have 17% of the total share of employed professional and technical migrants in OECD countries indicates the impact that government migration policies can have (Figure 7).

In terms of the governance of migration, states employ a variety of options ranging from a general openness to a selective recruitment of skilled personnel. The EU is promoting the latter approach - its Blue Card scheme set out in the Directive on the Entry and Residence for High Skilled Workers which is targets skilled migrants by offering them a fast-track entry and a range of socio-economic rights. This scheme is due to come into effect in June 2011 and represents part of a broader agenda on harmonisation of EU policy on legal migration. However, despite a rapid increase in EU competency in the area of border management, including moves towards harmonisation of visa and asylum policy, immigration policy is a politically sensitive subject and remains largely in the hands of member states, a position reinforced by the 2008 European Pact on Immigration and Asylum [22]. It is little surprise then that a number of countries are expected to opt out of the Blue Card scheme, including leading biotech countries such as Germany [105].

How will the global flows of scientific expertise affect the field of regenerative medicine? Early career stem cell science researchers are reported to be seeking out opportunities in Europe, usually citing as reasons a better variety of choice and more potential for longer term career prospects in the EU than in the US (except California) [106]. However, there is no hard data to support this view and there have been few examples of leading scientists moving from the US to Europe. Given the huge difference in research funding between the two regions it seems likely that the general trend of a flow of scientific expertise from Europe to the US will not be easy to reverse.

Governing the market

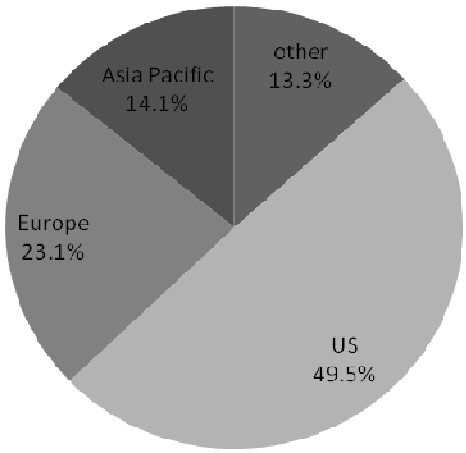
As we stated in the introduction, the current financial crisis has raised serious concerns about the adequacy of current governance mechanisms for supporting the EU's biopharma sector. Whilst much of the concern is currently focused on supply side issues relating to the availability of investment capital, there are also a number of demand-side issues.

Industrial strength

Industrial R&D is a further area where Europe lags behind its main global rival. Just under half of global share of industry health R&D expenditure is by US firms (Figure 9), Europe's share is just under a quarter (although well ahead of the Asia Pacific region). As with public R&D investment, the US has an even more commanding lead in the biotech sector (Figure 10). Figures published by Ernst and Young give a total global R&D expenditure of $31,806M; 81% of this sum was spent by US companies and just 14% by European firms. However, here there is a clear European advantage over the AP region,

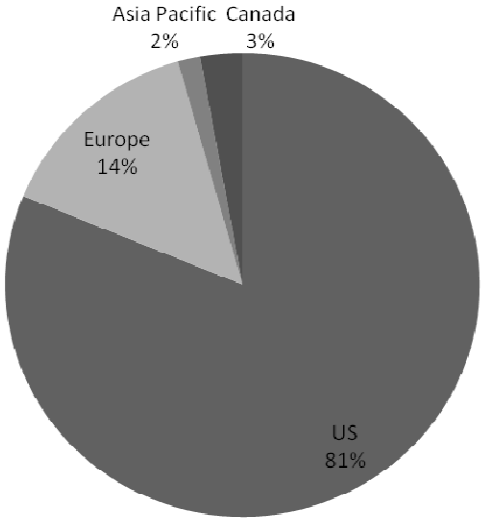
which accounted for just 2% of the total figure [23]. A similar pattern is seen in biotech revenues: the US has 77%, Europe 15% and Asia Pacific just 5%

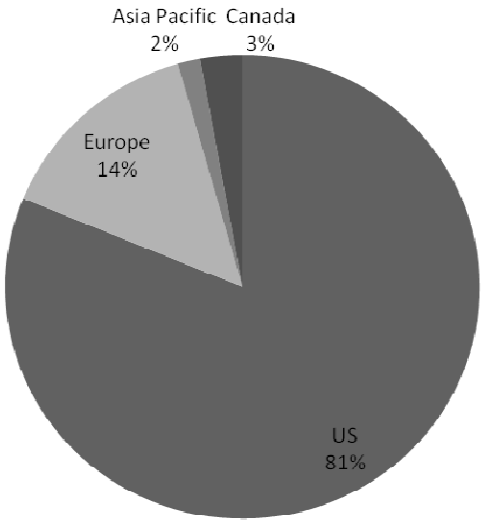
Figure 9 Global share of industry health R&D expenditure 2005 (US$ M)



Source: adapted from [10]

Figure 10: Global biotech industry R&D expenses in US$M





A similar pattern is seen in biotech revenues: the US has 77%, Europe 15% and Asia Pacific just 5%. Furthermore a 2007 study found that only 25% of biopharmaceuticals were developed by European companies (10% of these by Swiss companies) compared with 54% by US companies and that US companies had 75% more products in the pipeline than EU companies [12].

These figures set the context for consideration of the RM industry as a distinct part of the health biotech sector. It is unsurprising to discover that Martin et al's recent survey reveals a clear US lead at least in terms of number of firms and clinical products in development. The US has 107 primary and secondary tissue engineering firms and 78 products in development, Europe has 37 firms and 42 products in development and Asia Pacific has 17 firms and ten products in the pipeline. A further concern is that the US dominates the newer areas of stem cells and first generation allogeneic products, whereas Europe is specialising in autologous therapies which have thus far proved a commercial disappointment. [24]

VC investment

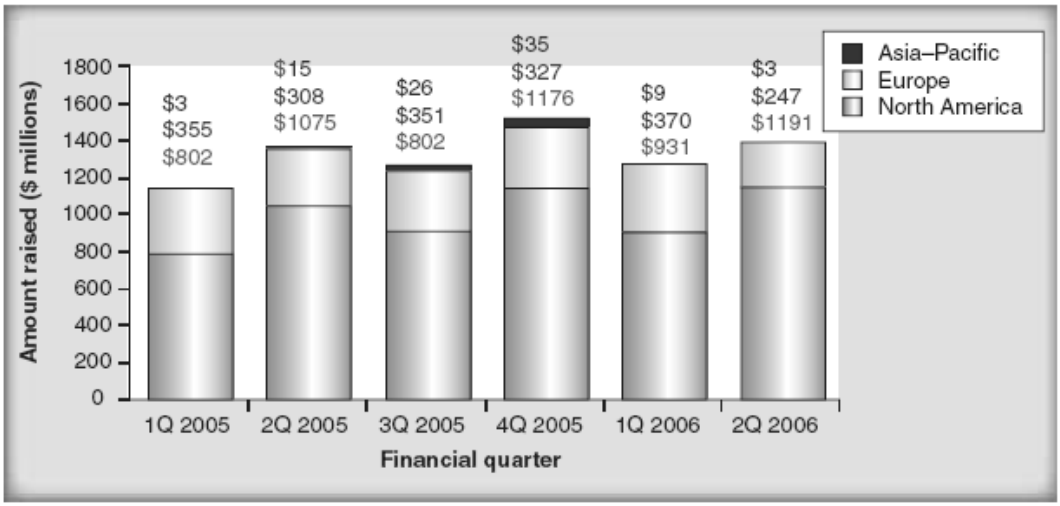
The US advantage in the RM market and health biotech is reinforced by its superior access to a key component of the innovation process: venture capital (VC) finance. In general terms, EU VC investment is one-third of that in the US [25]. Ang reports other US advantages:

US biotech companies tend to have larger amount of investment received per VC firm, larger number of investing VC firms and greater biotech investment experience of the investing VC firms [26].

As noted in the introduction, Europe's relatively weak VC market has been exacerbated by the current recession producing a downward trend in both VC financing in general and VC support for biotech in particular. A recent UK policy report states that: "The flow of finance to emerging biotech companies from institutional investors has virtually ceased." [27]. However, Europe has a strong advantage over Asia-Pacific in terms of access to VC

finance, as indicated by the figures for funding in 2005-6 (see Figure 11, [107]). At least in 2004 the Australian biotech sector still lacked a "critical mass of downstream venture capital or other financial support to fund continued growth." [28] China has failed to attract substantial VC investment, and India currently lacks a stock market with sufficient volume and liquidity to attract substantial international investment in support of early-stage and high-risk stem cell ventures [29].

Figure 11 Global biotech venture capital investment by region



Source: [107]

If VC finance does not return to previous levels in Europe the domestic biotech sector may lose one of its sources of advantage over Asia Pacific nations, many of whom are compensating for lack of private capital through state investment in industry. Likewise, European biotech companies have long relied on state grant funding as a preferred secondary source of funding after VC finance although it is doubtful whether the amounts currently available can compete with some of the AP states [30].

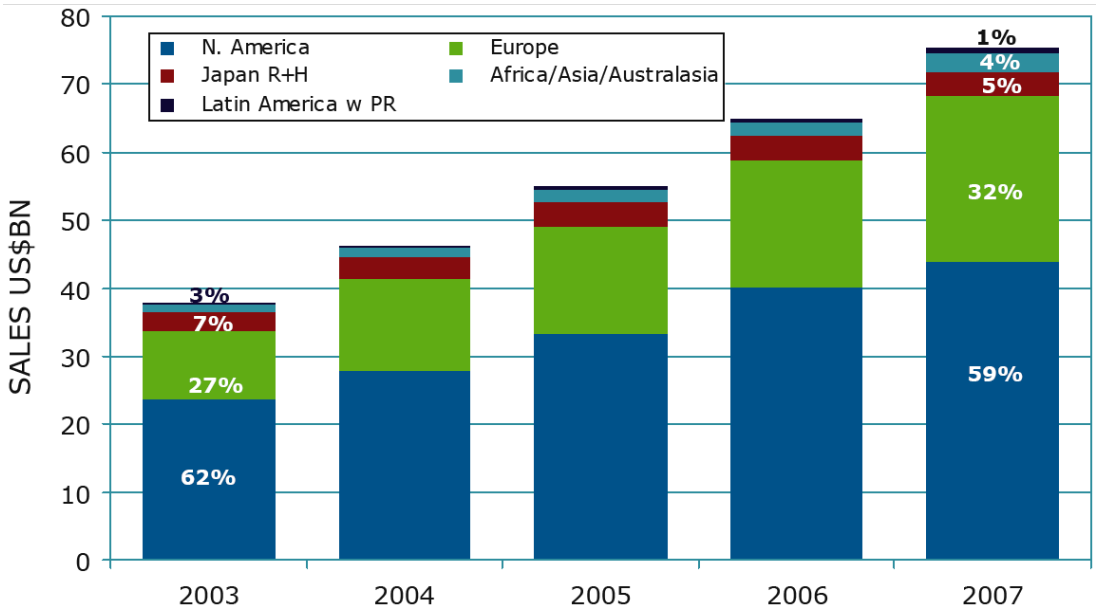
Governance initiatives at EU level to deal with the VC issue include the European Investment Bank (EIB)'s Innovation 2010 Initiative, the EIB's Risk-Sharing Finance Facility (RSFF) which combines funding from EIB and the EC, and the European Investment Fund's venture capital instruments which are focused primarily on the high-tech sector [2]. However, some of this funding is only available to firms which are already profitable, ruling out many of the biopharma companies which urgently require assistance today. For instance, thus far only a small number of biopharma companies have gained funding from the RSFF [2]. An alternative source of potential support comes from the FP7 programme where the proportion of project funding which can go to industry has been raised from 50% in FP6 to 75%. Industry can now lead projects rather

than simply being a support partner and has greater control over IP arising from the research [25].

Demand-side issues in the RM sector – market size, openness to innovation and price sensitivity

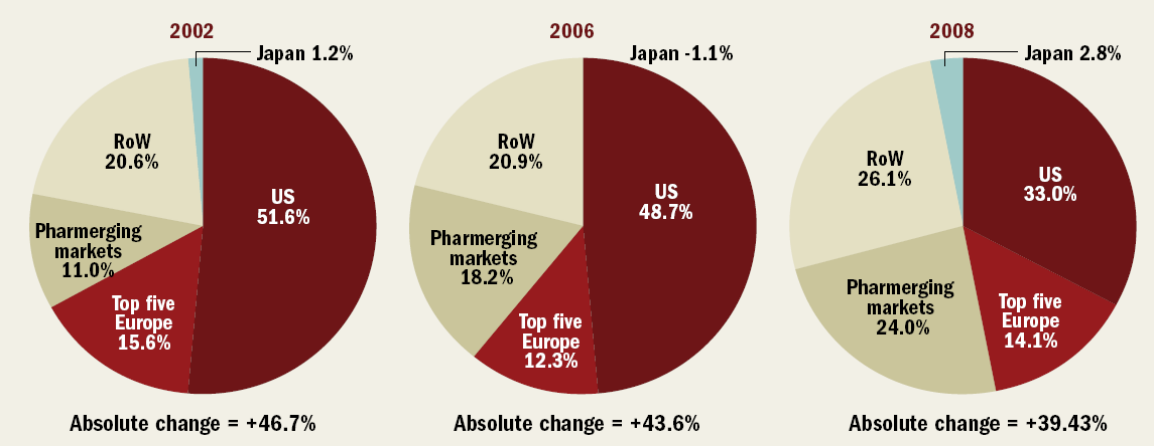
Although governance support for the market usually focuses on the supply side of the equation, the demand side may be equally critical for the creation of innovation capacity in a particular area of the life sciences. Indeed, the European Commission has cited demand side issues as a major factor in the failure of European pharma and biotech companies to keep up with the US [31]. The US is the single largest market for healthcare biotech products with sales nearly twice that of Europe, although between 2003 and 2007 Europe's share increased by 5% and the US share declined by 3%. (see figure 12) [108]. A recent survey of UK SMEs in the medical technology industries found that "More than half of the companies (14/22) were or were becoming US centric and notably the success of 5 mature companies rested largely on the success of their US operation." [32]. However, this is an area where the growth of NIEs can clearly be seen. Whilst European and Japanese markets have remained stable, there has been a dramatic decline in the US market share relative to the growth of what Edery terms the pharmerging markets (China, India, Brazil, South Korea, Mexico, Turkey and Russia) and the rest of the world (see Figure 13, [109]).

Figure 12: Health biotech regional sales



Source: [108]

Figure 13: Regional shares of global pharmaceutical market



Source: [109]

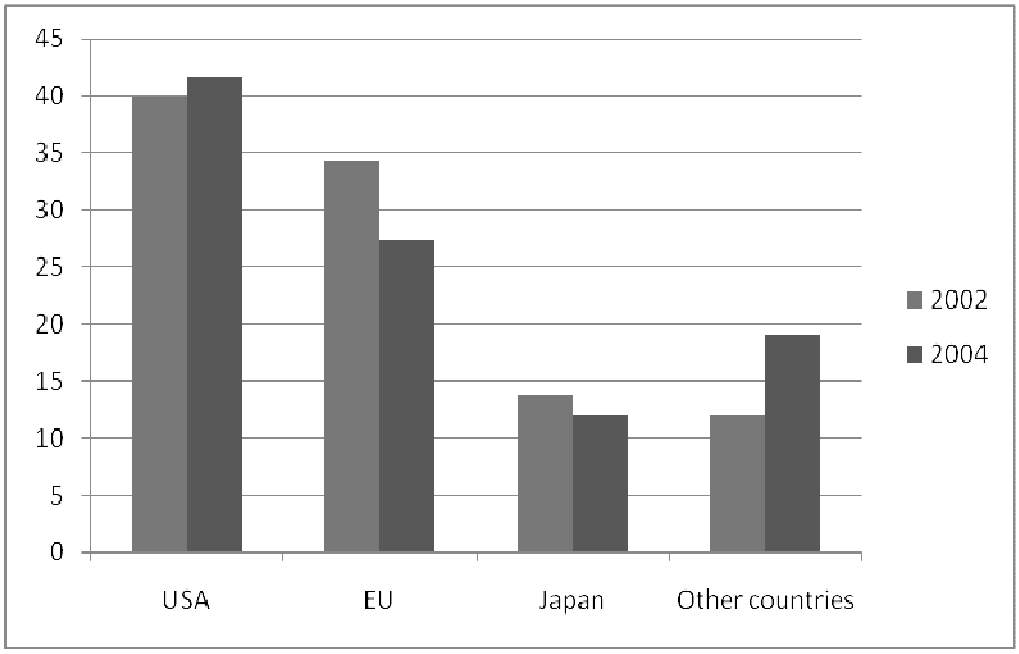
Size is not the only attraction of the US market for innovative health biotech. On average, manufacturers gain 50% higher prices for equivalent products marketed in the US compared with Europe and there is a more rapid adoption of new pharmaceuticals [33].Whether the price differential applies to the same degree with biotech drugs is unclear. Calfee and Dupree suggest that the gap is closer for first-generation biotech products such as human growth hormone and interferons and that for more recent targeted therapeutics such as Herceptin and Gleevec the US is paying less than Europe [34]. Similarly, Danzon and Furukawa find that there is less of a price gap for biologics than for other drugs but that nevertheless the US had the highest per capita spending on this class of drugs, spending more than double most other countries as a result of "greater availability of new molecules and greater use of more-costly products and formulations" [35].

For the EC the governance problem is that its capacity for intervention on demand-side issues is very limited. Differing approaches to reimbursement and pricing between and even within Member States preclude the development of a single market for healthcare products.

Patenting activity

The last indicator of innovation strength we will discuss here is patenting. Figure 14 shows that the US has established a dominant position as the country most active in biotech patenting. However, the EU as a whole enjoys a position close to that of the US and far ahead of its next nearest rival Japan. Between 1997 and 2002 the general trend was towards convergence in performance between these three players [36]. However, the figures for 2004 and 2006 indicate a greater share for other nations and a diminished share for Japan and Europe whilst the US share has increased slightly (see figures 14) [37].

Figure 14 Global share of biotechnology patents filed at the EPO, 2002 and 2004



Source: [36,37]

However, in the field of RM the US has a more dominant position. The USA had 51% of all priority filings in stem cell research for the period between 2001 and 2005 (Marks and Clerk, 2006) [38], and a 2007 study confirms the trend [39]. There are a variety of issues that affect stem cell patenting in the EU. These include differences between member states on patenting law, continuing ethical disagreement over the issuing of stem cell patents and Community opposition to the patenting of products of human origin. The European Patent Office has been wrestling for some time with the European Biotechnology Directive of 1998 which states that human embryos should not be used for industrial or commercial purposes [40].

However, many of the obstacles faced by biotech SMEs wanting to patent their inventions in Europe do not relate to ethical controversy. The European patent system is heavily criticized by many stakeholders:

for its cost and complexity ... its high level of fragmentation and its translation requirements [which] make it the most expensive, most complex patent system in the world. Indeed, despite the explicit 1978 objective of creating a Community Patent (one patent valid for all member states), the European Patent system is still fragmented: once a patent is granted by the European Patent Office (EPO) it must be enforced (i.e., translated, validated and renewed each year) in each desired national jurisdiction [41].

The ability of patenting governance in Europe to adapt to construct a solution to these ethical and operational problems is constrained by the fact that it is composed of not one system of multi-level governance but two quite separate ones with their own distinct legal identities and administrative systems: the European Patent Organisation (EPO) and the

arrangements contained within the EU's 1998 Directive on the legal protection of biotechnological inventions (Directive 98/44/EC – commonly known as the Biotech Directive). Established in 1977 on the basis of the European Patent Convention (EPC) signed in Munich in 1973, the EPO is an intergovernmental organisation currently with 35 member states [109]. The Directive, meanwhile, applies to the 27 member states of the European Union, all of whom are also signatories to the EPC, and acts within the legal system of the EU with the European Court of Justice (ECJ) as the final arbiter.

The EU 2020 vision has identified the creation of a single EU patent and a specialised patent court as part of the innovation agenda but these are goals which have existed for a decade. In December 2009 the EU member states agreed on some of the general principles of the new European patent regulation, and they must now await a legal opinion from the European Court of Justice on their proposals. However, the contentious issue of translating patents into the languages of all member states has yet to be resolved. Thus it remains unclear how quickly progress can be made on these goals [42].

3. Governing society

According to a 2005 Eurobarometer Survey there is significant support for stem cell research across Europe as a whole, but an effective system of governance is seen as an important mechanism for maintaining public trust.

> Providing it is tightly regulated there is considerable support for embryonic stem cell research across Europe …. Europeans lean towards [a] utilitarian view; the possible benefits for health and the alleviation of diseases tend to outweigh possible moral objections [43].

Public support for biotechnology requires modes of regulatory governance that can address issues of risk and safety as well as cultural sensitivities that may be stimulated by the new science. In the case of regenerative medicine, states face policy choices about the appropriate level and form of such regulation at every stage of the innovation process, from bench to bedside. As we describe below, regenerative medicine is a field where there is significant regulatory divergence within the EU both at the beginning of the innovation process in the area of basic scientific research (at least in the case of hESC) and at the end of the innovation process at the stage of adoption.

Regulating basic science

With RM now focused on stem cell applications, the ethics of human embryonic stem cell (HESC) research has become an important governance issue which may, or may not, be circumvented by the arrival of induced pluripotent stem (IPS) cells. The policy options which states face can be placed on a continuum extending from "restrictive" (of scientific freedom through protection of the embryo) to "liberal" (facilitative of science, industry, and certain social interests):

1. Prohibition of procurement of HESCs from human embryos
2. Prohibition of procurement but allowing importation
3. Allowing procurement of HESCs from supernumerary human embryos

4. Prohibition of creation of human embryos for research purposes including cloning
5. Allowing creation of human embryos for research purposes including cloning

A 2007 global survey of national hESC policy gathered data on thirty-nine countries, and found that only seven have prohibited the procurement of HESCs from human embryos (option1) [44]. They are all EU member states. By contrast none of the AP countries have chosen the most restrictive policy options, and more than half have chosen the most liberal policy: permitting the creation of human embryos for research purposes, including cloning (option 5), whereas only two of the 29 European countries have chosen this option. The ethical controversy affecting RM funding in Europe is mirrored in the US where there has been a similar divergence in approaches at state level and constraints on federal funding. This may give an advantage to the Asia Pacific region which has experienced no comparable level of opposition.

Much of the European opposition can be attributed to religious convictions, particularly in Catholic states but there are also secular sources of opposition to research on human embryonic stem cells, for instance the opposition of the Greens and Socialists in Germany [45]. There is no clear correlation between state support for biotechnology and the positions taken. Of the seven leading investors in biotech in the EU [12], three have adopted restrictive policies: Austria, Germany and Ireland, but four have adopted a more liberal approach: Belgium, Finland, France and Ireland.

There appears to be a distinct trend for countries to move in a more liberal direction including European countries such as Denmark, France, Germany, and the UK. Italy is the only country moving in a less liberal direction. Even in the seven states where Policy Option 1 prohibits the procurement of HESCs from human embryos, there are indications that this position may not be sustainable in the medium to longer term. Two of these states have adopted a political compromise by nevertheless allowing the importation of HESC lines (option 2), and even Catholic Spain has adopted a more permissive policy.

At the EU level of governance, this diversity produced lengthy and acrimonious conflict between MS over the conditions that should govern the funding of hESC research under the FP6 and FP7 Programmes. Although a compromise was eventually reached that permits the funding of hESC stem cell line research but not the creation of such lines, given the entrenched differences of MS on the moral status of the human embryo, it remains very much a live governance issue.

Regulating RM products

The statutory regulation of healthcare products is characterised by both global convergence and competition. The trend towards convergence is facilitated by the work of transnational policy fora such as the International Committee on Harmonisation (ICH) for pharmaceuticals, and the Global Harmonisation Task Force (GHTF) for medical devices. However, some experts argue that the regulation of pharmaceuticals has been characterised as much by inter-state competition as by convergence, with EU member states touting for regulatory business by providing faster approval times [46].

In the last decade the field of RM has seen worldwide trend towards the establishment of risk-based systems of regulation of cell therapy products in the USA, Canada, Australia and Europe with different regulatory pathways for different types of products [110]. In the European Union RM products are regulated under Regulation 1394/2007 on Advanced Therapy Medicinal Products. The impetus for an EU-wide approach to the regulation of RM came from industry concerns that wide variations in regulation across member states had created a "heterogeneous and segmented market in Europe." [47]. Prior to the 2007 regulation RM products were regulated by different member states as either devices, drugs, biologics or a combination of them, or dealt with specifically as cell therapy products. The new regulation brings them under the framework of pharmaceutical regulation with authority for product approval vested in the European Medicines Agency (EMA). It is too early to tell whether the common EU framework for market approval of RM products will provide a competitive advantage for the European market. However, it seems likely that the single market regulation offers a distinct advance on the heterogeneous patchwork of regulation that existed across member states prior to the introduction of the new regulation. Furthermore, the success in creating a unified governance approach for product approval reinforces the view of the European Union as a 'regulatory' state which has particular strengths in the production of regulatory policy [48]. This in turn reinforces the view that comparative advantage in the bioeconomy will often come from the adaptation of existing governance structures rather the *de novo* creation of completely new systems and processes.

Regulating reimbursement

In the face of unlimited demand, governance arrangements to maximise the social benefit of limited health care resources has become a central plank of state health policy in the last twenty years. In this respect, the governance of society has significant implications for the governance of the market. Healthcare systems have placed increasing emphasis on the systematic evaluation of clinical effectiveness and cost-effectiveness with the result that Health Technology Assessment (HTA) has become the 'fourth hurdle' in the innovation process. Companies developing healthcare products with reimbursement and coverage decisions are frequently dependent on favourable HTA evaluations because these determine the national healthcare market for their product. In this context, Rowley and Martin report that the UK RM industry views NICE evaluations as "a significant issue and companies consider the outcomes of these evaluations to be quite unpredictable." [49]. As we saw earlier, this is a policy field where it is difficult for EU member states to move towards a harmonized system of governance because the principle of subsidiarity respects the operation of national health care systems.

Conclusion: the future of regenerative medicine in the EU

The UK's Office of Life Sciences recent report *Life sciences 2010: Delivering the blueprint* includes all of the above areas of governance in its discussion of how the government can best support the UK's future position in the bioeconomy [1]. It does not mention the EU. The message for the new EC Commissioner of Innovation is clear: for MS, national interest is the primary driver in the formation of modes of innovation governance.

This is not to deny that European RM science has strong indicators pointing towards a potentially competitive position within the global RM bioeconomy. There is a solid research base, a high level of scientific output and the introduction of rigorous standards for cell lines and laboratory protocols should facilitate international collaboration within the EU. FP6 funding has allowed rich patterns of scientific alliances to develop between scientists in different member states and this trend is continuing under FP7. However, the global picture in the wider biotech sector suggests that the US will rapidly establish an unchallengeable position as the dominant player. It has three key advantages – far higher levels of R&D funding, greater access to VC finance for biotech start-ups, and the single largest market for health technologies.

If Europe is to mount a serious challenge to this dominance its approach to innovation governance has to change. A recent EC report painted a bleak picture of how the EU's multi-level system of governance has severely restricted the implementation of the Lisbon agenda:

> The coordination of policies to support innovation at regional, national and EU level has to improve significantly and a better governance system is needed, based on the principles of subsidiarity, but better exploiting the added value of setting common objectives, agreeing on common actions and sharing best practices among Member States [3].

But it is not merely a question of better internal coordination. External governance has a role to play as well. An imaginative approach to governance would recognize the utility of harnessing the rise of the Asia-Pacific region and the emergence of an increasingly globalised system of open innovation. For example, in developing their R&D strategies policymakers could now assess the advantage to be gained from contracting out certain components of the innovation process to the NIEs of the Asia Pacific region. Access to fast-growing new markets for health care technologies provides an opportunity for companies to generate additional revenues. It may be that with some health technologies these NIEs leapfrog, adopting them more rapidly and extensively than in the West where existing technologies are more embedded in clinical care. In such a situation provision could be made for European scientists to benefit from collaborations with colleagues in the AP region, providing an alternative to the US, the traditional overseas partner of choice. In addition, countries such as China and India may also offer to European policy makers alternative models of both innovation governance and biotech business.

In some respects the EU multilevel governance framework closely resembles that of the United States, with individual states competing for comparative advantage within a unified framework and with strong regional differences (for instance in their approach to hESC research). The historic advantage enjoyed by the US in biotechnology means that in new areas such as regenerative medicine a national strategy may not be necessary for the country to enjoy a leading position. Can the same be said for the EU? Is it sufficient to rely on the efforts of those countries most committed to the biotech sector, and would the EU's competitive position be best enhanced by providing additional support to these leaders or by trying to drag the stragglers up to their levels?

Appendix one
Stem cell projects funded by European Union under FP6
All data from [102]

Figure one: FP6 stem cell projects: partners by country

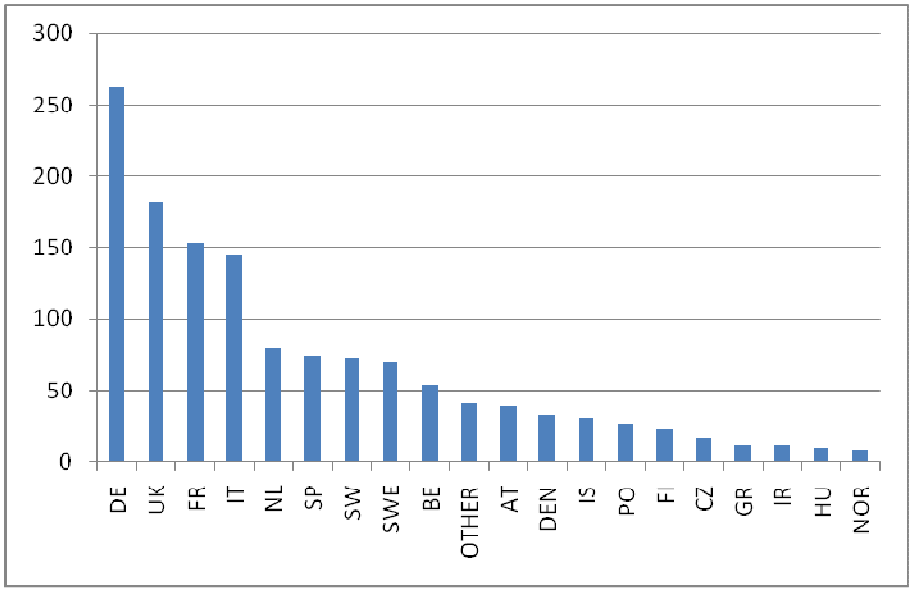


Figure two: FP6 cell therapy projects: coordinating partner by country

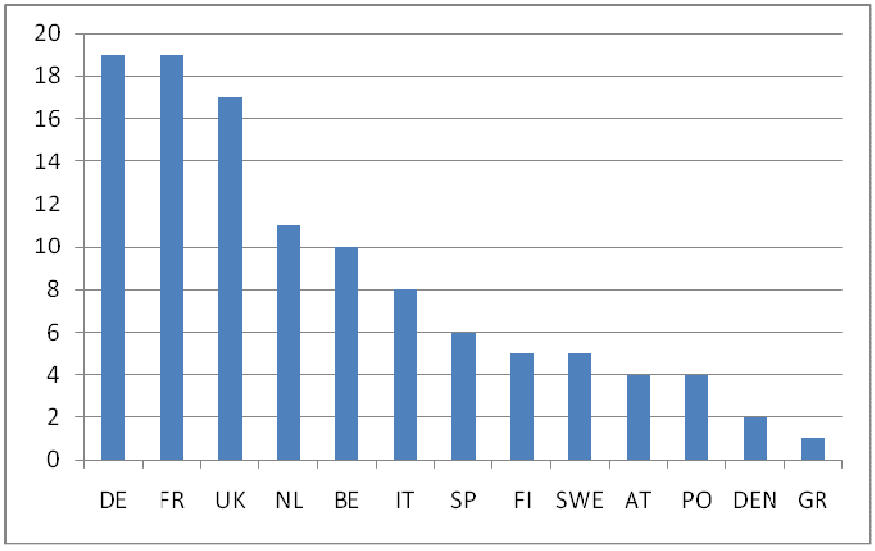


Figure three
Partners in projects coordinated by the UK (17 PROJECTS, 15 COUNTRIES, 188 PARTNERS)

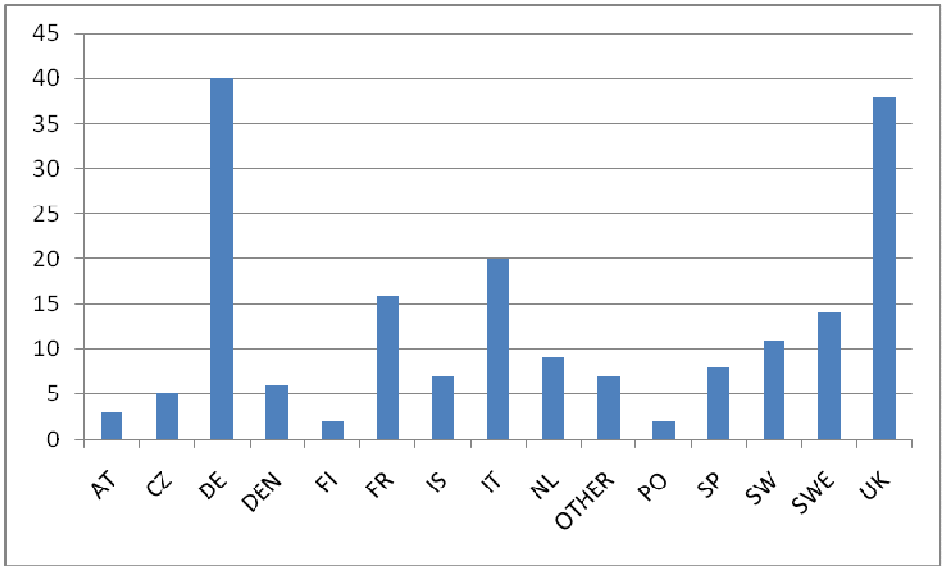


Figure four
Partners in projects coordinated by France (19 PROJECTS, 20 COUNTRIES, 195 PARTNERS)

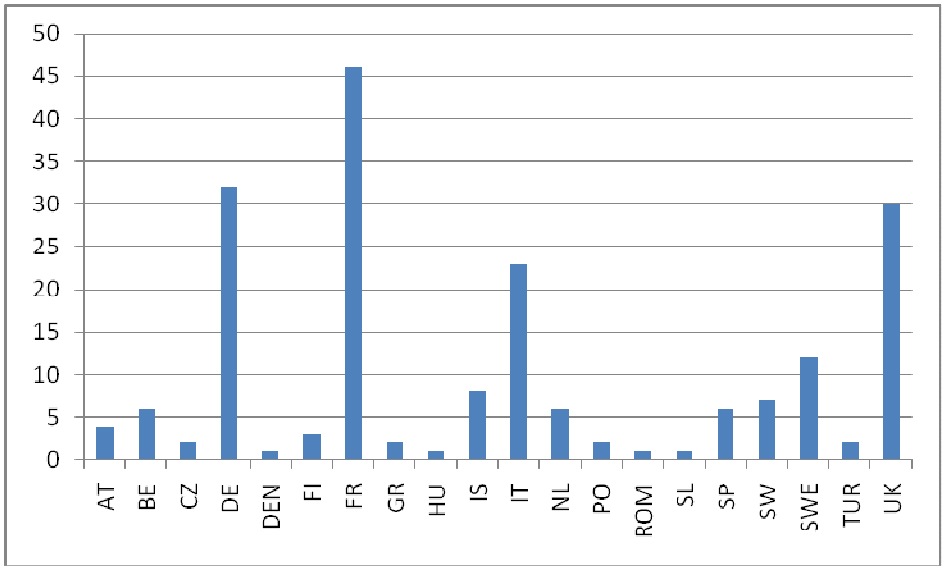


Figure five
Partners in projects coordinated by Netherlands (11 PROJECTS, 18 COUNTRIES, 153 PARTNERS)

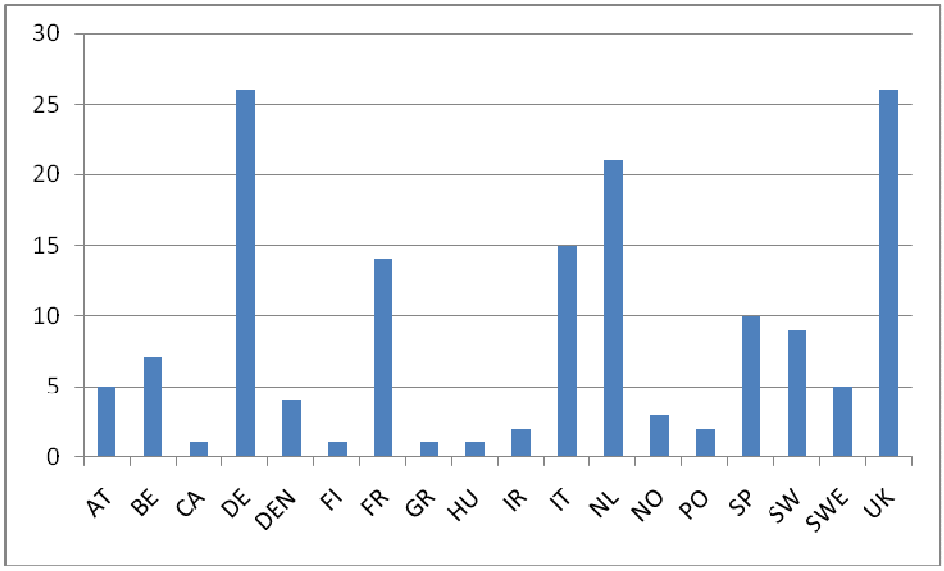


Figure six
Partners in projects coordinated by Germany (19 PROJECTS, 31 COUNTRIES, 333 PARTNERS)

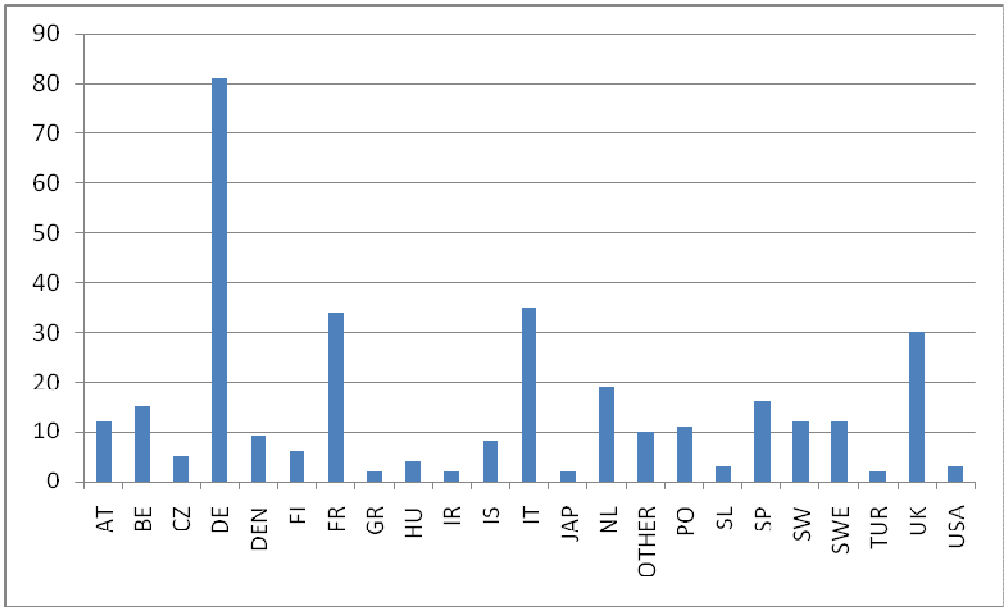


Figure seven
Partners in projects coordinated by Belgium (10 PROJECTS, 21 COUNTRIES 113 PARTNERS)

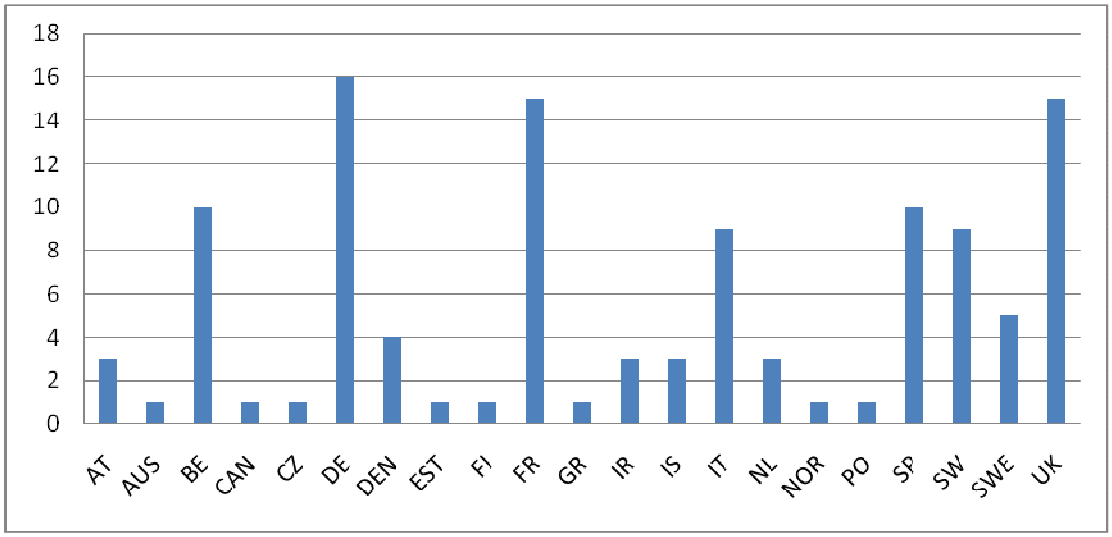


Table one FP6 projects involving stem cells

Name	Start date	Funding	Instrument	Duration	Coordinator
CELLS INTO ORGANS	2004	7,200,000	NoE	5	NL
DNA REPAIR	2005	11,500,000	IP	4	NL
EMBRYOMICS	2005	1,449,850	NEST-ADVENTURE	3	FR
EPISTEM	2006	2,500,000	IP	4	BE
ESTOOLS	2006	12,000,000	IP	5	UK
EUCOMM	2006	13,000,000	IP	3	DE
EUGENE2	2004	8,000,000	NoE	4	SWE
EuReGene	2005	10,500,000	IP	5	DE
EURO-Laminopathies	2006	2,565,000	STREP	3	AT
EuroBoNet	2006	13,218,960	NoE	5	NL
EuroHear	2004	12,500,000	IP	5	FR
EUROPEAN MCL NETWORK	2004	2,493,900	STREP	3	DE
EURYTHRON	2004	2,875,996	Marie-Curie RTN	4	NL
EuTRACC	2007	9,600,000	IP	4	NL
EVI-GENORET	2005	10,000,000	IP	4	BE
FunGenES	2004	8,500,000	IP	3	DE
HeartRepair	2006	11,400,000	STREP	4	NL
INTERDEVO	2005	2,000,000	STREP	3	SP

LYMPHANGIOGENOMICS	2004	9,000,000	IP	5	FI
MCSCs	2006	2,150,068	STREP	5	NL
MSCNET	2006	2,740,000	STREP	3	DEN
MUGEN	2005	11,000,000	NoE	5	GR
MYORES	2005	12,000,000	NoE	5	FR
ONCASYM	2006	2,820,000	STREP	3	DE
Plurigenes	2006	2,500,000	STREP	3	FR
REGULATORY GENOMICS	2004	2,200,000	STREP	4	FI
SIROCCO	2007	11,781,445	IP	4	UK
THE EPIGENOME	2004	12,500,000	NoE	5	AT
TRANSCODE	2005	1,000,000	STREP	3	IT
Anti-tumor targeting	2005	2,420,000	STREP	3	AT
CONSERT	2004	11,635,000	IP	4	NL
CRYSTAL	2007	2,400,000	STREP	3	DE
E.E.T.-Pipeline	2007	4,000,000	STREP	3	DE
EPI-VECTOR	2005	2,100,000	STREP	3	UK
EURO-THYMAIDE	2004	12,000,000	IP	5	BE
EuroCSC	2007	1,900,000	STREP	3	DE
EUROSTEMCELL	2004	11,906,400	IP	4	UK
EUROXY	2004	8,000,000	IP	5	DEN
EVGN	2004	9,000,000	NoE	5	FR
GIANT	2005	9,700,000	IP	5	UK
INTHER	2005	2,800,000	STREP	3	DE
KIDSTEM	2006	2,463,000	Marie-Curie RTN	4	UK
magselectofection	2006	2,800,000	STREP	4	DE
MODEST	2007	2,755,468	SME-STREP	3	DE
MOL CANCER MED	2004	4,000,000	IP	4	UK
MYOAMP	2006	2,480,000	SME-STREP	3	FR
NEURONE	2005	8,300,000	NoE	4	UK
NEUROscreen	2006	2,050,000	STREP	3	UK
NSR	2004	2,600,335	Marie-Curie RTN	4	FR
OsteoCord	2006	2,486,000	STREP	3	UK
SKINTHERAPY	2005	2,079,900	STREP	3	FR
STEM-HD	2006	2,500,000	STREP	3	FR
STEMS	2006	2,400,000	STREP	3	FR
SyntheGeneDelivery	2005	2,400,000	STREP	3	FR
TherCord	2006	1,800,000	STREP	3	IT
TUMOR-HOST GENOMICS	2005	2,700,000	STREP	3	FI
X-ALD	2004	1,800,000	STREP	3	AT
3G-SCAFF	2005	1,699,998	STREP	3	SWE
AUTOBONE	2004	2,296,892	STREP	4	IT

BARP+	2004	2,495,600	STREP	3	FR
BIOSYS	2005	1,999,700	STREP	3	DE
CellPROM	2004	17,599,928	IP	4	DE
CORNEA ENGINEERING	2004	2,558,797	STREP	3	FR
Custom-IMD	2007	5,400,000	IP	4	SP
EXPERTISSUES	2004	7,300,000	NoE	5	PO
GENOSTEM	2004	8,752,000	IP	4	FR
HIPPOCRATES	2004	2,896,000	STREP	4	PO
LIVEBIOMAT	2005	2,299,906	STREP	3	DE
NANOBIOCOM	2005	2,017,616	STREP	3	SP
NanoEar	2006	10,499,957	IP	4	FI
NEWBONE	2006	4,400,000	IP	4	FI
SILKBONE	2005	1,599,304	SME-Coop. Research	2	UK
SmartCaP	2005	1,796,814	STREP	3	SP
STEPS	2005	13,063,154	IP	4	IT
VASCUPLUG	2005	2,300,000	STREP	3	DE
ARTEMIS	2007	1,985,420	STREP	3	SP
CARCINOGENOMICS	2006	10,440,000	IP	5	NL
CONTROL CANCER STEM	2005	1,499,892	NEST-ADVENTURE	3	BE
INVITROHEART	2007	2,701,611	SME-STREP	3	SWE
M3CS-TU TH	2004	2,942,447	Marie-Curie RTN	4	IT
NEURO	2005	1,945,500	NEST-ADVENTURE	3	IT
PREDICTOMICS	2004	2,259,754	STREP	3	SP
ReProTect	2004	9,100,000	IP	5	DE
VITROCELLOMICS	2006	2,942,000	STREP	3	SWE
BETACELLTHERAPY	2005	11,788,000	IP	5	BE
EuroSTEC	2007	7,828,500	IP	5	NL
MYOCARDIAL REPAIR	2005	400,000	SSA	2.5	PO
RESCUE	2005	2,700,000	STREP	3	FR
SC&CR	2004	1,954,200	STREP	3	IT
STEMSTROKE	2007	2,475,508	STREP	3	SWE
STROKEMAP	2006	2,400,000	STREP	3	BE
THERAPEUSKIN	2005	1,523,000	STREP	3	FR
Ulcer Therapy	2005	2,392,000	STREP	3	IT
ALLOSTEM	2004	8,000,000	IP	3.5	UK
CLINT	2007	500,000	SSA	2	UK
EUROPEAN LEUKEMIANET	2004	6,000,000	NoE	5	DE
FIRST	2004	1,500,000	IP	2	NL
RISET	2005	10,000,000	IP	5	BE

STEMDIAGNOSTICS	2007	2,500,000	SME-STREP	3	UK
TRANS-NET	2005	4,539,456	Marie-Curie RTN	4	UK
TRIE	2007	450,000	SSA	1.5	BE
EMRS	2004	675,000	SSA	4	FR
EU hESC registry	2007	1,000,000	SSA	3	DE
EUROCITS	2005	500,000	SSA	1.5	BE
imgbchimerashybrids	2005	600,424	CA	2	DE
INDUSTRYVECTORTRAIN	2004	176,000	SSA	2	FR
INVIVOVECTORTRAIN	2003	161,620	SSA	2	FR
REPROGENETICS	2004	980,000	STREP	3	BE
SENECA	2006	142,800	SSA	2	PO
StemCellPatents	2005	249,257	SSAS	4	UK
CORDCELLBANKING STUDY	2002	13,000		0.5	UK
111 projects	TOTAL	532,712,377			

Bibliography

Websites

101. ‘EU to convene subgroup of 'innovation commissioners' 19 April, 2010 EurActiv http://www.euractiv.com/en/innovation/eu-convene-subgroup-innovation-commissioners-news-461155

102. European research projects involving stem cells in the 6th Framework Programme http://ec.europa.eu/research/fp6/p1/stemcells/pdf/stemcell_eu_research_fp6_en.pdf#view=fit&pagemode=bookmarks

103. Science / Business Innovation Board 2008 *Clustering for growth - how to build dynamic innovation clusters in Europe.* http://www.sciencebusiness.net/documents/clusterbooklet.pdf

104. National Science Foundation. Science and Engineering Statistics 2008. http://www.nsf.gov/statistics/seind08/

105. SpiegelOnline (2008) Germans reject fast-track EU immigration scheme http://www.spiegel.de/international/europe/0,1518,513241,00.html

106. Webb, S. and Pain, E. (2006). Navigating the Stem-Cell Research Maze, *Science,* Careers Forum, 1st of December. Available at: http://sciencecareers.sciencemag.org/career_development/previous_issues/2006

107. Presentation by Professor Brian Clark, Life Sciences Partnering China and Europe. www.e-unlimited.com/LSPCE/Event/London2006/default.asp?mp=presentations.asp

108. IMS 2008 Global biotech perspective http://www.imshealth.com/deployedfiles/imshealth/Global/Content/StaticFile/biotech_slides_for_internet.pdf

109. Edery, E:. Market divergence softens growth. *World Pharmaceuticals Frontiers,* March (2008) http://www.worldpharmaceuticals.net/editorials/013_march08/013_market.pdf

110. European Patent Office http://www.epo.org/

110. Burger, S: Overview of regulations and standards for cell therapy: an international perspective. Presented at: International Stem Cell Therapy Society workshop 2006. http://www.ac-gt.com/talks/pdfs/Cell%20Therapy%20Regulations%20-%202006%20SCT%20Workshop.pdf

References

1. UK Office of Life Sciences *Life sciences 2010: Delivering the blueprint* London, UK, Department for Business, Innovation and Skills.

2 . European Commission: *The financing of biopharmaceutical product development in Europe. Study on the competitiveness of the European biotechnology industry*. Brussels, European Commission (2009)

3. European Commission: *Reviewing Community innovation policy in a changing world.* Brussels, European Commission (2009)

4. European Commission: *Towards world-class clusters in the European Union: Implementing the broad-based innovation strategy.* Brussels, European Commission (2008)

5. European Commission: *Life sciences and biotechnology: a strategy for Europe.* Brussels: European Commission. (2002)

6. European Commission: *Mid term review of the Strategy on Life Sciences and Biotechnology*. Brussels: European Commission (2007).

7. Salter B and Salter C: Governing innovation in the biomedicine knowledge economy: stem cell science in the USA. *Science and Public Policy* 37(2), 87-100 (2010).

8. European Commission: *European Innovation Scoreboard 2009 Brussels.* European Commission (2009).

9. European Commission: *A more research-intensive and integrated European Research Area. Science, technology and competitiveness: key figures report 2008/2009* Luxembourg, Office for Official Publications of the European Communities (2008).

10. Burke M and Matlin S (eds): *Monitoring financial flows for health research 2008.*

prioritizing research for health equity. Geneva, Switzerland, Global Forum for Health Research (2008)

11. Galama T and Hosek J: *U.S. competitiveness in science and technology.* Santa Monica, USA RAND (2008).

12. Enzing C et al: *BioPolis: Inventory and analysis of national public policies that stimulate biotechnology research, its exploitation and commercialisation by industry in Europe in the period 2002–2005*. Luxembourg, Office for Official Publications of the EU (2007)

13. Kessler, C: EU support for stem cell research. Presented at: *EMA workshop on stem cell-based therapies*. London, UK, 10 May 2010.

14. Kessler, C: European policies and priorities for stem cell research. Presented at*: Beyond Pattison: Challenges to Stem Cell Translation and Policy*. London, UK, 7-8 May 2009.

15. Organisation for Economic Co-Operation and Development. 2006. *Innovation in pharmaceutical biotechnology: comparing national innovation systems at the sectoral level.* (Paris: OECD)

16. Cooke, P: New economy innovation systems: biotechnology in Europe and the USA. *Industry and Innovation*, 8(3), 267-289 (2001).

17. European Commission. 2008. *Towards world-class clusters in the European Union: Implementing the broad-based innovation strategy.* Brussels: European Commission (2008).

18. NERA: *Key factors in attracting internationally mobile investments by the research-based pharmaceutical industry.* London, UK, NERA Economic Consulting (2007).

19. Organisation for Economic Co-Operation and Development: *Science, technology and industry outlook 2008*. Paris, France, OECD (2008)

20. European Commission: *The European Research Area Partnership, 2008 initiatives.* Brussels, European Commission (2009)

21. Organisation for Economic Co-Operation and Development: *Science, technology and industry outlook 2007*. Paris, France, OECD (2007).

22. Collett, E: Beyond Stockholm: overcoming the inconsistencies of immigration policy. *European Policy Centre Working Paper 32* Brussels, European Policy Centre (2009)

23. Ernst and Young:. *Beyond Borders: Global Biotechnology Report 2008* Ernst and Young, (2008)

[24] Martin P, Hawksley, R and Turner, A: *The commercial development of cell therapy – lessons for the future?* Nottingham, Nottingham University (2009)

25. Nasto, B: Chasing biotech across Europe, *Nature Biotechnology*, 26, 283-288 (2008)

26. Ang, S: Country-of-origin effect of VC investment in biotechnology companies. *Journal of Commercial Biotechnology*, 13, 12–19 (2006).

27. Bioscience Innovation and Growth Team: *The review and refresh of Bioscience 2015: a report to government.* Bioscience Innovation and Growth Team, London, UK (2009).

28. Herpin, T et al: Australian biotech companies: navigating the maze. *Journal of Commercial Biotechnology*, 11(2): 110–120 (2004).

29. Salter, B: Governing stem cell science in China and India: emerging economies and the global politics of innovation. *New Genetics and Society*. 27(2): 145–159 (2008).

30. European Commission *Competitiveness of the European biotechnology industry* Brussels, European Commission (2007)

31. European Commission: *Life science research: US a healthy challenger to Europe. Factsheet 1* Brussels, European Commission (2004).

32. Williams, D Hourd, P and Chandra, A: *Enhancing the competitiveness of health technology SMEs – paper for the Ministerial Medical Technology Strategy Group.* Loughborough, UK, Loughborough University (2008).

33. Farrell, D, Jensen, E and Kocher, B: Why Americans pay more for health care. *McKinsey Quarterly*, December (2008).

34. Calfee, J and DuPre, E: The emerging market dynamics of targeted therapeutics. *Health Affairs* 25(5), 1302-1308 (2006)

35. Danzon, P and Furukawa, M: Prices and availability of biopharmaceuticals: an international comparison. *Health Affairs* 25(5), 1353-1361 (2006).

36. van Beuzekom, B and Arundel, A: *OECD Biotechnology Statistics – 2006.* Paris, France, OECD (2006)

37. van Beuzekom, B and Arundel, A: *OECD Biotechnology Statistics – 2009.* Paris, France, OECD (2009)

38. Marks and Clerk: *Biotechnology Report 2006*. London: Marks and Clerk (2006).

39. Bergman, K. and Graff, G. 2007. The global stem cell patent landscape: implications for efficient technology transfer and commercial development. *Nature Biotechnology*, 25(4): 419-424.

40. Gill, S: European patent law developments in stem cell research. *Pathology in Practice*. Feb (2007)

41. van Pottelsberghe de la Potterie, B and Mejer, M: The London Agreement and the cost of patenting in Europe *ECORE discussion paper* Louvain (2008).

42. Tait, N: Ministers back EU patent reform plan. *Financial Times* 4 December (2009).

43. Gaskill, G et al: Europeans and Biotechnology in 2005: Patterns and Trends. *Eurobarometer* 64.3 (2006).

44. Salter, B: 'The global politics of human embryonic stem cell science' *Global Governance*, 13, 277-98 (2007).

45. Paarlberg, R: The great stem cell race. *Foreign Policy*, May/June (2005).

46. Abraham, J and Lewis, G: *Regulating medicines in Europe: competition, expertise and public health*. London, Routledge (2000).

47. Hughes-Wilson, W. and Mackay, D. 2007. European approval system for advanced therapies: good news for patients and innovators alike. *Regenerative Medicine*, 2(1): 5-6.

48. Majone, G: *Regulating Europe*. London, Routledge (1996).

49. Rowley E and Martin P: *Barriers to commercialisation and utilisation of regenerative medicine in the UK*. Nottingham, UK, Nottingham University (2009).