

Regenerative Medicine

The Patent Landscape in 2011

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This report was prepared by the Intellectual Property Office Patent Informatics Team, June 2011

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Executive Summary

Growth in the Regenerative Medicine field has been found to slow to a steady level since 2003 worldwide and since 2007 in the UK. Granted patents have declined since 2003 and do not reflect the earlier growth in applications. It is not clear from this study whether this is due to fundamental legal issues of patentability of the subject matter, patent quality, or patenting strategies within the industry. However, holdings sizes suggest that the industry still has space for further growth and increased expertise, leading to larger portfolios of patents. At present, 47% of inventions worldwide belong to small portfolios, rising to 67% of inventions for the UK.

The US leads other countries by a large margin both in Regenerative Medicine and in the life sciences more generally, and is the source country for almost half of all the inventions in this study. Other leading countries are Japan, Germany, China, and Canada, with the UK in sixth position. However, when a correction is applied to sift out the countries which tend to patent more frequently for all industries, it is found that Israel, Australia, Canada, and the US show greater than expected levels of invention. China, Korea, Germany, France, and Japan show a lower level of invention than expected. Inventions in the UK are just below the expected level, with four or five additional inventions per year sufficient to bring Regenerative Medicine to the expected level for UK industry overall, or six additional inventions per year to bring Regenerative Medicine to the level of the higher performing life sciences.

The largest subject areas in terms of patent classifications are "Materials for grafts/prostheses/coating containing added animal cells", "Cells from the blood or immune system: haematopoietic stem cells, uncommitted or multipotent progenitors", and "Embryonic cells: pluripotent cells e.g. embryonic stem cells". Focus within the UK is generally the same as that found worldwide.

The leading applicants are University of California, General Hospital Corp., and Massachusetts Institute of Technology, with five of the top ten applicants being universities, and all but one (Japan Science and Technology Agency) being in the US. The leading applicants in the UK are University of Edinburgh, Smith and Nephew, Imperial College London and University of Sheffield. Five of the top ten applicants in the UK are universities. The leading inventors are David C Rueger, Anthony Atala, and James A Thomson, all in the US. David C Rueger, Charles M Cohen, and Hermann Oppermann's inventions all have a high grant rate of around 70%, and all three are associated with Creative Biomolecules Inc., Stryker Corp., and Curis Inc., which are not in the top ten applicant organisations. Leading inventors in the UK are Gerard Austin Smith, Peter Andrews, and Qi-Long Ying. In the UK, however, the leading inventors do tend to be associated with the leading applicant organisations. Overall, 25% of inventions are from the academic sector, and in the UK, 32%.

Collaborations are revealed between organisations when they are named as coapplicants. Strong collaborations were found by all of the leading universities in the UK, both with other universities and with industry, and including overseas **Regenerative Medicine**

collaborations. The smaller size of the industry in the UK and the limited numbers of active individuals appear to be conducive to collaboration. As the sector grows in the UK, however, as may be expected from the indicators in the patent data, increased fragmentation may occur as new entrants appear and grow, and competition develops.

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1 Introduction

In August 2006 the IPO (then The Patent Office) produced a patent analysis of Regenerative Medicine for BIS (then DTI). This was based around the following definition of Regenerative Medicine:

Those technologies that provide substitute tissues (both synthetic and natural) and/or cells for implantation into the body that promote tissue regeneration or remodelling for the purpose of replacing, repairing, regenerating, reconstructing or enhancing function."

The leading companies at the time were Ethicon Endo Surgery Inc., Asahi Medical Co., and Human Genome Services Inc. The earliest country of filing by these companies was mainly the US or Japan. However, when considering only the most recently available data, DePuy (a branch of Johnson and Johnson), Tigenix NV, and Wyeth showed signs of growth.

The US was the most common country of first filing, with the UK being the sixth. Regenerative Medicine as a whole was showing high levels of patenting activity from 2001-2005.

This report updates the 2006 analysis in line with the present requirements of BIS. Techniques used in patent landscaping have also evolved since the first report so the analysis in this project is specifically based around the country of residence of patent applicants. This gives a better indication as to the location of any innovative activity. The time period covered is 1991 to the present.

2 Updated Analysis

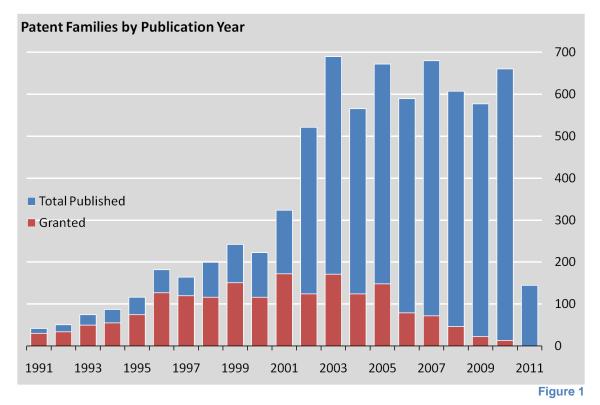
2.1 The dataset

A dataset was obtained by searching the European Patent Office (EPO) EPODOC database using patent classification terms and word searching. For further details of the data, see Appendix A.

Over 20,000 patent publications were included in the dataset, which were divided into 7,500 unique patent families (or inventions).

2.2 Patent Trends and Lifecycle

Patent activity in Regenerative Medicine is high but rather steady in the second half of the period covered, compared to the high growth seen over the first half of the period. Figure 1 shows the number of patent family representatives published each year (blue bar) from 1991-2011.

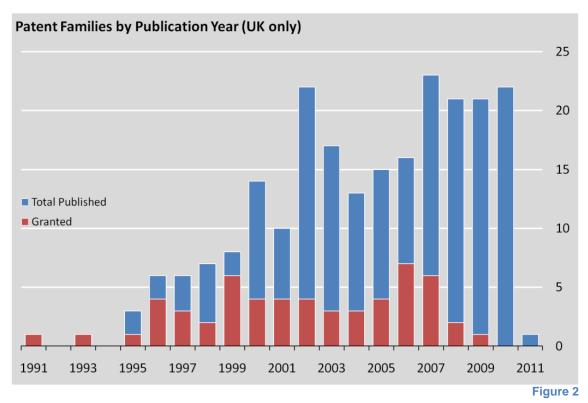


The use of patent families corrects for the effect of several patent applications in different countries by the same applicant and for the same invention; that is, each single invention should only be counted once. The number of families which include a granted patent each year is shown in red. There are two notable points concerning patent grants, particularly in the Regenerative Medicine field. Firstly, the proportion of granted patents falls far short of the number of applications, and, secondly, the grant of patents lags applications by a number of years, showing a general decline from 2003 to the present.

Although tempting, it would be wrong to conclude that the blue bars in Figure 1 necessarily represent "failed" applications, because several factors are at play in determining whether an application ever proceeds to grant. In particular, in the field

of Regenerative Medicine, there are ongoing legal issues which have caused the European Patent Office (EPO) to defer consideration of any patent application for grant, resulting in an even greater dearth of granted patents than may be expected generally. The patenting strategies of applicants may also contribute because applicants may file more applications than they ever intend to pursue. The inherent lag in patent grants, which is variable from patent office to patent office, but which is generally measured in years, means that figures for patent grants are less up date and less indicative of current trends than applications. Nevertheless, it is surprising that the large surge of patent applications between 2000 and 2003 (blue bars) is not reflected at all in the rates of granted patents (red bars), despite the inclusion of patent granting authorities other than the EPO. Therefore, the figures for published applications are considered a more robust measure of the level of invention than the figures for granted patents.

Figure 2 shows only the number of patent family representatives published each year which have a UK applicant. The trend appears level for the years 2007-10 but generally grew steadily from 1993-2007. Growth has therefore continued in the UK until more recently than internationally. The grant rate in the UK also lags the application rate and fails to reflect the growth in applications.

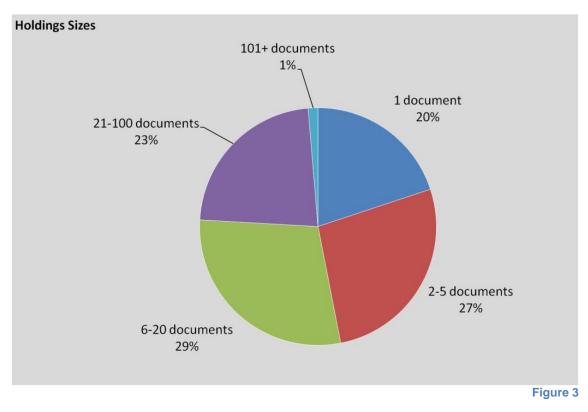


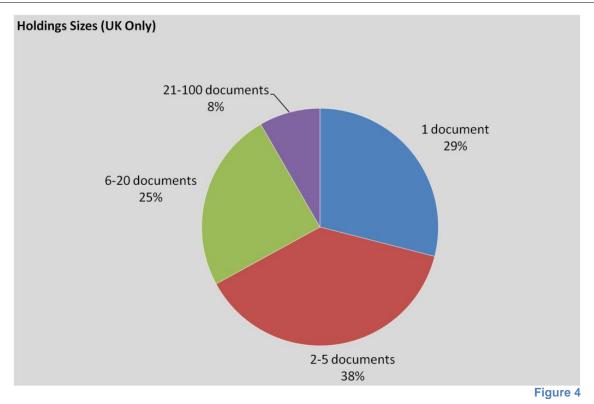
The development of technology over time may be tracked thus, but the lifecycle of a technology may be tracked by studying the size of the patent holdings belonging to applicant organisations. In the early, emerging stage, a large proportion of new entrants are found amongst the applicants, and the applicant turnover is high. This manifests as a high proportion of small sized patent holdings, and very few large sized ones (or even none, if the study occurs early enough). As the sector develops, specialisation sets in and a small number of organisations begin to develop large portfolios of patents through their own innovation and through acquisition. The

proportion of larger sized holdings therefore expands and squeezes out the smaller ones. Figure 3 illustrates the holdings sizes for the present dataset.

Fully 20% of patent families belong to applicants having a single patent family. 47% of patent families sit within a portfolio of just five or fewer families. These numbers suggest the industry has considerable room for expansion and maturity ahead.

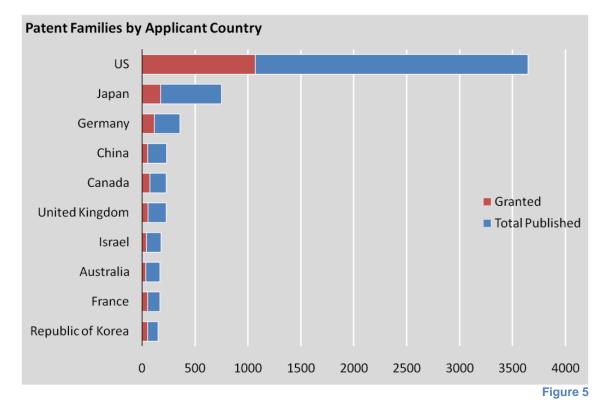
For the UK only (see Figure 4), as many as 67% of patent families belong to portfolios of five or fewer families. There are no portfolios of greater than 100 documents in size. Thus the UK industry appears to be at a nascent stage with considerable room for development.



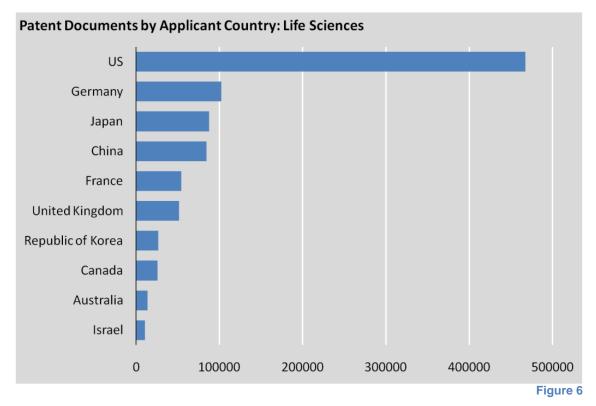


2.3 Country of Origin

Turning to the country of origin of Regenerative Medicine inventions, Figure 5 shows the number of patent families originating in each applicant country for the whole time period (1991-2011). Almost half of all inventions originate in the US, and this is, unsurprisingly, unchanged from the last report. The grant rate follows in approximate proportion amongst all the entrants in the chart, at around 30%.



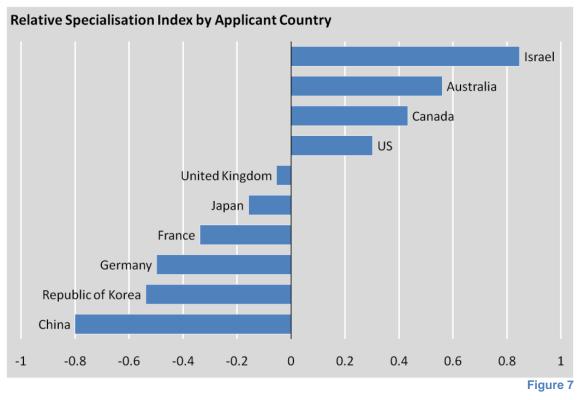
By way of context, similar figures¹ for patent documents in life sciences generally are shown in Figure 6. The pattern appears very similar, but the lead of the US in all life sciences is slightly less than for Regenerative Medicine. The total number of patents in the life sciences is 1.7 million, and for Regenerative Medicine is just over 20,000, forming nearly 7,500 families.



It is, however, well known that there is a greater propensity to patent in certain countries than others, and this picture may change if the figures are corrected for this difference in behaviour. Therefore, the Relative Specialisation Index (RSI)² for each applicant country has been calculated to give an indication of the level of invention in Regenerative Medicine for each country compared to the overall level of invention in that country, and is shown in Figure 7.

¹ Figures given are numbers of patents, rather than families

² See Appendix B for details

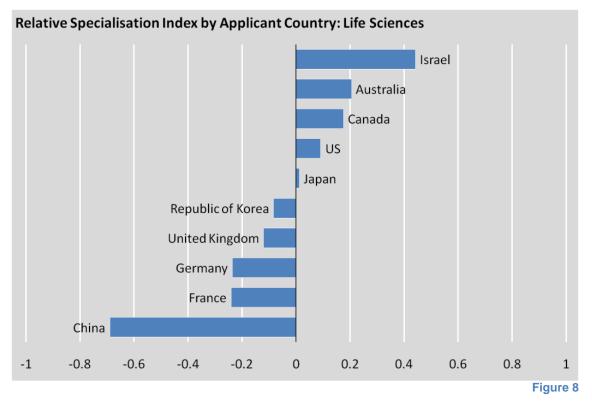


The picture is, indeed, different. The US is relatively specialised in the field of Regenerative Medicine but is now reversed in its ranking compared to Israel, Australia, and Canada. These show much greater levels of patenting in Regenerative Medicine than expected, despite their modest absolute levels of patenting. Patent filings by UK applicants are around the level expected, given the mildly negative value of RSI at -0.05.

The significance of this for the UK may not be clear in absolute terms: how badly is the UK performing? In terms of real numbers, this RSI represents a "shortage" of 86 regenerative medicine inventions in the UK (662 compared to the 748 that would be required for an RSI of zero) over the whole time period (1991-2011). Put another way, the UK would only need, on average, four or five additional regenerative medicine inventions per year in order to perform on par with other UK industries on average.

Applicants from the remaining countries are less interested in Regenerative Medicine than expected, given their strongly negative RSI values. In particular, Chinese applicants display a level of interest in Regenerative Medicine far below what would be expected from their large general growth in patenting.

A further way to gauge patenting levels is to use life sciences patents generally as a benchmark for comparison, rather than all patents. RSI has therefore been recalculated and expressed in Figure 8 on this basis.



The pattern is in fact broadly similar, although the UK drops below Japan and the Republic of Korea. In comparison to other life sciences, the regenerative medicine sector has a "shortage" of 211 regenerative medicine inventions (662 compared to 873 that would be required for an RSI of zero), or around ten patents per year, on average. On a positive note, this drop in RSI indicates that patenting in the life sciences as a whole in the UK relatively outperforms other industries.

2.4 Patent Classifications

All patents have classification terms allocated to them by patent examiners. There are a number of classification schemes used throughout the world, including an International Patent Classification (IPC) scheme, which comprises a hierarchical structure covering all fields of technology. The European Patent Office produces an enhanced scheme based on the IPC but containing greater detail. The most frequent EPO classification (ECLA) terms used on all inventions in the regenerative medicine dataset are listed in Table 1, and those used only on inventions from the UK are listed in Table 2.

It is clear that patents in the UK are found mostly in the same classification areas as worldwide (the only exception being A61L27/60 – materials for grafts/prostheses/coating for use in artificial skin – which finds higher prominence in the UK than in general).

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ECLA (hyperlinked)	Description	Total Published	Granted
<u>A61L27/38</u>	Materials for grafts/prostheses/coating containing added animal cells	681	209
<u>C12N5/06B11P</u>	Cells from the blood or immune system: haematopoietic stem cells, uncommitted or multipotent progenitors	651	198
<u>C12N5/06B2P</u>	Embryonic cells: pluripotent cells e.g. embryonic stem cells	523	105
<u>C12N5/06B21P</u>	Cells from the bone marrow stroma: mesenchymal stem cells	464	88
<u>C12N5/00S</u>	Substrates for cell culture of undifferentiated human, animal or plant cells	410	145
<u>A61L27/36</u>	Materials for grafts/prostheses/coating containing ingredients of undetermined constitution or reaction products thereof, e.g. Transplant tissue, natual bone, extracellular matrix	373	103
<u>C12N5/06B8P</u>	Cells of the nervous system: stem cells, progenitor cells, precursor cells	369	97
<u>A61K38/18</u>	Growth factors, growth regulators for medicinal preparations containing peptides from animals or humans	329	69
<u>G01N33/50D2F14</u>	Testing or evaluating the effect of chemical or biological compounds involving stem cells	269	46
<u>A61K38/19</u>	Cytokines, lymphokines, interferons for medicinal preparations containing peptides from animals or humans	220	40

Table 1: ECLA classifications. Terms are hyperlinked

Regenerative Medicine

Updated Analysis

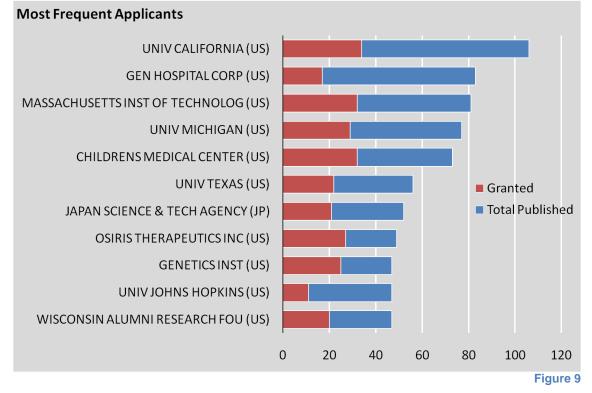
ECLA (hyperlinked)	Description	Total Published	Granted
<u>C12N5/06B2P</u>	Embryonic cells: pluripotent cells e.g. embryonic stem cells	52	14
<u>C12N5/06B8P</u>	Cells of the nervous system: stem cells, progenitor cells, precursor cells	22	7
<u>A61L27/38</u>	Materials for grafts/prostheses/coating containing added animal cells	21	7
<u>C12N5/00S</u>	Substrates for cell culture of undifferentiated human, animal or plant cells	17	5
<u>C12N5/06B21P</u>	Cells from the bone marrow stroma: mesenchymal stem cells	17	5
G01N33/50D2F14	Testing or evaluating the effect of chemical or biological compounds involving stem cells	17	3
A61L27/60	Materials for grafts/prostheses/coating for use in artificial skin	12	6
<u>C12N5/06B11P</u>	Cells from the blood or immune system: haematopoietic stem cells, uncommitted or multipotent progenitors	10	3
<u>A61L27/36</u>	Materials for grafts/prostheses/coating containing ingredients of undetermined constitution or reaction products thereof, e.g. Transplant tissue, natual bone, extracellular matrix	9	4
<u>A61K38/19</u>	Cytokines, lymphokines, interferons for medicinal preparations containing peptides from animals or humans	8	1

Table 2: ECLA classifications, UK only. Terms are hyperlinked

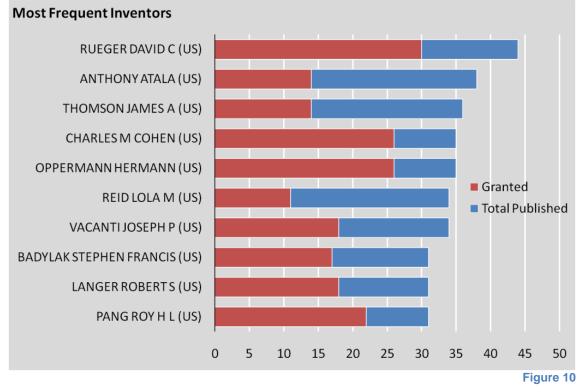
2.5 Applicants and Inventors

The details of the most frequent applicants are shown in Figure 9. Applicants are generally companies or organisations because inventions made by employees are normally assigned to the employer with employees retaining the right to be credited as inventors. As might be expected from the results presented in Figure 5, all but one (*JAPAN SCIENCE & TECH AGENCY*) of the entries in the top ten most frequent applicants are of US origin. The entrants are ranked by total number of publications, but it can be seen that the grant rates associated with each entrant vary (from 20% for *GEN HOSPITAL CORP* to 55% for *OSIRIS THERAPEUTICS INC*). There is a significant academic presence in Figure 9, which is expected from a science-intensive field such as Regenerative Medicine.





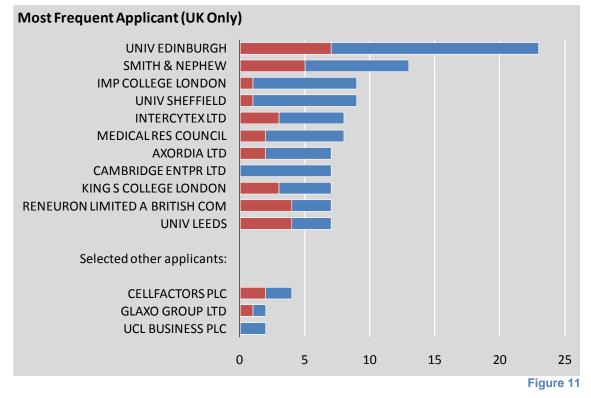
The most frequent inventors are listed in Figure 10. Inventors are the named individuals to whom the invention is credited, even if those individuals are employed by an organisation which has acquired the patent rights. The top inventors do not correlate with top applicants: *RUEGER DAVID C* is associated with *CREATIVE BIOMOLECULES INC*, *STRYKER CORP*, and *CURIS INC*, none of which appear in Figure 9 (they fall in positions 32, 35, and 38 respectively). This individual is named on more patent documents than anyone else, and also has a high success rate in terms of patents granted (68%). CHARLES M COHEN and *OPPERMANN HERMANN* also have high success rates, at 74% each. These individuals are also affiliated with CREATIVE BIOMOLECULES INC, STRYKER CORP, and CURIS INC.



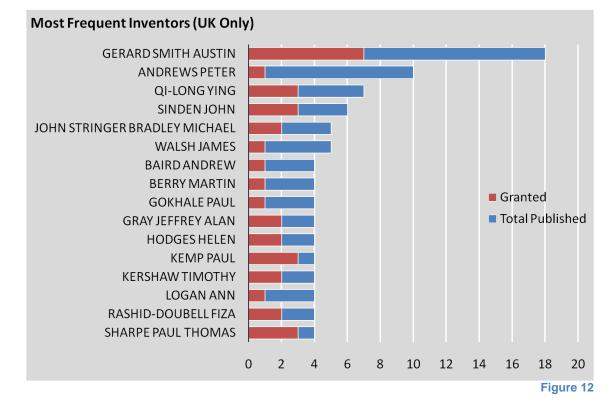
The most frequent UK applicants are given in Figure 11. Grant rates vary between 0% (*CAMBRIDGE ENTERPR LTD*) and 57% (*RENEURON LIMITED*), but no great weight may be given to these numbers because of the small sizes of the portfolios. There is similarly a significant academic presence in Figure 11, demonstrating the research-based and science-intensive Regenerative Medicine field follows the same trend in the UK as elsewhere.

There are some notable absences from these lists, for example Pfizer and University of College London (UCL). In fact, just five inventions are listed under the name Pfizer in this dataset, and two inventions under the name UCL Business PLC (responsible for transfer of UCL emerging technologies). This serves to underline that patent analysis does not offer a complete picture of the technology sector because it is susceptible to the varying strategies and levels of participation of organisations within the patent system. Nevertheless, it opens a window onto the behaviours of those who do participate.

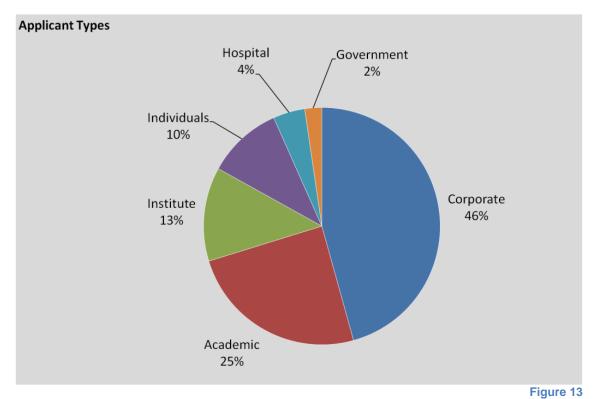
Some details of some of the latest inventions from UK applicants are given in Appendix C.

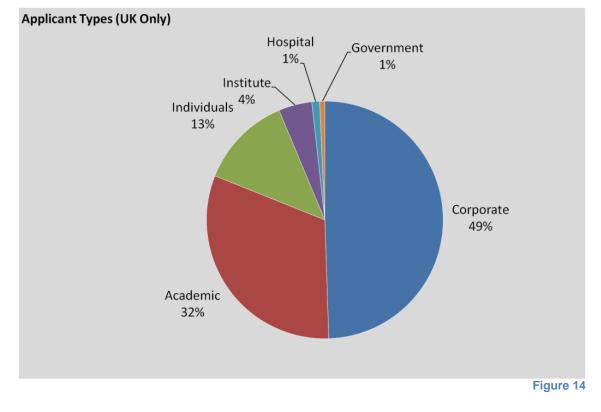


UK inventors are illustrated in Figure 12. *GERARD SMITH AUSTIN* and *QI-LONG YING* are associated with UNIV EDINBURGH, and ANDREWS PETER is associated mainly with UNIV SHEFFIELD, and to a lesser degree with AXORDIA LTD, *INTERCYTEX LTD*, and EXAUDIO CO LTD. Thereby, in the case of UK, there is some degree of correlation between the top inventors and top applicants. The smaller sizes of the patent portfolios probably allow an employee individual to exert a greater influence on an employer organisation.



Applicant types are shown in Figure 13. In the field of Regenerative Medicine, there is a relatively small proportion of corporate applicants, at 46%. The academic sector, at 25%, is much larger than is the case generally. This result reflects the science-intensive nature of Regenerative Medicine, which has already been noted above with reference to frequent applicants. For the UK, applicant types are shown in Figure 14. Here, the academic sector is even more significant, at 32%, whilst the institute, hospital, and government sectors are smaller.





2.6 Collaborations

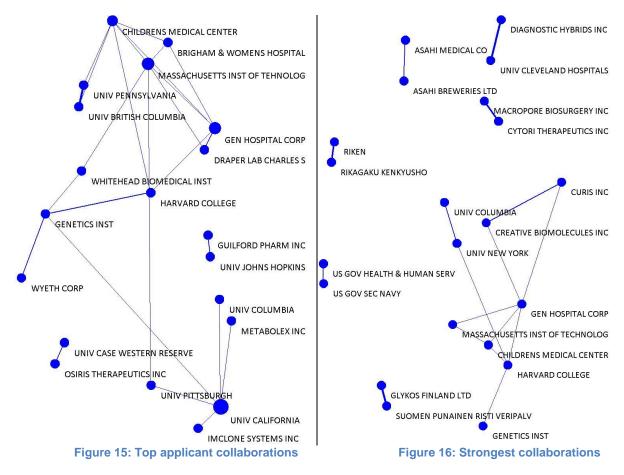
Collaborations are revealed in patent documents when the collaborating parties are named as co-applicants. Team working and personal connections are also revealed when the individuals are named as co-inventors. These collaborations and connections may be presented as links as shown in Figures 13-18. Collaborations of the most frequent applicants are shown in Figure 15.

However, the most frequent applicants are not necessarily the most frequent collaborators. Figure 16 shows the applicants who have collaborated most frequently and therefore discloses the strongest links between organisations in terms of Regenerative Medicine related research. Organisations and associated individuals who have retained assignee rights separately would ordinarily manifest as links but have been removed. Of more interest are links between organisations which are not related other than through their collaborative patenting. Examples of these are *CREATIVE BIOMOLECULES INC* with *CURIS INC* and *GEN HOSPITAL CORP*; *SUOMEN PUNAINEN RISTI VERIPALV* with *GLYKOS FINLAND LTD*; *MASSACHUSETTS INST OF TECHNOLOG* with *CHILDRENS MEDICAL CENTER* and *GEN HOSPITAL CORP*; *UNIV NEW YORK* with *UNIV COLUMBIA* and *HARVARD COLLEGE*; *HARVARD COLLEGE* with *GENETICS INST*; *UNIV CLEVELAND HOSPITALS* with *DIAGNOSTIC HYBRIDS INC*.

Figure 17 illustrates links between individual inventors. Clusters of inventors may arise because they work for a common applicant. This is the case for the dense cluster of inventors towards the top left of Figure 17, all of whom are associated with *CREATIVE BIOMOLECULES INC, CURIS INC,* and *STRYKER CORP*. However, links also arise between inventors associated with different organisations, even when those organisations are not co-applicants, thereby revealing additional collaborative information. This appears to hold true for *REID LOLA M*, who, although mainly associated with *UNIV NORTH CAROLINA* and *EINSTEIN COLL MED*, has links with inventors associated with *UNIV YESHIVA* and *UNIV PENNSYLVANIA*.

Links between the most frequent UK applicants and their collaborators are shown in Figure 18. All of the universities in the top ten most frequent UK applicants have collaborations, some of which are with overseas organisations, for example UNIV EDINBURGH with UNIV MICHIGAN and MOUNT SINAI HOSPITAL CORP, and UNIV BIRMINGHAM with SELECTIVE GENETICS INC. Turning to the strongest links throughout all UK applicants, in Figure 19, it can be seen that there are a number of strong collaborations between universities and industry. Some collaborations appear to be spin out companies from the universities; for example UNIV DURHAM with REINNERVATE LTD. and IMP COLLEGE LONDON with NOVATHERA LTD. Others appear not to be spin-out companies; examples of these are UNIV ABERDEEN with PLASMA BIOTAL LTD, KINGS COLLEGE with SELECTIVE GENETICS INC and ODONTIS LTD, UNIV SHEFFIELD with INTERCYTEX LTD, and ROSLIN INST EDINBURGH (at the University of Edinburgh) with GERON CORP. (Geron Corporation wholly owns a subsidiary based in Edinburgh.) Although links between organisations and associated individuals have been removed (for clarity), two individuals remain in Figure 19 since are applicant/inventors and are not associated with any organisation: DELLA BITTA RUGGERO with FRANKS CHRISTOPHER RALPH.

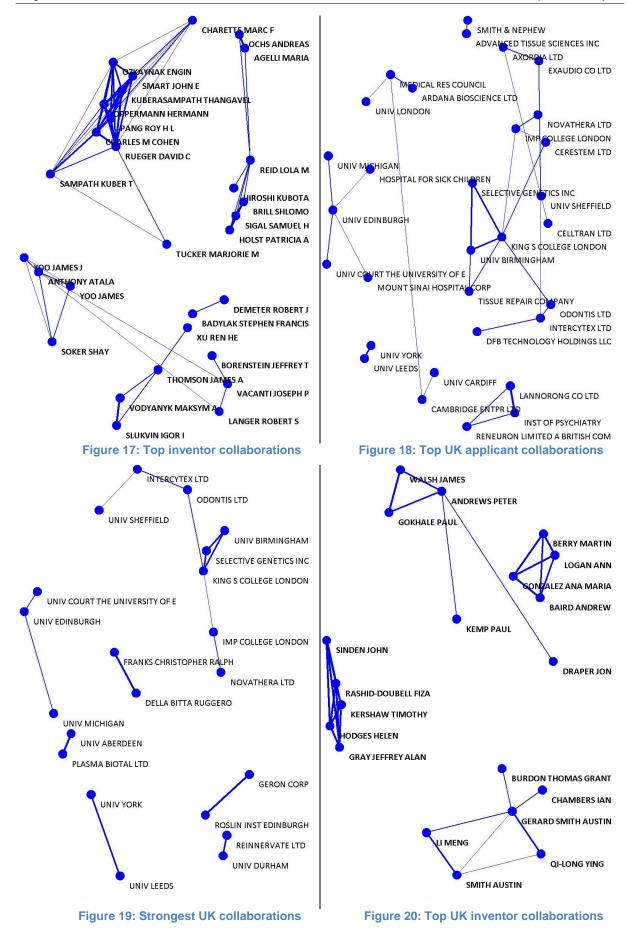
Figure 20 shows inventor links within the UK. The cluster at the bottom right is associated with the University of Edinburgh. The cluster at the left is associated with Reneuron Limited. The triangle of *WALSH JAMES*, *ANDREWS PETER*, and *GOKHALE PAUL* reveals a potential link between *AXORDIA* and *INTERCYTEX* in terms of people that is not apparent from applicant information (these organisations are never co-applicants). The remaining cluster at the top right reflects the *KINGS COLLEGE*, *SELECTIVE GENETICS INC*, and *UNIV BIRMINGHAM* cluster.



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Updated Analysis



2.7 Landscape Map

A landscape map is provided in Patents are clustered according to the themes appearing in the titles and abstracts, and contours are produced to indicate the density of patents. The themes are given on the map and it can be seen how commonly they occur and how closely they are related.

Figure 21, showing the major themes occurring throughout the whole dataset. Patents are clustered according to the themes appearing in the titles and abstracts, and contours are produced to indicate the density of patents. The themes are given on the map and it can be seen how commonly they occur and how closely they are related.

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Figure 21: Landscape map © Thomson Reuters

3 Conclusions

Regenerative Medicine saw growth during the period 1991-2003, with especially strong growth in 2000-2003, but since 2003 activity has remained steady at around 650 inventions per year. In the UK the growth period has lasted to a more recent point (2007), and also remains steady from 2007-present, at just over 20 inventions per year. However, the growth both in general and in the UK has not been reflected in numbers of granted patents, which have stumbled along with slow growth over the period 1991-2001 but with a slow decline from 2003-present. Notably, a large surge in inventions between 2000 and 2003 is totally lacking from the pattern in granted patents. Therefore, early signs of promise appear to have led to a stalling. Although legal issues resulting in delays in granting some European patents would be expected to strongly influence these trends, the inclusion even of other patent granting authorities appears not to change them.

Holdings data do suggest that Regenerative Medicine is still at a relatively early stage of development, with a relatively large proportion of activity from smaller, newer entrants to the industry, and this is even more true for the UK. Development of any industry may be expected to occur in fits and starts and the recent lack of growth may merely be a part of that. There appears to be still more room for development and for the accumulation of expertise to lead to greater levels of patenting and larger portfolios of patents to be built up yet.

The US leads the way in absolute numbers of inventions in Regenerative Medicine specifically, and in the life sciences more generally. Other leading countries respectively are Japan, Germany, and China, with the UK in sixth position. However, when adjusted for expected levels of invention when compared to general performance, Israel, Australia, Canada, and the US show higher than expected levels of invention in Regenerative Medicine. However China, Republic of Korea, Germany, France, and Japan show a lower level of invention in Regenerative Medicine compared to general performance. The UK falls close to, but just below, the expected level of performance compared to general performance, which translates into a shortfall of four or five inventions per year. However, the shortfall is six inventions per year compared to the life sciences because the life sciences perform better than the UK average, but Regenerative Medicine does not share in this level of performance.

UK inventions tend to be classified into the same categories as worldwide inventions, indicating that the focus of activity is fairly homogenous.

The leading applicants are mostly of US origin, as would be expected from the abundance of US inventions discussed above. The Japan Science and Technology Agency is the only exception in the top ten. There is a significant academic presence amongst the leading applicants: half of the top ten applicants are universities. Similarly, in the UK, half of the top ten applicants are universities. This presence is not limited only to the top ten lists: 25% of inventions overall and 32% of inventions in the UK are from universities. Corporate applicants account for 46% of inventions overall and 49% of inventions in the UK. This contrasts with the general pattern found in most patent studies, in which corporate applicants generate the vast majority of inventions.

Leading inventors are entirely of US origin, although they do not necessarily work for the leading applicant organisations. David C Rueger, Charles M Cohen, and Hermann Oppermann are associated with Creative Biomolecules Inc., Stryker Corp., and Curis Inc., none of which are near the top ten applicants. These individuals demonstrate a relatively high grant rate. In the UK, the leading inventors do work for leading applicant organisations. The smaller size of the portfolios found within the UK perhaps allows individuals to exert greater influence and to shine brighter.

Collaborations show links between organisations and between individuals. Collaboration by UK universities appears to be greater than found in general worldwide, with all of the leading universities demonstrating strong collaborations, either with other universities or with industry. Several overseas collaborations are also apparent. Inventor collaborations show the teams within the organisations, although occasionally links occur between individuals associated with different organisations. The smaller size of the Regenerative Medicine industry in the UK and the limited numbers of active individuals unsurprisingly appear to be conducive to collaboration. Greater fragmentation may be expected to occur if the sector grows, and further entrants and competitors appear.

Appendices

A Notes on Patent Data

A.1 Basis for Report

For this project the European Patent Office (EPO) database EPODOC was interrogated, which holds bibliographic and abstract data of published patents and patent applications derived from the majority of leading industrialised countries and patent organisations, for example the World Intellectual Property Organisation (WIPO), EPO and the African Regional Industry Property Organisation (ARIPO). It should be noted that patent applications are generally published eighteen months after filing.

A.2 Priority Date, Application Date and Publication Date

There are generally three dates which can be associated with a patent application as follows:

Application date: The date on which an application for a patent was made.

Priority date: The application date of an earlier, related patent application containing the same invention. A patent can claim a priority date from an earlier application which contains the same subject matter. The priority date is the earliest available indication of the date of invention.

Publication date: The date when the patent application was published. This is normally eighteen months after the priority date or the application date, whichever is the earlier.

A.3 WO and EP Patent Applications

International Patent Applications (WO) and European Patent Applications (EP) may be made through the World Intellectual Property Organization (WIPO) and the European Patent Office (EPO) respectively.

International Patent Applications may designate any signatory states or regions to the Patent Cooperation Treaty (PCT) and will have the same effect as national or regional patent applications in each designated state or region, leading to a granted patent in each state or region.

European Patent Applications are regional patent applications which may designate any signatory state to the European Patent Convention (EPC), and lead to granted patents having the same effect as a bundle of national patents for the designated states.

A.4 Patent Documents Analysed

The document dataset was identified through European Classification (ECLA) codes and word searching of abstracts in conjunction with patent examiner technologyspecific expertise. The applicant and inventor data were cleaned as far as practicable to remove duplicate entries arising from spelling errors, initialisation, international variation (Ltd, Pty, GmbH etc.), or equivalence (Ltd., Limited, etc.).

B Relative Specialisation Index

Relative Specialisation Index (RSI) was calculated as a correction to absolute numbers of patent families in order to account for the fact that some countries file more patent applications than others in all fields of technology. In particular, US and Japan inventors are prolific patentees. RSI compares the fraction of Regenerative Medicine patents found in each country to the fraction of patents found in that country overall. A logarithm is applied to scale the fractions more suitably. The formula is given below:

 $\log_{10} \left(\frac{\frac{n_i}{n_{total}}}{\frac{N_i}{N_{total}}} \right)$

 $n_{i=1}$ number of Regenerative Medicine patents in country *i* n_{total} =total number of Regenerative Medicine patents in dataset $N_{i=1}$ =total number of patents in country *i* N_{total} =total number of patents in dataset

The effect of this is to highlight countries (in this study, Israel in particular – see Figure 7) which have a greater level of patenting in Regenerative Medicine than expected from their overall level of patenting, and which would otherwise languish much further down in the lists, unnoticed.

C Recent UK Inventions

Publication Number	Applicant Name	Title of Invention
US2010234966	ORTHOGEM LTD	BONE REPAIR OR AUGMENTATION DEVICE
WO2010001175	GREATER GLASGOW HEALTH BOARD	MODIFIED CELLS AND METHODS OF MONITORING THEIR VIABILITY
WO2010007353	SMITH & NEPHEW	CATABOLIC AGENTS
WO2010023463	UNIV EDINBURGH	POLYMER BLENDS
WO2010029288	AXORDIA LTD	GROWTH FACTOR
EP2195417	UNIV EDINBURGH	REGIONALISED ENDODERM CELLS AND USES THEREOF
WO2010052508	UNIV BRISTOL	LIGANDS OF VITAMIN D NUCLEAR RECEPTORS WITH CELL MATURATION PROMOTION FACTORS
GB2466073	UNIV MANCHESTER	TISSUE REPAIR SCAFFOLD
GB2466481	UCL BUSINESS PLC	ALGINATE ENCAPSULATED HIGH DENSITY BIO-ARTIFICIAL LIVER
WO2010028846	BIOCOMPATIBLES UK LTD	TREATMENT OF ACUTE MYOCARDIAL INFARCTION (AMI) USING ENCAPSULATED CELLS ENCODING AND SECRETING GLP-1 PEPTIDES OR ANALOGS THEREOF