

# The global stem cell patent landscape: implications for efficient technology transfer and commercial development

Karl Bergman & Gregory D Graff

**Characteristics of the complex and growing stem cell patent landscape indicate strategies by which public sector research institutions could improve the efficiency of intellectual property agreements and technology transfers in stem cells.**

The debate over access to research tools essential for stem cell research and development has been waged most strongly over patents granted in the United States to the Wisconsin Alumni Research Foundation (WARF) for work done at the University of Wisconsin on embryonic stem cells<sup>1,2</sup>. Although those WARF patents are now being widely licensed, the concerns that they raised<sup>3-7</sup> may soon be overshadowed by a more subtle but more chronic problem. Patent filing activity in stem cells has been growing steadily since the late 1990s. Given the particular characteristics of stem cells as a broadly enabling technology, many expect the field to be particularly susceptible to the emergence of a patent thicket<sup>8-13</sup>, also known in property rights theory as an 'anti-commons'<sup>14</sup>. In a patent thicket, the existence of many overlapping patent claims can cause uncertainty about freedom to operate, impose multiple layers of transaction costs and stack royalty payments beyond levels that can be supported by the value of single innovations. By blocking pathways to market and dampening investor interest in commercialization, a patent thicket has the potential to slow and

skew the overall development of new technical applications.

Proposals that seek to solve the patent thicket problem by altering, reducing or eliminating the granting of problematic property rights beforehand are important to consider for the long-term efficiency of the patent system<sup>15,16</sup>. This approach is fundamentally policy-oriented, seeking changes in patent law, particularly in scope and subject matter, or changes in patent administration and enforcement. In the short to medium term, however, this approach has at least two major drawbacks. First, changes in law tend to require a critical mass of political support. Second, the die has already been cast: the existing patent estates in the field of stem cells have already been created under current law and practice. Academia and industry must continue to operate under this legacy for the next two decades.

A second approach seeks more efficient exchange, transaction or redistribution of granted property rights after the fact<sup>17-21</sup>. This approach is market- or institutionally oriented, seeking ways that existing assets can be put to use more efficiently, regardless of the initial grant or scope of rights. This may be a more feasible approach in the short to medium term and, under the right conditions, a more efficient solution in the long term. Examples include mechanisms ranging from compulsory licensing, to open source licensing, to the formation of patent pools and other forms of collective action. Such approaches do not depend necessarily upon new legislation or legal interpretation. Instead they depend upon the voluntary construction of market or institutional mechanisms that operate within

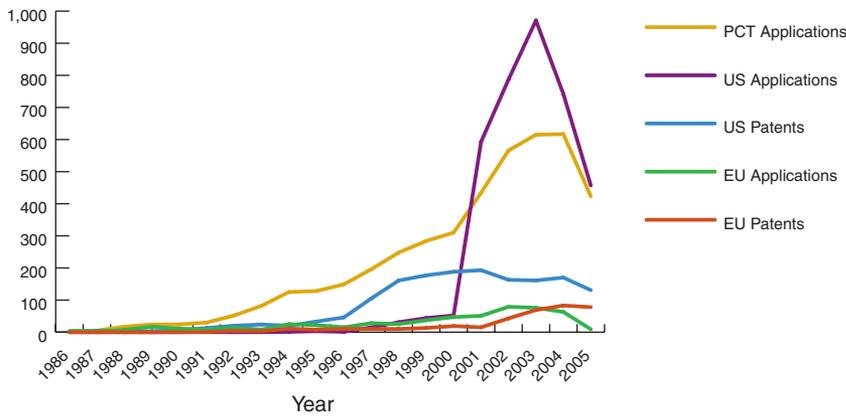
the existing environment to facilitate transactions in a more efficient manner than would be achieved under multiple rounds of one-on-one negotiations.

## Issues in stem cell patenting and licensing

Until now, stem cell research within many academic settings has proceeded without paying heed to the patent environment. However, university research administrators and technology transfer offices are becoming more concerned, particularly when universities engage in commercially sponsored research projects or look for opportunities to license out university inventions. Specific issues that have arisen with the broad WARF patents may be indicative of future developments in the field. In industry, access to intellectual property has been a concern for some time, but at the same time has often been overshadowed by even greater concerns about ethical and regulatory constraints on the commercial viability of stem cell technologies and products based on them<sup>22</sup>. The emerging shape of the complexity of the field holds important implications about where bottlenecks are most likely to affect the rate and direction of stem cell research, development and commercial application.

The WARF patents, claiming all primate and human embryonic stem cell lines, embody one of the strongest possible property claims in the field of stem cells, establishing control at the very root of all possible lineages of cellular differentiation. Beyond this central starting point, however, navigation of intellectual property rights is potentially fraught with challenges due to the sheer complexity of the 'tree' of cellular

*Karl Bergman is at the Göteborg International Bioscience Business School and Center for Intellectual Property Studies, Chalmers University of Technology and Göteborg University, Göteborg, Sweden and Gregory D. Graff is at the Public Intellectual Property Resource for Agriculture (PIPRA), University of California, Davis, California 95616, USA. e-mail: mail@karlbergman.se or gdgraff@ucdavis.edu*



**Figure 1** A core collection of published patent documents constructed to encompass all stem cell related technologies contains 10,681 applications and granted patents from the US Patent and Trademark Office, the European Patent Office and WIPO's Patent Cooperation Treaty (PCT) filing system. Applications filed and patents granted at each office are shown for years 1986–2005.

differentiation. In theory all cell types could be initiated from pluripotent stem cells, through the general pathways differentiating first into multipotent endodermal, mesodermal and ectodermal cells, and then on into increasingly specific cellular lineages. Furthermore, several studies have suggested that lineage- or tissue-specific adult stem cells may be able to transdifferentiate into cell types of other lineages, even of other germ layers<sup>23</sup>, or to regain pluripotency and plasticity, in essence by dedifferentiating through nuclear reprogramming<sup>24</sup>. Stem cells need specific culture conditions and specific growth factors, proteins, hormones or small molecules to be led step-wise through the stages of cellular differentiation, transdifferentiation or dedifferentiation. Many of these are separately patented technologies that will not have many alternatives, and thus they control the main 'thoroughfares' that must be traveled by all who wish to manipulate embryonic or adult stem cells into specific cell lineages. In addition, other core technologies where congestion and inefficiency may be caused by multiple overlapping patent claims include genetic transformation and nuclear transfer methods for altering genetic characteristics of stem cells and assays to determine potency or typology of stem cells. In each of these areas, component technologies are likely to exhibit high degrees of interdependence while at the same time being widely employed in the development of therapeutic applications.

**A global data set of filed and granted patents on stem cell technologies**

An understanding of the main trends in stem cell patenting activity is essential for confirming where patent proliferation is likely to be most problematic and how researchers and policy-

makers might best address problems of technology access. To answer questions about the broad trends in stem cell patenting, we constructed a comprehensive data set of patent documents covering any and all "uses, methods, or compositions involving human or animal stem cells."<sup>25</sup> Of the resulting 10,681 documents, 1,724 were patents granted by the US Patent and Trademark Office (USPTO); 3,711 were US patent applications. By comparison, there were 421 patents granted and 560 applications published by the European Patent Office (EPO) and 4,265 applications processed and published through World Intellectual Property Organization (WIPO)'s Patent Cooperation Treaty (PCT) mechanism.

**Annual stem cell patent applications and grants.**

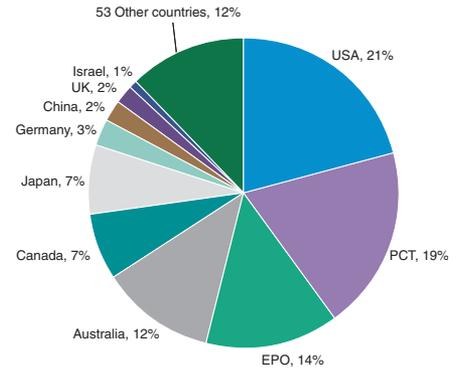
Annual numbers of applications filed and patents granted indicate the rate of innovation (Fig. 1). Stem cell patent applications through the PCT showed steady growth from the late 1980s to a peak of almost 600 in 2004. Applications in the US followed a similar trend, peaking at almost 1,000 in 2003. The rate of stem cell patent grants by the USPTO was more modest. After growing rapidly in the mid 1990s, they leveled off around 200 per year after 1998 and have been in gradual decline since 2001. In Europe, both applications and grants have grown more slowly, but grants continued to trend upwards through 2005. Overall, extremely rapid growth in filings was seen between 2000 and 2002, yet this seemed to have been tempered more recently (even after correcting for data truncation). The causes of this apparent stagnation in the young field of stem cells are uncertain.

**Stem cell patenting activities by country.** The countries in which patents are filed indicate

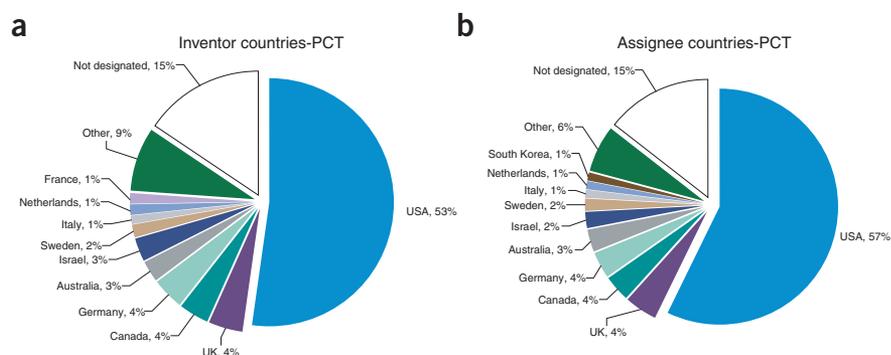
those markets that inventors and owners consider to be the most important in which to protect their technology. To compare stem cell patent filing activity in all countries around the globe, we expanded the core collection using international patent family data for each of the records in the core collection. This resulted in an expanded global collection of stem cell patent families consisting of 47,467 documents (Fig. 2). After the PCT, US and EPO, the most active countries for stem cell filings were Australia, Canada, Japan, Germany, China, the United Kingdom and Israel. The remaining 12 percent of global stem cell filings were thinly dispersed across 53 additional countries. It is noteworthy that the Australian and Canadian markets had attracted more filings than Japan and Germany. Israel also stood out as a relatively small market with a large share.

The organization that takes assignment to a patent is most often the organization that employed the inventor. Country of residence of inventors is thus tightly correlated with the country of the assignee (Fig. 3). After accounting for undesignated assignee and inventor country data, it seemed that roughly two thirds (61 to 66 percent) of all stem cell inventions filed through the PCT originated with or belong to US organizations. The contribution of every other country was at least an order of magnitude smaller.

Comparison between issuing country, assignee country and inventor country provides some insights into global activity in stem cell research and patenting. In these data the US, Europe (EPO member countries considered together) and Israel had higher shares of



**Figure 2** The core collection of US, EPO and PCT documents expanded to include the full 'patent family' for each document: the corresponding patent filing made in any of 60 additional countries on the same invention. This resulted in a global collection of stem cell patent families consisting of 47,467 documents. The figure shows the distribution of these overlapping documents worldwide.



**Figure 3** National contributions to the global stock of stem cell inventions indicated by the distribution by country of the first inventor listed and the first assignee listed in the 4,265 PCT applications in the core collection of stem cell documents identified in this study. Since inventors (a) and assignees (b) were not designated on 15 percent of the PCT documents, estimates for countries' contributions are 15 percent greater than those indicated in the figure. For example, the estimated share to US assignees is 66 percent (the observed 57 percent plus 9 of the unobserved 15 percent).

stem cell inventors and assignees relative to the shares of the global collection of stem cell documents published by their patent offices, indicating net exports of stem cell knowledge. In fact, the US was by far the most prolific innovator and exporter of stem cell technologies. Europe, however, had a higher ratio of inventors to assignees than did the US, indicating, all else being equal, a net assignment of patents by European inventors to US-based assignees. Other countries, including Australia, Canada, Japan, Germany, China and several other major emerging economies, showed decidedly lower shares of inventors and assignees globally relative to their patent offices' respective shares of published stem cell documents globally, indicating in some cases substantial net inflows of stem cell filings by foreigners.

**Distribution and concentration of stem cell patent ownership by sector and assignee.** The interrelated questions of concentration of ownership and distribution of ownership between public and private sector entities can be crucial in determining how readily intellectual property may be accessed and redistributed. We characterized all assignees as (i) private sector organizations (including privately held companies, publicly traded corporations and individuals) or (ii) public sector organizations (including government agencies and academic or nonprofit research institutions).

Of US granted stem cell patents, 44 percent were assigned to public sector entities and 56 percent to private sector entities (Fig. 4a). This contrasts sharply with the distribution of ownership of all patents granted by the USPTO between 1986 and 2005, where just 3 percent are assigned to public sector entities. Of course, stem cells are still an early-stage technology,

and medical research is perhaps the greatest priority of publicly funded R&D.

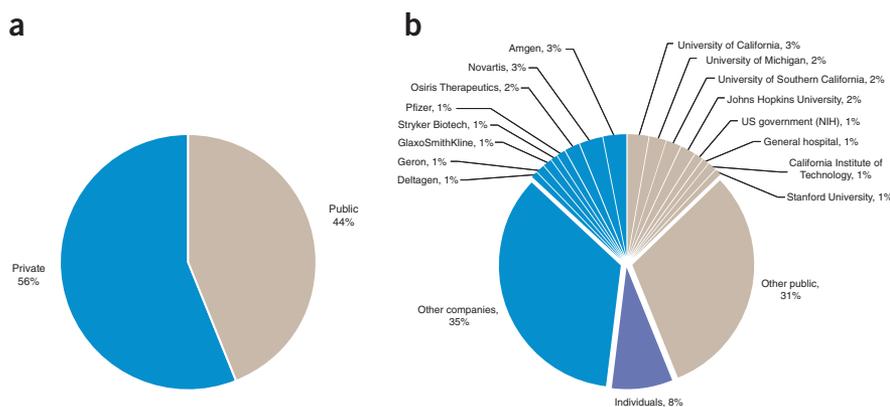
Among both public institutions and private companies, ownership of stem cell technologies was very fragmented (Fig. 4b). No single company, even after accounting for mergers and acquisitions, held more than 3 percent of the total. Interestingly, the top eight public sector institutions likewise owned 13 percent of the total. Half of these were located in California. The strong showing of large biotech and pharmaceutical companies was somewhat surprising. Amgen, Novartis, Pfizer and GlaxoSmithKline are rarely mentioned by market analysts as prominent players in stem cell research. Instead, it is the smaller companies with a specific focus on stem cells, such as Geron, that are more frequently cited. These larger companies are probably not putting major effort into stem cells

but have nonetheless accumulated significant stem cell positions in their patent portfolios through mergers and acquisitions executed for other technical or business reasons.

**Major technical areas of stem cell patenting.**

A technical categorization of the documents in the collection enables us to see the major topographic features of the stem cell patent landscape. Under the newest version of International Patent Classification (IPC), the technical field of a patent's primary 'inventive steps' are reported. We used these to analyze the technologies contained in the core collection. No single category contained or described all stem cell technologies: the collection covered a wide range of IPC codes. Yet, several stood out. The single largest class present was stem cell lines and culture media (C12N 5/), of which 3,587 were animal cells or tissues (C12N 5/06) and 968 were human cells or tissues (C12N 5/08). Thus, only about 20 percent of patents describing stem cell lines or preparations referred specifically or limited their claims to just human cells. Other main classes included the 9,634 occurrences of polypeptides, growth factors (medicinal preparations) and enzymes (A61K 38/, C07K 14/ and C12N 9/), and the 4,182 technologies related to genetic engineering (C12N 15/). Less numerous but also substantial were the 878 documents on new animal breeds involving nuclear transfer or cloning (A01K 67/), 3,050 on prostheses, stents and tissue scaffolds (A61F 2/ and A61L 27/), 1,769 on immunoglobulins or antibodies that target or signal stem cells (C07K 16/) and 2,620 on assays and diagnostics that identify stem cells (C12Q 1/ and G01N 33/).

**The most dominant stem cell patents.** A relatively small number of patents cover the most fundamental technologies on which most stem



**Figure 4** The distribution of ownership between private sector and public sector entities of granted US patents over stem cell technologies (a), and a breakdown of their ownership (b). This picture contrasts greatly with the distribution of holdings in most industries and fields of technology.

cell R&D is dependent. These are the technologies that inform and support the wider field, and these patents have proportionately greater potential for blocking commercialization of a range of stem cell applications. One measure of the importance or scope of a patent is the number of 'forward references' that have been made to it by other patents issued later. The list of forward references made to a patent provides a summary of the assessments made by others within the technical and legal community who are highly knowledgeable about the field. An additional indicator of importance or dominance is simply its mention and discussion within the legal and trade literatures. We employed these two indicators to select a list of the 50 most dominant patents in stem cell R&D today (Table 1). The majority of the listed patents covered stem cell lines, preparations and methods of culturing or inducing differentiation in stem cells, reflecting the inventive-step IPC composition of the documents in the core collection.

**The lay of the landscape.** Already a substantial number of patents have been granted within this field. Large numbers have been filed in recent years, particularly since 2001. If grant rates follow these trends, there will soon be a significant mass of intellectual property claims through which commercial products will have to navigate to reach market. Yet by some indications, patenting activity in stem cells may have already peaked—some time between 2001 and 2003, and certainly well before the field has seen any real commercial applications.

The technical content of the patent landscape is highly complex. Stem cell lines and preparations, stem cell culture methods and growth factors show the most intense patenting activity but also have the most potential for causing bottlenecks, with component technologies expected to show high degrees of interdependence while being widely needed for downstream innovation in stem cell applications.

The United States clearly dominates most aspects of stem cell research, invention and patenting. The top public sector organizations by patent assignment are all in the US. Yet Europe in particular is beginning to close the gap with the United States, at least in numbers of patents granted. Nationality of invention and ownership is likely to become more evenly or proportionately distributed.

Finally, ownership of stem cell patents is quite fragmented across multiple organizations. No single one dominates, with the largest assignees accounting for no more than three percent of all documents in the sample, and with even dominant patents broadly distributed among many assignees. Under such conditions of

fragmentation the task of coordinating access to complex key technologies could involve an intensive and costly coordination process. Government, academic and nonprofit institutions account for an inordinately large share of the patents in the field. Under the typical technology transfer strategy of offering single patents for license, these are not likely to integrate complex supporting-technology platforms. However, there may be significant potential for sourcing all of the necessary components for such from public sector institutions.

### Conclusions and recommendations

The characteristics of the stem cell patent landscape are consistent with conditions that could give rise to a patent thicket. Under these conditions—including the rapid growth in numbers of patents, their dispersal among many owners and over complex interrelated technologies—navigating and negotiating freedom to operate within the field is likely to become increasingly difficult. Given the difficulties of enacting patent law reform and the legacy effect of already granted patents on industry and academia, strategies to facilitate efficient exchange of existing property rights *ex post* are more likely to provide effective remedies.

**An intellectual property clearinghouse for stem cells.** Following the second approach to addressing the patent thicket problem, in order to enhance exchange in stem cell technologies and to complement market function in key areas where it may be most prone to fail, we propose what we call an 'intellectual property clearinghouse mechanism' for the stem cell R&D community. Of key importance, such a strategy should find its origins among those organizations, particularly those that are public sector or academic institutions, most deeply engaged in stem cell R&D who share mutual concerns about the dampening effects that the emerging patent thicket may have on opportunities for investment, innovation and commercialization. The primary functions of an intellectual property clearinghouse mechanism would be to provide (i) information on patents available for licensing (through a common database or other means) in order to reduce uncertainties and enhance transparency, thereby supporting market discovery and subsequent market exchanges in patent rights and (ii) principles of best practices in licensing to address other common goals such as adopting terms that encourage use of the most ethically acceptable of possible approaches to stem cell research. Such primary functions would help reduce the likelihood of strategic or short-sighted behaviors on the part of participating patent owners and would aid research managers

in making important technical decisions as they plan future projects.

For those stem cell technologies where several substitutes are available, the intellectual property clearinghouse would facilitate the market by providing a 'universal listing' that included the respective technical characteristics, allowing the different technology options to compete as fairly and transparently as possible. By analyzing patterns of demand for common stem cell research tools, which technologies are most often employed in R&D projects and in which combinations, as well as assembled information about which technologies are available for licensing, the clearinghouse could pool technologies characterized by high complementarity and license them jointly to meet identified demand more efficiently. These pooled research tools could be marketed widely, to serve the goal of facilitating downstream R&D in stem cells. Participation in any single patent pool would be a voluntary decision of the technology owners, based on negotiations facilitated by the clearinghouse, but motivated by their own commercial or institutional policy considerations. All terms of participation in and disposition of the pools would be negotiated independently of the more general issues of participating in the governance and activities of the intellectual property clearinghouse.

These functions reflect the basic model being pursued by one existing intellectual property exchange or clearinghouse mechanism known as the Public Intellectual Property Resource for Agriculture (PIPRA), a coalition of over 40 universities and research institutes seeking a more efficient exchange of patent rights over plant biotechnologies to facilitate R&D for 'neglected' applications—cases where the patent thicket seems to have affected agricultural innovation, and thereby social welfare<sup>26–28</sup>. This initiative involves WARF, the University of California and several other universities also prominent in stem cell research, sharing data on the patents in their agricultural portfolios that are available for licensing, identifying the intellectual property bottlenecks over key research tools, and developing patent pools—drawn from the patent holdings of the coalition members—designed to alleviate those bottlenecks. As both major patent owners and active researchers in the field, the universities and research institutions involved are precisely those that have the greatest vested interests in improved intellectual property exchange. Other coalition-based initiatives, such as the HapMap Project, have been undertaken to establish common mechanisms for accessing well-defined technologies to enable R&D broadly in the life sciences.

**Table 1 The 50 most important stem cell patent documents published from 1992 onwards**

Publication date	Patent number	Title	Assignee (and likely current owner) <sup>a</sup>	Times cited <sup>b</sup> ; discussed in lit. <sup>c</sup>
April 11, 1995	US5405772	Medium for long-term proliferation and development of cells	Amgen	25
November 24, 1992	US5166065	<i>In vitro</i> propagation of embryonic stem cells	Amrad (Zenyth Corporation)	26; <sup>c</sup>
March 9, 1993	US5192553	Isolation and preservation of fetal and neonatal hematopoietic stem and progenitor cells of the blood and methods of therapeutic use	Biocyte Corporation	27
June 4, 1996	US5523226	Transgenic swine compositions and methods	Biotechnology R&D Corp. and University of Illinois	29
December 31, 1996	US5589376	Mammalian neural crest stem cells	California Institute of Technology	28
September 30, 1997	US5672499	Immortalized neural crest stem cells and methods of making	California Institute of Technology	20
July 13, 1993	US5226914	Method for treating connective tissue disorders	Arnold Caplan and others (Osiris Therapeutics)	42
March 30, 1993	US5197985	Method for enhancing the implantation and differentiation of marrow-derived mesenchymal cells	Arnold Caplan and others (Osiris Therapeutics)	26
January 7, 1997	US5591625	Transduced mesenchymal stem cells	Case Western Reserve University	21
April 29, 1993	WO9308268	Methods for selectively expanding stem cells	Cellpro (Baxter)	13
June 3, 1997	US5635387	Methods and device for culturing human hematopoietic cells and their precursors	Cellpro (Baxter)	17
May 19, 1998	US5753506	Isolation, propagation and directed differentiation of stem cells from embryonic and adult central nervous system of mammals	CNS Stem Cell Technology	43
April 28, 1992	US5108753	Osteogenic devices	Creative BioMolecules (Curis)	18
October 19, 1999	US5968829	Human CNS neural stem cells	Cytotherapeutics (StemCell)	16
October 1, 2002	US6458589	Hepatocyte lineage cells derived from pluripotent stem cells	Geron Corporation	0; <sup>c</sup>
June 10, 2003	US6576464	Methods for providing differentiated stem cells	Geron Corporation	0; <sup>c</sup>
November 4, 2003	US6642048	Conditioned media for propagating human pluripotent stem cells	Geron Corporation	0; <sup>c</sup>
October 5, 2004	US6800480	Methods and materials for the growth of primate-derived primordial stem cells in feeder-free culture	Geron Corporation	0; <sup>c</sup>
April 6, 1993	US5199942	Method for improving autologous transplantation	Immunex (Amgen)	54
July 18, 2000	US6090622	Human embryonic pluripotent germ cells	Johns Hopkins University	7; <sup>c</sup>
June 12, 2001	US6245566	Human embryonic germ cell line and methods of use	Johns Hopkins University	4; <sup>c</sup>
May 13, 2003	US6562619	Differentiation of human embryonic germ cells	Johns Hopkins University	0; <sup>c</sup>
June 22, 1999	US5914268	Embryonic cell populations and methods to isolate such populations	National Jewish Center for Immunology & Respiratory Medicine	0; <sup>c</sup>
April 28, 1994	WO9409119	Remyelination using neural stem cells	Neurospheres (Novartis)	15
May 11, 1994	WO9410292	Biological factors and neural stem cells	Neurospheres (Novartis)	19
May 12, 1998	US5750376	<i>In vitro</i> growth and proliferation of genetically modified multipotent neural stem cells and their progeny	Neurospheres (Novartis)	37
December 22, 1998	US5851832	<i>In vitro</i> growth and proliferation of multipotent neural stem cells and their progeny	Neurospheres (Novartis)	31
March 18, 1997	US5612211	Stimulation, production and culturing of hematopoietic progenitor cells by fibroblast growth factors	New York University and Sloan-Kettering Institute	16
January 23, 1996	US5486359	Human mesenchymal stem cells	Osiris Therapeutics	48
June 17, 1997	US5639618	Method of isolating a lineage-specific stem cell <i>in vitro</i>	Plurion	16
March 6, 1997	WO9707668	Unactivated oocytes as cytoplasm recipients for nuclear transfer	Roslin Institute	12; <sup>c</sup>
November 14, 2000	US6147276	Quiescent cell populations for nuclear transfer in the production of non-human mammals and non-human mammalian embryos	Roslin Institute (Geron Corporation)	4; <sup>c</sup>
May 2, 1995	US5411883	Proliferated neuron progenitor cell product and process	Somatix Therapy Corporation	33
January 20, 2004	US6680198	Engraftable human neural stem cells	The Children's Medical Center Corporation	0; <sup>c</sup>
April 20, 1995	WO9510599	Embryonic stem cell-like cells	University of Melbourne	13
July 9, 1992	WO9211355	Method for culturing and transforming human stem cell-containing compositions	University of Michigan	17
March 21, 1995	US5399493	Methods and compositions for the optimization of human hematopoietic progenitor cell cultures	University of Michigan	34
August 1, 1995	US5437994	Method for the <i>ex vivo</i> replication of stem cells, for the optimization of hematopoietic progenitor cell cultures, and for increasing the metabolism, GM-CSF secretion and/or IL-6 secretion of human stromal cells	University of Michigan	22

**Table 1, continued The 50 most important stem cell patent documents published from 1992 onwards**

Publication date	Patent number	Title	Assignee (and likely current owner) <sup>a</sup>	Times cited <sup>b</sup> ; discussed in lit. <sup>c</sup>
July 8, 1997	US5646043	Methods for the <i>ex vivo</i> replication of human stem cells and/or expansion of human progenitor cells	University of Michigan	13
September 23, 1997	US5670351	Methods and compositions for the <i>ex vivo</i> replication of human hematopoietic stem cells	University of Michigan	15
October 28, 2003	US6638763	Isolated mammalian neural stem cells	University of Tennessee Research Foundation	0; <sup>c</sup>
November 7, 1995	US5464764	Positive-negative selection methods and vectors	University of Utah Research Foundation	14
May 2, 2006	US7037720	Neuroepithelial stem cells and glial-restricted intermediate precursors	University of Utah Research Foundation	0; <sup>c</sup>
September 26, 1995	US5453357	Pluripotential embryonic stem cells and methods of making same	Vanderbilt University	36; <sup>c</sup>
September 23, 1997	US5670372	Pluripotential embryonic stem cells and methods of making same	Vanderbilt University	19
November 25, 1997	US5690926	Pluripotential embryonic cells and methods of making same	Vanderbilt University	20; <sup>c</sup>
January 21, 1993	WO9301275	Novel growth factor responsive progenitor cells which can be proliferated <i>in vitro</i>	Samuel Weiss and Brent Reynolds (Novartis or Stem Cell Therapeutics)	35
February 11, 1992	US5087570	Homogeneous mammalian hematopoietic stem cell composition	Irving Weissman and others (Novartis or StemCells)	51
December 1, 1998	US5843780	Primate embryonic stem cells	Wisconsin Alumni Research Foundation	29; <sup>c</sup>
March 13, 2001	US6200806	Primate embryonic stem cells	Wisconsin Alumni Research Foundation	16; <sup>c</sup>

Patents covering critical technologies for stem cell R&D, selected based on citation rates from other patents in the core collection or on discussions in the literature. Patents are listed alphabetically by assignee.

<sup>a</sup>Likely current owner based on mergers and acquisitions or other industry information. <sup>b</sup>Times cited by other documents in the core collection. <sup>c</sup>Discussed in the literature by patent legal experts<sup>3,6,7,12,13</sup>.

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Pursuing an intellectual property clearinghouse can be a sensible business opportunity to the extent that it can increase efficiency of intellectual property agreements and technology transfer under normal conditions as well as alleviating the more severe restrictions of a patent thicket. Simply, under the conditions of a patent thicket, there is even greater latent value to unlock, making the undertaking that much more valuable. In addition, multiple efforts are not mutually exclusive. Competition among intellectual property clearinghouse initiatives and the technology platforms that they might each assemble and promote would in the end benefit everyone who hopes some day to realize the potential that stem cells hold for solving some of humanity's most intractable health problems.

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**COMPETING INTERESTS STATEMENT**

The authors declare no competing financial interests.

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