Research on Stem Cell Patent Valuation and Transfer-Transformation Strategies [Supported by Shanghai Soft Science Research Program (18692115002)] Postprint

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Abstract

Objective: To construct an indicator model for stem cell patent value assessment and analyze factors beyond indicator content that affect stem cell patent transfer and transformation in real-world scenarios. Methods: Based on the "Patent Value Analysis Indicator System" of China Technology Exchange, a patent value assessment framework suitable for stem cells was developed, employing the analytic hierarchy process to determine indicator weights and using case analysis to verify the model' s operability. Results: An indicator system for stem cell patent value assessment was established based on stem cell technical characteristics and indicator operability, comprising three primary indicators (technical value, market value, and legal value) and nine secondary indicators (including technical advancement, technical maturity, and technical cost). Technical advancement, technical maturity, policy adaptability, and market demand were identified as the most influential indicators for stem cell patent value assessment. In analyzing other factors, core technical advantage emerged as the key determinant affecting stem cell patent transfer and transformation, while technical feasibility, quality control, and long-term returns also significantly impact successful transfer and transformation of stem cell technology. Conclusion: The patent value assessment model and factor analysis developed in this study can be applied to patent valuation in the stem cell domain, facilitating effective development and industrialization of patented technologies.

Full Text

Preamble

Research on Stem Cell Patent Value Evaluation and Transfer Transformation Strategies

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Abstract

Objective: To construct an indicator model for stem cell patent value evaluation and analyze factors affecting stem cell patent transfer and transformation beyond the indicator content in real-world scenarios.
Methods: Based on the Patent Value Analysis Indicator System developed by China Technology Exchange, we constructed a patent evaluation system suitable for stem cells, determined weights using the Analytic Hierarchy Process (AHP), and verified the operability of the indicator model through case analysis.
Results: An indicator system for evaluating stem cell patents was established based on the technical characteristics of stem cells and indicator operability, comprising three first-level indicators (technical value, market value, and legal value) and nine second-level indicators (including technological advancement, technological maturity, and technical cost). Technological advancement, technological maturity, policy adaptability, and market demand were identified as the most influential indicators for stem cell patent value evaluation. In analyzing other factors, the core technical advantage emerged as the key determinant affecting stem cell patent transfer and transformation. Additionally, technical feasibility, quality control, and long-term benefits all significantly impact the successful transfer and transformation of stem cell technologies.
Conclusion: The patent value evaluation model and factor analysis established in this paper can be applied to patent value assessment in the stem cell field, helping to promote effective development and industrialization of patented technologies.

Keywords: Stem Cells; Patent Evaluation; Transfer and Transformation

Introduction

Since the world' s first bone marrow transplant in 1968, stem cell technology officially entered the clinical application stage. Over the past half-century, stem cell technology has been widely used in treating various diseases including cancer, diabetes, Parkinson' s disease, and respiratory diseases, with multiple stem cell therapy drugs receiving regulatory approval. According to a market research report by Markets and Markets, the global stem cell manufacturing market was valued at $10.19 billion in 2017 and is projected to grow at a compound annual growth rate of 6.3% over the next five years, reaching an estimated $14.61 billion by 2023. Given the broad application prospects and enormous market potential of stem cell technology, numerous research institutions and enterprises have invested heavily in this innovative medical technology, yielding

significant research achievements and actively pursuing patent applications for technological layout.

Analysis using the Clarivate Analytics patent search platform Thomson Innovation reveals that from 2008 to 2017, global patent applications in the stem cell field maintained a consistently high volume, totaling 102,349 applications. China accounted for 12,666 applications (12.4% of the global total), with a rapid growth rate averaging 7.8% annually from 2008 to 2016 (2017 data was excluded from growth calculations due to database collection delays and patent publication review timelines). [Figure 1: see original paper]

Stem cell patent applications were filed in nearly 70 countries or regions worldwide. The top five jurisdictions were the United States, China, Japan, South Korea, and Australia, forming a strong competitive landscape in stem cell technology. The United States, as the largest filer, had 24,540 applications, with 58,077 applications claiming US priority—approximately seven times that of China, which ranked second. This demonstrates America' s absolute advantage in stem cell research and market deployment. China filed 12,328 applications, with 8,608 claiming Chinese priority, ranking second globally. Since priority countries generally represent the source of technological innovation, this indicates that beyond foreign institutions'patent deployment in China, China has developed abundant independent innovations in stem cell technology. In terms of patent holder distribution, universities and research institutions remain China' s primary patent owners, accounting for 86% of the top 20 domestic patent holders in the stem cell field.

Despite China' s high patent application volume, most patents have not realized practical value in further R&D, industrial application, or patent portfolio development. The transfer and transformation of stem cell patents remain insufficient, with a disconnect between the growing technological achievements of innovators and market demand, constraining the development of stem cell technology and industrialization. The *Amendment to the Law for Promoting the Transformation of Scientific and Technological Achievements (Draft)* published in early 2015 stipulated that "research institutions and higher education institutions established by the state shall strengthen management, organization, and coordination of scientific and technological achievement transformation, build transformation teams, optimize processes, and conduct technology transfer through internal technology transfer offices or independent technology transformation service agencies."In this context, the importance of enhancing intellectual property utilization capabilities through patent operations has become increasingly prominent, with patent value evaluation and transfer transformation strategy formulation comprising critical components of patent operations. This paper constructs a stem cell patent value evaluation model based on the Patent Value Analysis Indicator System developed by China Technology Exchange, combined with characteristics of the stem cell field. Additionally, we summarize key elements for enhancing the competitiveness of stem cell patent transfer and transformation based on development characteristics and practical

issues in industrial transfer, providing references for patent management and transfer transformation in the stem cell technology field.

1.1 Information Sources

Patent literature searches were conducted primarily using the National Intellectual Property Administration' s patent search system, Clarivate Analytics' Thomson Innovation platform, and the incoPat database. Journal literature was searched using CNKI, Wanfang Data, and Web of Science. Additionally, company market analysis reports, national policy information, and institutional official news served as important information sources.

1.2 Analytical Methods

This paper employs indicator analysis for stem cell patent value evaluation, optimizing the Patent Value Analysis Indicator System from China Technology Exchange to create a patent value evaluation indicator system suitable for the stem cell field. Thirteen experts from the Chinese Academy of Sciences (including five stem cell researchers, five patent management professionals, and three life science information researchers) were invited to score indicator importance, with final weights determined using AHP. To verify the model' s operability, we conducted a case analysis on the patent "Small Molecule Compound Composition for Efficiently Inducing Differentiation of Human Pluripotent Stem Cells into Cardiomyocytes" (Application No. 201610038160.4), demonstrating application considerations.

Additionally, expert interviews were conducted with CAS stem cell specialists regarding patent transfer and transformation, summarizing factors beyond the evaluation system that affect stem cell patent transfer and transformation.

2.1.1 Indicator Selection

Through investigation of existing domestic patent value evaluation systems, the Patent Value Analysis Indicator System developed by China Technology Exchange demonstrates high recognition and practicality, making it suitable as a reference for stem cell patent evaluation indicator selection. However, its evaluation criteria are not fully applicable to the stem cell field—some indicators lack representativeness, some are overly subjective with difficult data acquisition, and the excessive number of indicators hinders control of time and labor costs. Therefore, beyond comprehensiveness and scientific rigor, this paper prioritized whether indicators reflect stem cell technology characteristics and demonstrate good operability.

At the technical value dimension, we retained technological advancement, technological maturity, and technical substitutability while adding technical cost to evaluate stem cell patent technical value. For technological advancement, stem cell technologies demonstrate varying advancement levels across different

processes (isolation/purification, culture, preservation/transportation, modification, characterization, induction, differentiation, transplantation) and disease applications. For example, hematopoietic stem cell transplantation has become a widely used leukemia treatment globally, while stem cell research for Alzheimer' s disease remains in early stages. For technological maturity, the clinical stage is a crucial evaluation criterion—as a therapeutic technology approaches market launch, risks decrease and value increases. For technical substitutability, lower substitutability indicates greater monopoly value and higher potential industrialization returns. For technical cost, different technologies involve varying raw materials, equipment, risk costs, and labor costs, all affecting stem cell value.

At the economic value dimension, since stem cells represent an emerging field with clinical applications in early stages, long-term market value is the primary focus, making direct evaluation of market application, share, and competition difficult. We retained market size prospects and policy adaptability while adding market demand to evaluate economic value. For market demand, different stem cell products target different patient populations—diseases with large patient populations, wide incidence, and lack of effective treatments create greater market demand and value. For market size, this reflects economic factors beyond demand, including pricing. Products with large market demand and high pricing demonstrate greater market size and long-term returns. For policy adaptability, this is a critical consideration in stem cell patent value evaluation. Following China' s "stem cell chaos" period, clinical research has gradually opened. On April 11, 2017, China' s first two officially registered stem cell clinical research projects ("Neural Progenitor Cells Derived from Human Embryonic Stem Cells for Parkinson' s Disease" and "Retinal Pigment Epithelial Cells Derived from Human Embryonic Stem Cells for Dry Age-Related Macular Degeneration") launched at the First Affiliated Hospital of Zhengzhou University. On December 22, 2017, the CFDA released the *Technical Guidelines for Research and Evaluation of Cell Therapy Products (Trial)*, marking the beginning of a comprehensive, orderly era of stem cell clinical treatment in China. However, no stem cell drugs have been approved domestically, and future policy tightening remains possible, significantly impacting stem cell technology application and patent value.

At the legal value dimension, we merged patent stability, design-around potential, dependency, and infringement detectability into a single patent protection strength indicator for clarity and focus, while retaining patent term for legal value evaluation. For patent protection strength, this comprehensively reflects four factors—stability (for ungranted patents, likelihood of grant through three-pronged analysis; for granted patents, ability to withstand invalidation requests), design-around potential, dependency, and infringement detectability. Stronger protection indicates higher value. For patent term, longer remaining protection for granted patents indicates higher value.

2.1.2 Indicator System Establishment

After selecting evaluation indicators across three dimensions, we defined each indicator clearly and established baseline values and scoring scales for future application.

2.1.3 Indicator Weight Determination

The Analytic Hierarchy Process (AHP) converts multi-objective, multi-criteria decision problems that are difficult to quantify into multi-level single-objective problems, providing a concise and practical method suitable for calculating indicator weights. We designed the "Mesenchymal Stem Cell Patent Value Evaluation Indicator Expert Scoring Form" and invited 13 CAS experts (five stem cell researchers, five patent managers, and three information researchers) to score indicator importance, yielding 10 valid responses. As AHP methodology is well-established, detailed calculation processes are omitted. Consistency tests were performed on all expert responses; inconsistent results were adjusted using the maximum direction improvement method to obtain final indicator weights. Weighted averages of the 10 expert ranking vectors were calculated and normalized to produce final weights.

The resulting stem cell patent value evaluation model reveals that technological advancement, technological maturity, policy adaptability, and market demand are the four most important indicators, with policy adaptability considered the most influential. This demonstrates that national clinical approval processes, industrial support, and successful product launch and clinical application significantly impact Chinese stem cell patent value.

2.1.4 Case Analysis

The patent "Small Molecule Compound Composition for Efficiently Inducing Differentiation of Human Pluripotent Stem Cells into Cardiomyocytes" (Application No. 201610038160.4) from the Shanghai Institute of Life Sciences, Chinese Academy of Sciences, shows strong transfer transformation potential and is a priority for institutional transfer. We evaluated this patent using our model.

Since the patent is not yet granted, the "patent term" indicator was excluded, making the total weighted score 9 points. For intuitive comparison, results were converted to a 10-point scale. Through in-depth analysis of technical, market, and legal value dimensions, the patent scored 8.15 points. The evaluation process requires objective assessment based on literature, patent, and product research data to avoid subjective speculation. Taking the technical value dimension as an example:

For technological advancement, the patent uses a small molecule composition containing mTOR pathway inhibitors and Wnt pathway promoters for induced differentiation. Research on these compounds in cardiomyocyte differentiation has primarily emerged in the last three years, particularly regarding the mTOR

inhibitor rapamycin, with key results published in 2017, representing the field' s most advanced achievements. For technological maturity, while the patent uses human embryonic stem cell lines (H9-cTnT-eGFP, H9, H7) and human pluripotent stem cell line U-Q1—advancing beyond animal cell experiments—it has not entered clinical trials, indicating room for maturity improvement. For technical cost, the method adds small molecule compounds to culture medium to promote differentiation, offering lower operational difficulty than cell transfection methods and higher stability than cytokine induction methods. The patent description notes this method can save half the culture medium and additives, effectively controlling costs. For technical substitutability, while small molecule-based cardiomyocyte differentiation methods have research foundations, this patent achieves differentiation rates above 90%, significantly higher than existing journal articles and patents (e.g., patent CN201110286477.7 achieved maximum 40% differentiation rate). Therefore, while alternative technologies exist, this patent holds functional advantages.

Accordingly, we scored the patent' s technical value dimension: technological advancement (9 points), technological maturity (3 points), technical cost (7 points), and technical substitutability (7 points).

2.2 Other Factors in Stem Cell Patent Transfer and Transformation

Patent transfer and transformation involves subsequent experimentation, development, application, and promotion to create new products, processes, materials, and industries. As one of the most complex therapeutic products in pharmaceutical history, stem cells present challenges for both developers and regulators. Unlike chemically defined drugs such as chemical medicines and antibiotics, stem cell products' dynamic and heterogeneous nature requires additional considerations from both transfer parties. While the 2017 *Technical Transfer Service Specification* national standard by the Torch High Technology Industry Development Center of the Ministry of Science and Technology, WHO' s *Guidelines on Transfer of Technology in Pharmaceutical Manufacturing*, and ISPE' s new drug transfer guidelines address pharmaceutical technology transfer, no literature, guidelines, or standards specifically address factors in stem cell patent technology transfer. Based on stem cell technology characteristics and interviews with multiple CAS stem cell transfer experts, we analyze factors beyond the patent value evaluation model that, while not reflected in patent texts, are closely related to stem cell patent value. Detailed data provision by technology providers on these factors can significantly facilitate transfer and transformation.

2.2.1 Patent Core Advantage We consider a patent' s technological innovation point and characteristics as its core advantage—the decisive factor for successful transfer and transformation. Both parties must clearly understand the patent' s core innovation, technical advantages, and limitations, and assess its match with transfer objectives. Using the previously evaluated patent "Small

Molecule Compound Composition for Efficiently Inducing Differentiation of Human Pluripotent Stem Cells into Cardiomyocytes" (CN201610038160.4) as an example, we analyze its core advantages through in-depth examination of claims and description content against current field developments.

2.2.2 Technical Feasibility Factors When deciding on stem cell technology transfer, the technology recipient first conducts reproducibility verification experiments to confirm whether the technology quality matches patent descriptions. Key considerations include ethical compliance, resource matching between parties, technical operability, and equipment/personnel requirements. Technological maturity from the evaluation model is revisited here as a crucial feasibility factor—stem cell technologies or products that have entered clinical trials face lower investment risks and higher likelihood of market launch.

2.2.3 Quality Control Factors For stem cell patent transfer and transformation, especially for patented products, quality control throughout the product or technical process is a critical consideration. Referencing the *General Requirements for Stem Cells* released by the Chinese Society for Cell Biology in December 2017, transfer parties must comprehensively consider quality characteristics, raw materials, excipients, and risk control.

2.2.4 Long-term Benefit Factors Most stem cell patented technologies or products are not yet marketed or even in clinical stages, so recipients seek long-term benefits. Market factors are primary considerations, alongside transfer-generated costs and payback periods. Comprehensive risk control throughout the process ensures smooth transfer and transformation.

Conclusion

This paper' s stem cell patent value evaluation model optimizes existing indicator systems by incorporating stem cell technology development characteristics, evaluating patent value across technical, market, and legal dimensions, enabling scoring for patent classification management. In applying indicator analysis, in-depth understanding of evaluated patent technologies and objective analysis of patent text protection capabilities are crucial. Existing literature often focuses on patent analysis methods or indicator systems while neglecting domain applicability and patent content analysis importance. Using the patent "Small Molecule Compound Composition for Efficiently Inducing Differentiation of Human Pluripotent Stem Cells into Cardiomyocytes" as an example, we demonstrated the model' s application—practically executable through collaboration between patent analysts and stem cell experts. Furthermore, in actual transfer processes, technology recipients often require additional information from providers, including ethical compliance, experimental procedures, equipment, and undisclosed technical details (technical feasibility factors); product stability, raw material and excipient sources (quality control factors); and technology-

recipient matching and potential value (long-term benefit factors). Stem cell researchers and patent managers can reference this paper to improve patent management efficiency and proactivity in transfer transformation, thereby promoting technology transfer.

References

[1] Meuwissen H J, Gatti R A, Terasaki P I, et al. Treatment of lymphopenic hypogammaglobulinemia and bone-marrow aplasia by transplantation of allogeneic marrow. Crucial role of histocompatiility matching, New England Journal Of Medicine, 1969, 281(13).

[2] Bacakova L, Zarubova J, Travnickova M, et al. Stem cells: their source, potency and use in regenerative therapies with focus on adipose-derived stem cells - a review. Biotechnology Advances, 2018, 36(4): 1111-1126.

[3] Stem Cell Manufacturing Market by Product (HSCs, MSCs, iPSCs, ESCs, Instruments, Media, Consumables), Application (Research, Target Identification, Therapy (Autologous, Allogeneic), Cell Banks), End User (Pharma, Hospitals) - Global Forecast to 2023. [2018-3-31]. https://www.marketsandmarkets.com/Market-Reports/stem-cell-manufacturing-market-70743403.html.

[4] Huo G Q. The sticking points and solutions of China' s scientific and technological achievement transformation. Think Tank: Theory & Practice, 2016, 1(2): 119-125.

[5] Amendments to the law for promoting the transformation of scientific and technological achievements (Draft). [2015-3-2]. http://www.npc.gov.cn/npc/xinwen/lfgz/flca/2015-03/02/content_{1906948}.htm

[6] China Technology Exchange. Operating Manual of Patent Value Analysis Indicator System. Beijing: Intellectual Property Publishing House, 2012: 5-32.

[7] de Alvarenga E C, Silva W N, Vasconcellos R, et al. Promyelocytic leukemia protein in mesenchymal stem cells is essential for leukemia progression. Annals of Hematology, 2018, 97(10): 1749-1755.

[8] Cao N, Liao T L, Liu J J, et al. Clinical-grade human umbilical cord-derived mesenchymal stem cells reverse cognitive aging via improving synaptic plasticity and endogenous neurogenesis. Cell Death & Disease, 8(8): e2996.

[9] The first clinical research projects on embryonic stem cells in China were launched today. [2017-4-11]. http://politics.people.com.cn/n1/2017/0411/c1001-29202930.html.

[10] Ding J Y, Lu Y. Patent evaluation and analytic hierarchy process (AHP). Patent Literature Research, 2007, 6: 1-7.

[11] Qiu X X, Liu Y, Zhang Y F, et al. Rapamycin and CHIR99021 Coordinate Robust Cardiomyocyte Differentiation From Human Pluripotent Stem

Cells Via Reducing p53-Dependent Apoptosis. JOURNAL OF THE AMERICAN HEART ASSOCIATION, 2017, 10(6): e005295.

[12] Lu Q, Liu Y A, Wang Y, et al. Rapamycin efficiently promotes cardiac differentiation of mouse embryonic stem cells. [2017-6-7]. http://www.bioscirep.org/content/ppbioscirep/37/3/BSR2

[13] Xiamen University. Method for inducing cardiac differentiation of stem cells by utilizing small molecule compounds. CN104447417A. 2015-03-25 [2018-08-18]. http://www.pss-system.gov.cn/sipopublicsearch/patentsearch/showViewList-jumpToView.shtml.

Note: Figure translations are in progress. See original paper for figures.