

Observing the Intellectual Landscape and New Developments of Drugs

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Drug development is a broad research field involving biological therapies, stem cell treatments and tissue engineering. As research in these areas advances rapidly, this study aimed to investigate the thematic patterns, landmark articles and emerging trends in drug development for observing its intellectual landscape through a scientometric analysis. Five critical articles, representative clusters and three pivotal references were explored. Burst detections of citations also provided insightful guidance for navigating the fast-changing intellectual landscape of the relevant literature. This study not only elucidates research themes in the drug development community, but also helps demonstrate how research interests and trends evolve over time.

Keywords: Drug development, Scientometrics, Intellectual landscape, Cluster visualization.

Introduction

Drug development is a broad research field involving biological therapies, stem cell treatments and tissue engineering¹. The potential of reprogramming patients' own cells for biological therapy, tissue repair and regeneration is critical to drug developments². As research in these areas advances rapidly, this study aimed to detect the thematic patterns, landmark articles and new developments in drug research for identifying its intellectual landscape through a scientometric analysis.

Method and Data

Scientometric tool

Our analysis was guided by a scientometric method implemented in *CiteSpace*³. *CiteSpace* is used to generate and analyze networks of co-cited references based on bibliographic records retrieved from the Web of Science Core Collection (WoSCC). Through *CiteSpace*'s network modeling and visualization, intellectual landscape and new developments are computationally detected and visually depicted.

Network modeling and visualization

CiteSpace characterizes an intellectual landscape and emerging trends in a co-citation network in terms

of a variety of visual attributes. The size of a node indicates how many citations the associated reference has received. The thickness of the purple ring indicates the degree of its *betweenness centrality*. Citation rings in red indicate the time slices in which citation bursts are detected.

Bibliographic records

The 9,760 records published between 2000 and 2015 were retrieved from the WoSCC. The search records, consisting of original research articles and review articles, include information on the titles, authors, keywords, abstracts, journals, years, and other publication information.

Intellectual Landscape and New Developments

Top-cited articles

Based on the document co-citation analysis in *CiteSpace*, the five top-cited articles between 2000 and 2015 are summarized in Table 1. The first work is by Takahashi and Yamanaka⁴, who demonstrated how pluripotent stem cells can be directly generated from mouse somatic cells by introducing only a few defined factors. The second work⁵, by the same group of researchers, further demonstrated how differentiated human somatic cells can be reprogrammed into pluripotent stem cells using the same factors.

Cluster visualization

The nodes in the clusters represent cited references from the collected articles, and the links between the

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Table 1 — Five critical articles					
Citation frequency	Title	Author	Year	Betweenness centrality	Journal
1,151	Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors	Takahashi K & Yamanaka S	2006	0.01	Cell
1,057	Induction of pluripotent stem cells from adult human fibroblasts by defined factors	Takahashi K, et al.	2007	0.00	Cell
1,014	Embryonic stem cell lines derived from human blastocysts	Thomson J A, et al.	1998	0.11	Science
1,000	Multilineage potential of adult human mesenchymal stem cells	Pittenger M F, et al.	1999	0.03	Science
772	Induced pluripotent stem cell lines derived from human somatic cells	Yu J, et al.	2007	0.00	Science

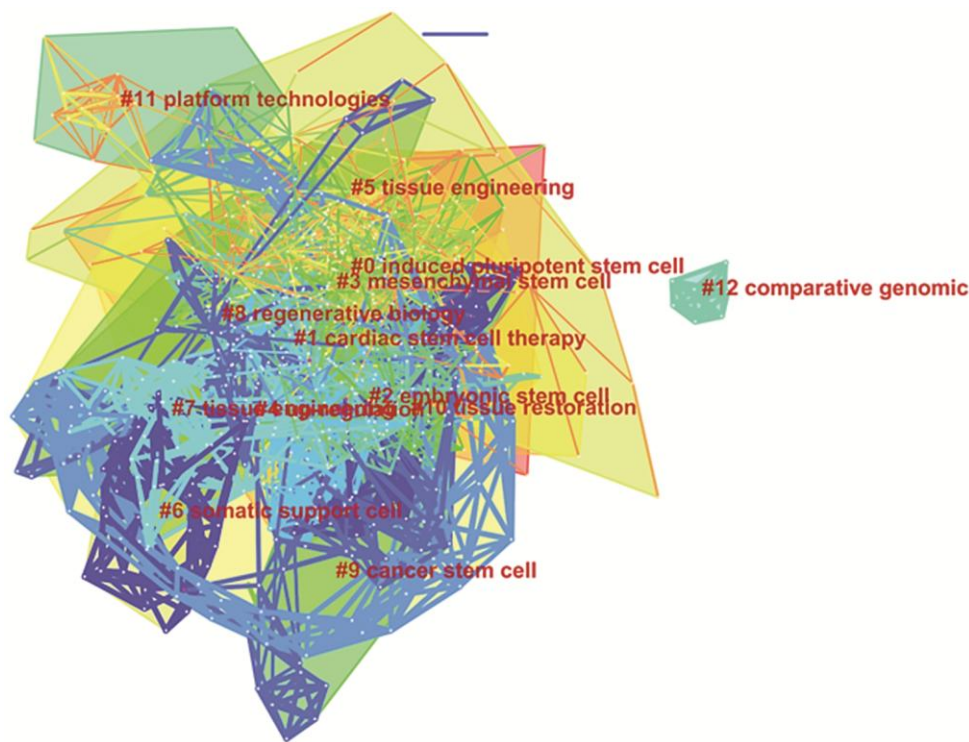


Fig. 1 — Cluster visualization based on a document co-citation network

nodes represent how often they are cited by the same articles. As shown in **Error! Reference source not found.**, the co-citation network consists of 23 clusters, 651 unique nodes and 5,338 links. Table also lists the top ranked clusters in details. As shown in **Error! Reference source not found.**, *induced pluripotent stem cell* and *myocardial infarction* are the two largest clusters. *Platform technologies* is the youngest clusters. The largest cluster, *induced pluripotent stem cell* (#0), consists of 107 member articles. According to the key citers in this cluster⁶, researchers interested in induced pluripotent stem cell (iPSC) focus on methods of iPSC production. Therefore, research works related to iPSC shape the foundation of the intellectual landscape. The second largest cluster (#1), *myocardial infarction*, has

103 member articles. According to the key citers in this cluster⁷, the discovery of cardiac stem cells that reside in the heart itself brings new prospects. The term *platform technologies* are the newest cluster, which has 16 member articles and an average year of 2009. Thus, research works related to *platform technologies* reflect the recent developments in the intellectual landscape of drug research.

Clusters with the strongest citation bursts

A citation burst is an indicator of a most active area of research. Fig. 2 shows four clusters—cluster #0, cluster #3, cluster #5 and cluster #11—with the strongest citation bursts. These clusters represent the major efforts of the research in this field since 2002. Cluster #0 is labeled as *induced pluripotent stem cell*.

Table 2 — Selected clusters

ID	Size	Silhouette	Label (TFIDF)	Label (LLR)	Label (MI)	Mean (cited year)
0	107	0.90	induced transdifferentiation	induced pluripotent stem cell	recent application	2008
1	103	0.65	cardiac stem cell	myocardial infarction	establishment	2000
2	96	0.63	transcriptional regulation	embryonic stem cell	exercise	2001
5	33	0.98	nanostructure	tissue engineering	engineering material	2005
11	16	0.99	tissue decellularization, cell sheet engineering	platform technologies	low oxygen tension	2009

TFIDF: term frequency-inverse document frequency
LLR: log-likelihood tests
MI: mutual information tests

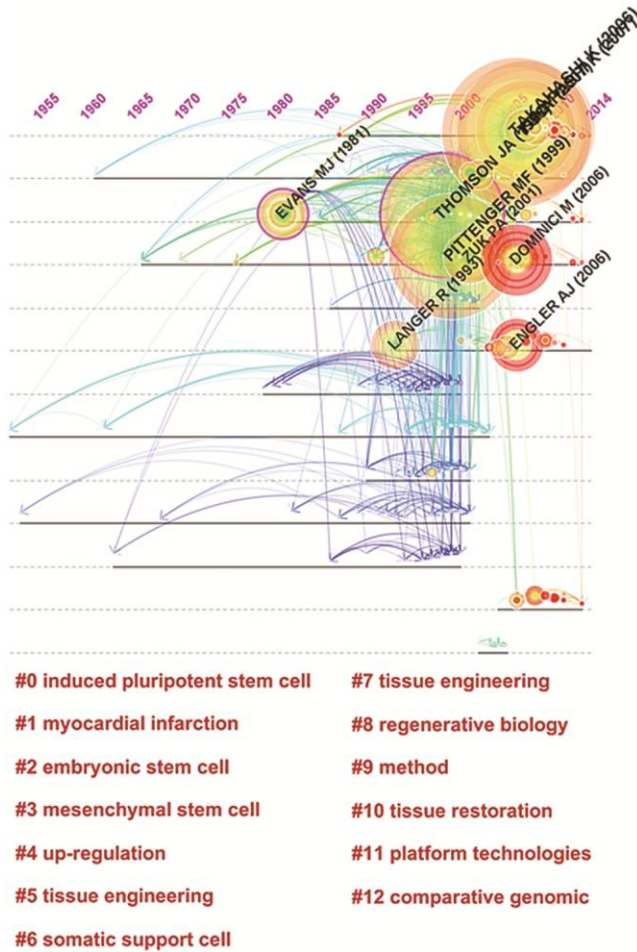


Fig. 2 — Timeline view

A common theme to this cluster is the derivation of human iPSCs with the use of nonintegrating episomal vectors⁹. Cluster #3 is labeled *mesenchymal stem cell*. A common theme to this cluster is the potential use of mesenchymal stem cell-based therapies¹⁰. Cluster #5 is labeled *tissue engineering*. A common theme to this cluster is the synthetic methods or microfabrication techniques of scaffold materials for tissue engineering applications¹¹. Cluster #11 is labeled *platform*

technologies. A common theme to this cluster is the creation of decellularized organs¹².

Conclusions

This scientometric analysis has revealed the intellectual landscape and new developments of drug research. Five critical articles were detected out of the 9,760 bibliographic records based on document co-citation analysis. According to the cluster visualizations, research works related to *induced pluripotent stem cell* and *myocardial infarction* shape the foundation of the intellectual landscape. Research works related to *platform technologies* reflect the recent research forefront of drug developments. The burst detection also provides insightful guidance for navigating through the fast-changing intellectual landscape of the relevant literature. Future research may incorporate an expanded dataset through forward-citation links to scientometric analysis.

References

- 1 Anitua E, Troya M, Zalduendo M, Tejero R & Orive G, Progress in the use of autologous regenerative platelet-based therapies in implant dentistry, *Curr Pharm Biotechnol*, **17** (2016) 402-413.
- 2 Zhang F, Lu M, Liu H, Ren T, Miao Y & Wang J, Sertoli cells promote proliferation of bone marrow-derived mesenchymal stem cells in co-culture, *Indian J Exp Biol*, **54** (2016) 309-314.
- 3 Lee Y C, Chen C & Tsai X T, Visualizing the knowledge domain of nanoparticle drug delivery technologies: A scientometric review, *Appl Sci*, **6** (2016) 1-14.
- 4 Takahashi K & Yamanaka S, Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors, *Cell*, **126** (2006) 663-676.
- 5 Takahashi K, Tanabe K, Ohnuki M, Narita M, Ichisaka T, Tomoda K & Yamanaka S, Induction of pluripotent stem cells from adult human fibroblasts by defined factors, *Cell*, **131** (2007) 861-872.
- 6 Masip M, Veiga A, Belmonte J C I & Simón C, Reprogramming with defined factors: from induced pluripotency to induced transdifferentiation, *Mol Hum Reprod*, **16** (2010) 856-868.

- 7 Lee S & Yoon Y S, Revisiting cardiovascular regeneration with bone marrow-derived angiogenic and vasculogenic cells, *Brit J Pharmacol*, **169** (2013) 290-303.
- 8 Yeo J-C & Ng H-H, The transcriptional regulation of pluripotency, *Cell Res*, **23** (2013) 20-32.
- 9 Yu J, Hu K, Smuga-Otto K, Tian S, Stewart R, Slukvin I I & Thomson J A, Human induced pluripotent stem cells free of vector and transgene sequences, *Science*, **324** (2009) 797-801.
- 10 Dominici M, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini F, Krause D, Deans R, Keating A, Prockop D & Horwitz E, Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement, *Cytotherapy*, **8** (2006) 315-317.
- 11 Slaughter B V, Khurshid S S, Fisher O Z, Khademhosseini A & Peppas N A, Hydrogels in regenerative medicine, *Adv Mater*, **21** (2009) 3307-3329.
- 12 Takebe T, Sekine K, Enomura M, Koike H, Kimura M, Ogaeri T, Zhang R-R, Ueno Y, Zheng Y-W & Koike N, Vascularized and functional human liver from an iPSC-derived organ bud transplant, *Nature*, **499** (2013) 481-484..