Follicle and melanocyte stem cells, and their application in neuroscience

A Web of Science-based literature analysis

Weifu Wu

Department of Dermatology, Jinzhou Central Hospital, Jinzhou 121001, Liaoning Province, China

Abstract

OBJECTIVE: To identify global research trends of follicle and melanocyte stem cells, and their application in neuroscience.

DATA RETRIEVAL: We performed a bibliometric analysis of studies from 2002 to 2011 on follicle and melanocyte stem cells, and their application in neuroscience, which were retrieved from the Web of Science, using the key words follicle stem cell or melanocyte stem cell, and neural, neuro or nerve.

SELECTION CRITERIA: Inclusion criteria: (a) peer-reviewed published articles on follicle and melanocyte stem cells, and their application in neuroscience, which were indexed in the Web of Science; (b) original research articles, reviews, meeting abstracts, proceedings papers, book chapters, editorial material, and news items. Exclusion criteria: (a) articles that required manual searching or telephone access; (b) documents that were not published in the public domain; and (c) a number of corrected papers from the total number of articles.

MAIN OUTCOME MEASURES: (1) Distribution of publications on follicle and melanocyte stem cells by years, journals, countries, institutions, in China, and most cited papers. (2) Distribution of publications on the application of follicle and melanocyte stem cells in neuroscience by years, journals, countries, institutions, and most cited papers.

RESULTS: Of the 348 publications from 2002 to 2011 on follicle and melanocyte stem cells, which were retrieved from the Web of Science, more than half were from American authors and institutes. The most prolific institutions in China for publication of papers on follicle and melanocyte stem cells were the Fourth Military Medical University and Third Military Medical University. The most prolific journals for publication of papers on follicle and melanocyte stem cells were the Journal of Investigative Dermatology, Pigment Cell & Melanoma Research. Of the 63 publications from 2002 to 2011 on the application of follicle and melanocyte stem cells in neuroscience, which were retrieved from the Web of Science, more than half were from American authors and institutes, and no papers were from Chinese authors and institutes. The most prolific journals for publication of papers on the application of follicle and melanocyte stem cells in neuroscience were the Journal of Investigative Dermatology, Pigment Cell & Melanoma Research.

CONCLUSION: Based on our analysis of the literature and research trends, we found that follicle stem cells might offer further benefits in neural regenerative medicine.

Key Words
skin stem cell; follicle stem cell; melanocyte stem cell; skin-derived precursor; neural crest stem cell; neuron; glial cell; differentiation; bibliometric; neural regeneration

Research Highlights
(1) We performed a bibliometric analysis of studies from 2002 to 2011 on follicle and melanocyte stem cells, and their application in neuroscience, which were retrieved from the Web of Science.
We analyzed the publication year, journals, countries, institutions, and institutions in China. Specifically, we analyzed all the data on follicle and melanocyte stem cells, and their application in neuroscience.

**INTRODUCTION**

Skin covers the surface of the body, and is the largest of all organs. It is composed of the epidermis, dermis, and subcutaneous tissue and appendages. The antigenicity of skin stem cells is weak, and they not only have the ability to self-renew, they also have multipotency and a strong proliferative ability. Skin stem cells can differentiate into various cells to repair cutaneous deficiencies, such as the cells of the skin, hair follicles, and sweat and sebaceous glands\(^1-3\).

**Data retrieval**

Follicle stem cells are located in the outer root sheath, i.e. the hair follicle bulge of the lower part of sebaceous glands. Follicle stem cells not only move downward to hair follicle roots to form hair follicles, but can also migrate upward from the hair follicle outer root sheath to generate the epidermis. These cells can even differentiate into neural crest stem cells and subsequently generate neurons and glial cells. Neural crest stem cells can also differentiate into melanocytes and smooth muscle cells, and can promote the repair of injured nerves. When neural crest stem cells in the hair follicle bulge are transplanted into injured peripheral nerves, they can promote axon growth and recovery of nerve functions. Thus, follicle stem cells can be used to repair spinal and auditory nerves to treat spinal cord injury and hearing disorders, respectively, and neurological degeneration\(^4-8\). Follicle stem cells proliferate rapidly in vitro and survive in long-term culture, do not show immunological rejection, and are not hindered by ethical issues. Thus, they can be used in regenerative medicine\(^9\). Melanocyte stem cells are also widely distributed in the hair follicle bulge. At present, there are relatively few studies of their application in neuroscience.

In this study, we analyzed the research trends of follicle and melanocyte stem cells, and their application in neuroscience, based on a bibliometric analysis of the papers in the Web of Science published from 2002 to 2011.

**DATA SOURCES AND METHODOLOGY**

This study used bibliometric analyses to quantitatively and qualitatively investigate research trends of studies on follicle and melanocyte stem cells, and their application in neuroscience. We searched the Web of Science, a research database of publications and citations selected and evaluated by the Institute for Scientific Information in Philadelphia, PA, USA, using the keywords follicle stem cell or melanocyte stem cell, and neural, neuro or nerve. We limited the publication period from 2002 to 2011, and compiled a bibliography of all articles related to follicle melanocyte stem cells, and their application in neuroscience. We downloaded the data on September 4\(^{\text{th}}\), 2012.

**Inclusion criteria**

The inclusion criteria are as follows: (1) published peer-reviewed articles on follicle and melanocyte stem cells, and their application in neuroscience, including original research articles, reviews, meeting abstracts, proceedings papers, book chapters, editorial material, and news items, which were indexed in the Web of Science; (2) the years of publication were 2002–2011; and (3) the citation database was Science Citation Index Expanded.

**Exclusion criteria**

We excluded articles that required manual searching or telephone access, documents that were not published in the public domain, and a number of corrected papers from the total number of articles analyzed.

The outcomes of all articles referring to skin stem cells were assessed using the following criteria. (a) Annual publication output of papers on follicle and melanocyte stem cells. (b) Distribution of publications on follicle and melanocyte stem cells by journals. (c) Distribution of publications on follicle and melanocyte stem cells by countries. (d) Distribution of publications on follicle and melanocyte stem cells by institutions. (e) Distribution of publications on follicle and melanocyte stem cells by institutions in China. (f) Most cited papers on follicle and melanocyte stem cells in the Web of Science from 2002 to 2011. (g) Annual publication output of papers on the application of follicle and melanocyte stem cells in neuroscience. (h) Distribution of publications on the application of follicle and melanocyte stem cells in neuroscience by journals. (i) Distribution of publications on the application of follicle and melanocyte stem cells in neuroscience by countries. (j) Distribution of publications on the application of follicle and melanocyte stem cells in
neuroscience by institutions. (k) Most cited papers on the application of follicle and melanocyte stem cells in neuroscience in the Web of Science from 2002 to 2011.

RESULTS

Annual publication output of papers related to follicle and melanocyte stem cells in the Web of Science from 2002 to 2011

A total of 348 publications on follicle and melanocyte stem cells from 2002 to 2011 were retrieved from the Web of Science. The number of relevant publications increased over the 10-year study period, in which five papers were published and included in the Web of Science in 2002, followed by an increase in the number of published papers to 72 in 2011. However, the numbers of papers published slightly decreased in 2007 (Figure 1).

Distribution of output by journal for publications on follicle and melanocyte stem cells in the Web of Science from 2002 to 2011

The Journal of Investigative Dermatology published 52 papers, followed by Pigment Cell & Melanoma Research, and Cell Stem Cell, which published 19 and 15 papers, respectively (Table 1). The next seven top journals were Development, Proceedings of the National Academy of Sciences of the United States of America, Cell, Experimental Dermatology, British Journal of Dermatology, American Journal of Dermatopathology, and Nature.

Distribution of output by country for publications on follicle and melanocyte stem cells in the Web of Science from 2002 to 2011

As shown in Figure 2, it was clear that most papers on follicle and melanocyte stem cells were published in the USA (191 papers), followed by Japan (79 papers). China published 12 papers and ranked 6th. The other prolific countries were the UK, Germany, Canada, Switzerland, France, Australia, and Italy.

Distribution of output by institution for publications on follicle and melanocyte stem cells in the Web of Science from 2002 to 2011

The University of California system and University of Pennsylvania in the USA were the most prolific research institutes (Table 2). Eight of the top 11 research institutes publishing in this field were in the USA, and the other three institutes were in Japan, the UK and Germany, respectively.
As shown in Table 3, the Fourth Military Medical University and Third Military Medical University were the most prolific research institutes in China for the publication of papers on follicle and melanocyte stem cells in the Web of Science from 2002 to 2011. Each university published three papers. So far at least, the number of papers on follicle and melanocyte stem cells published by Chinese institutions was very few.

Highly cited papers on follicle and melanocyte stem cells in the Web of Science from 2002 to 2011
A total of 348 papers on follicle and melanocyte stem cells were cited in the Web of Science from 2002 to 2011. “Capturing and profiling adult hair follicle stem cells”, published in 2004 by Nature Biotechnology [10], was cited 479 times, which was more citations than any other paper. Of the 10 most cited papers, four were published in Nature, two were published in Proceedings of the National Academy of Sciences of the United States of America, and the remaining four papers were published in four different journals. Of these 10 most cited papers, five were published in 2005, and one each was published in 2002, 2003, 2004, 2007, and 2008 (Table 4).

Annual publication output of papers related to the application of follicle and melanocyte stem cells in neuroscience in the Web of Science from 2002 to 2011 (Figure 3)
A total of 63 publications on the application of follicle and melanocyte stem cells in neuroscience from 2002 to 2011 were retrieved from the Web of Science. The number of relevant publications increased over the 10-year study period. No papers were published and included in the Web of Science in 2002, but the number of published papers had increased to 12 in 2008. However, the numbers of papers published had slightly decreased in 2004, 2007, 2009, and 2011.

**Distribution of output by journal for publications on the application of follicle and melanocyte stem cells in neuroscience in the Web of Science from 2002 to 2011** (Table 5)

| Journal                                      | ISSN        | Impact factor | No. of papers | % of total publications |
|----------------------------------------------|-------------|---------------|---------------|------------------------|
| Journal of Investigative Dermatology         | 0022-202X   | 6.314         | 6             | 9.524                  |
| Pigment Cell & Melanoma Research             | 1755-1471   | 5.059         | 4             | 6.349                  |
| Cell Cycle                                   | 1538-4101   | 5.359         | 3             | 4.762                  |
| Developmental Biology                        | 0012-1606   | 4.069         | 3             | 4.762                  |
| European Journal of Dermatology              | 1167-1122   | 2.526         | 3             | 4.762                  |
| Seminars in Cell Developmental Biology       | 1084-9521   | 6.646         | 3             | 4.762                  |
| American Journal of Dermatopathology         | 0193-1091   | 1.197         | 2             | 3.175                  |
| Cancer Research                              | 0008-5472   | 7.856         | 2             | 3.175                  |
| Cell Stem Cell                               | 1934-5909   | 25.421        | 2             | 3.175                  |
| Development                                  | 0950-1991   | 6.596         | 2             | 3.175                  |
| Journal of Cellular Biochemistry             | 0730-2312   | 2.868         | 2             | 3.175                  |
| Journal of Dermatology                       | 0385-2407   | 1.493         | 2             | 3.175                  |
| PLOS ONE                                     | 1932-6203   | 4.092         | 2             | 3.175                  |
| Proceedings of the National Academy of Sciences of the United States of America | 0027-8424 | 9.681 | 2 | 3.175 |

As shown in Figure 4, it was clear that most papers on the application of follicle and melanocyte stem cells in neuroscience were published in the USA (37 papers), followed by Japan (25 papers). The other prolific countries were Germany, the UK, and Switzerland. There is no paper in this area that was published in China.

**Distribution of output by institution for publications on the application of follicle and melanocyte stem cells in neuroscience in the Web of Science from 2002 to 2011**

Anticancer Inc and the University of California system in the USA were the most prolific research institutes (Table 6).

Seven of the top 15 research institutes publishing in this field were in the USA, four were in Japan, two were in Germany, and the other two institutes were in Switzerland and the UK, respectively.
Highly cited papers on the application of follicle and melanocyte stem cells in neuroscience from 2002 to 2011

A total of 63 papers on the application of follicle and melanocyte stem cells in neuroscience were cited in the Web of Science from 2002 to 2011. "Nestin expression in hair follicle sheath progenitor cells", published in 2003 by *Proceedings of the National Academy of Sciences of the United States of America*[^17^], was cited 150 times, which was more citations than any other paper. Of the 10 most cited papers, two were published in *Proceedings of the National Academy of Sciences of the United States of America, Cancer Research* and *Cell Cycle* respectively, and the remaining four papers were published in four different journals. Of these 10 most cited papers, five were published in 2005, two were published in 2006, and one each was published in 2003, 2007 and 2008 (Table 7).

### DISCUSSION

Based on Web of Science publications, bibliometric analysis identified several research trends over the past 10 years in studies of follicle and melanocyte stem cells, and their application in neuroscience.

The number of publications on follicle and melanocyte stem cells increased over the 10-year study period. The most prolific journals were the *Journal of Investigative Dermatology*, *Pigment Cell & Melanoma Research*, and *Cell Stem Cell*. Of the 348 publications from 2002 to 2011, which were retrieved from the Web of Science, more than half were from American authors and institutes. The most prolific institutions in China were the Fourth Military Medical University and Third Military Medical University.

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[^17^]: nestin expression in hair follicle sheath progenitor cells

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**Table 6** The top 15 institutions for publications on the application of follicle and melanocyte stem cells in neuroscience from 2002 to 2011

| Institution                        | Country    | No. of papers | % of total publications |
|------------------------------------|------------|---------------|-------------------------|
| Anticancer Inc                     | USA        | 16            | 25.397                  |
| University of California system    | USA        | 16            | 25.397                  |
| Kitasato University                | Japan      | 15            | 23.400                  |
| University of Lübeck               | Germany    | 5             | 7.937                   |
| University of Washington           | USA        | 4             | 6.349                   |
| RIKEN                              | Japan      | 3             | 4.762                   |
| Charité-Medical University Berlin  | Germany    | 2             | 3.175                   |
| Gifu University                    | Japan      | 2             | 3.175                   |
| Kyoto University                   | Japan      | 2             | 3.175                   |
| Massachusetts Institute of Technology | USA   | 2             | 3.175                   |
| New York University                | USA        | 2             | 3.175                   |
| Swiss Institute for Experimental Cancer Research | Switzerland | 2 | 3.175 |
| University of Manchester           | UK         | 2             | 3.175                   |
| University of Chicago              | USA        | 2             | 3.175                   |
| Yale University                    | USA        | 2             | 3.175                   |

**Table 7** The top 10 cited papers on the application of follicle and melanocyte stem cells in neuroscience from 2002 to 2011

| Title                                                                 | Author | Journal                                           | Publication year | Total citations | Average per year |
|-----------------------------------------------------------------------|--------|---------------------------------------------------|------------------|-----------------|------------------|
| Nestin expression in hair follicle sheath progenitor cells[^17^]      | Li L, Mignone J, Yang M, et al. | *Proceedings of the National Academy of Sciences of the United States of America* | 2003             | 150             | 15.00            |
| Pax3 functions at a nodal point in melanocyte stem cell differentiation[^18^] | Lang D, Lu MM, Huang L, et al. | *Nature* | 2005         | 138             | 17.25            |
| Implanted hair follicle stem cells form Schwann cells that support repair of severed peripheral nerves[^19^] | Amoh Y, Li L, Campillo R, et al. | *Proceedings of the National Academy of Sciences of the United States of America* | 2005             | 124             | 15.50            |
| Molecular characterization of melanocyte stem cells in their niche[^20^] | Osawa M, Egawa G, Mak SS, et al. | *Development* | 2005         | 86              | 10.75            |
| Hair follicle stem cells: Walking the maze[^21^]                       | Tiede S, Kloepper JE, Bodo E, et al. | *European Journal of Cell Biology* | 2007         | 69              | 11.50            |
| Nestin-linked green fluorescent protein transgenic nude mouse for imaging human tumor angiogenesis[^22^] | Amoh Y, Yang M, Li L, et al. | *Cancer Research* | 2005         | 68              | 8.50             |
| Hair follicle-derived blood vessels vascularize tumors in skin and are inhibited by doxorubicin[^23^] | Amoh Y, Li L, | *Cancer Research* | 2005         | 48              | 6.00             |
| Multipotent hair follicle stem cells promote repair of spinal cord injury and recovery of walking function[^24^] | Yang M, et al. | *Cell Cycle* | 2008         | 44              | 8.80             |
| Towards the development of a pragmatic technique for isolating and differentiating nestin-positive cells from human scalp skin into neuronal and glial cell populations: generating neurons from human skin[^25^] | Amoh Y, Li L, Katsuoka K, et al. | *Experimental Dermatology* | 2006         | 40              | 5.71             |
| The pluripotency of hair follicle stem cells[^26^]                     | Hoffman RM | *Cell Cycle* | 2006         | 36              | 5.14             |
The number of publications on the application of follicle and melanocyte stem cells in neuroscience increased over the 10-year study period. The most prolific journals were the Journal of Investigative Dermatology, Pigment Cell & Melanoma Research, and Cell Cycle. Of the 63 publications retrieved from the Web of Science, which were published from 2002 to 2011, more than half were from American authors and institutes, and no papers were from Chinese authors and institutes.

At present, scholars have made some achievements in the study of follicle and melanocyte stem cells, and their application in neuroscience[27-33], which provides new hope for treatments of nervous system disease by autologous cell transplantation and gene therapy. The technology to induce the differentiation of follicle stem cell is still at an experimental stage, and has not been widely or successfully used in clinical practice. Nevertheless, follicle stem cells have some advantages over other types of stem cells. Follicle stem cells can be obtained easily, proliferate rapidly in vitro, survive in long-term culture, do not undergo immunological rejection, and are not hindered by ethical issues[34-37]. Therefore, these cells are one of the best candidates for cell therapy of nervous system diseases. We have reason to believe that the research prospects in this area are long range. At present, there are relatively few studies on the application of melanocyte stem cells in neuroscience, and their availability has yet to be confirmed.

**Author contributions:** Weifu Wu retrieved the references, extracted the data, conceived and designed the study, and wrote the manuscript. The author approved the final manuscript.

**Conflicts of interest:** None declared.

**Author statements:** The manuscript is original, has not been submitted to or is not under consideration by another publication, has not been previously published in any language or any form, including electronic, and contains no disclosure of confidential information or authorship/patent application disputations.

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(Edited by Mu WJ/Song LP)