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# Olfactory ensheathing cell transplantation for spinal cord injury

## An 18-year bibliometric analysis based on the Web of Science<sup>★</sup>

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### Abstract

**OBJECTIVE:** Olfactory ensheathing cell (OEC) transplantation is a promising new approach for the treatment of spinal cord injury (SCI), and an increasing number of scientific publications are devoted to this treatment strategy. This bibliometric analysis was conducted to assess global research trends in OEC transplantation for SCI.

**DATA SOURCE:** All of the data in this study originate from the Web of Science maintained by the Institute for Scientific Information, USA, and includes SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED and IC. The Institute for Scientific Information's Web of Science was searched using the keywords "olfactory ensheathing cells" or "OECs" or "olfactory ensheathing glia" or "OEG" or "olfactory ensheathing glial cells" or "OEGs" and "spinal cord injury" or "SCI" or "spinal injury" or "spinal transection" for literature published from January 1898 to May 2012.

**DATA SELECTION:** Original articles, reviews, proceedings papers and meeting abstracts, book chapters and editorial materials on OEC transplantation for SCI were included. Simultaneously, unpublished literature and literature for which manual information retrieval was required were excluded.

**MAIN OUTCOME MEASURES:** All selected literatures addressing OEC transplantation for SCI were evaluated in the following aspects: publication year, document type, language, author, institution, times cited, Web of Science category, core source title, countries/territories and funding agency.

**RESULTS:** In the Web of Science published by the Institute for Scientific Information, the earliest literature record was in April, 1995. Four hundred and fourteen publications addressing OEC transplantation for SCI were added to the data library in the past 18 years, with an annually increasing trend. Of 415 records, 405 publications were in English. Two hundred and fifty-nine articles ranked first in the distribution of document type, followed by 141 reviews. Thirty articles and 20 reviews, cited more than 55 times by the date the publication data were downloaded by us, can be regarded as the most classical references. The journal *Experimental Neurology* published the most literature (32 records), followed by *Glia*. The United States had the most literature, followed by China. In addition, Yale University was the most productive institution in the world, while The Second Military Medical University contributed the most in China. The journal *Experimental Neurology* published the most OEC transplantation literature in the United States, while *Neural Regeneration Research* published the most in China.

**CONCLUSION:** This analysis provides insight into the current state and trends in OEC transplantation for SCI research. Furthermore, we anticipate that this analysis will help encourage international cooperation and teamwork on OEC transplantation for SCI to facilitate the development of more effective treatments for SCI.

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## Key Words

neural regeneration; spinal cord injury; olfactory ensheathing cells; cell transplantation; spinal cord transection; seed cells; Web of Science; bibliometrics; grants-supported paper; neuroregeneration

## Research Highlights

- (1) Bibliometrics is a set of methods to quantitatively analyze scientific and technical literature. Based on the Web of Science, this study summarizes the distribution characteristics of the last 18 years of literature on olfactory ensheathing cell transplantation for spinal cord injury in 10 aspects, including author, institution, classical references, countries/territories and funding agency.
- (2) This bibliometric analysis provides insight into the current state of the field and the dynamic tendencies of research on olfactory ensheathing cell transplantation for spinal cord injury. The results fulfill our initial design expectations.

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## INTRODUCTION

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Spinal cord injury (SCI) is caused by a variety of external and internal factors. Approximately 10 000–12 000 individuals suffer from spinal cord injuries each year in the United States<sup>[1]</sup>. In 2011, Fehlings *et al*<sup>[2]</sup> reported that more than 1 million people in the United States lived with SCI. SCI can be extremely physically and mentally debilitating and can bring forth financial and emotional burdens on family, friends and society. Many scholars around the world have made great efforts to improve treatment for SCI. These researchers have focused on traditional surgical techniques, drugs, physical training, and electrostimulation. However, the outcome for the patient generally remains unsatisfactory. In fact, the severing of nerve fibers, the formation of the glial scar and the lack of axonal regeneration in the injured spinal cord lead to permanent functional impairment. Thus, the key to successful treatment for SCI is to effectively regenerate functional synaptic connections<sup>[3-4]</sup>. In recent years, scholars have given much attention to tissue engineering and cell transplantation for the treatment of SCI, which makes the regeneration of functional synaptic connections possible and provides new hope to paraplegic and quadriplegic patients. Several types of cells have been used as tissue engineered seed cells, including olfactory ensheathing cells (OECs), neural stem cells, embryonic stem cells, cord blood monocytes, induced pluripotent stem cells, bone marrow stromal cells and Schwann cells. Among these seed cells, OECs are unique. OECs are neuroglial cells and are present in the olfactory mucosa, olfactory nerve and the olfactory bulb in the central nervous system. They have characteristics of both Schwann cells and astrocytes and assist in axonal regeneration and nerve functional improvement<sup>[5-7]</sup>. Raisman *et al*<sup>[8-9]</sup> held the view that nerve cells and nerve fibers in the adult brain and spinal

cord were alive. Furthermore, these nerve cells and fibers had the capacity and potential for new growth to establish new connections. Regrowth of axons is impeded by the loss of astrocytic pathways caused at the time of injury. The transplantation of cultured adult OECs into lesions is being investigated as a procedure to re-establish glial pathways permissive to the regeneration of severed axons and the recovery of function. Thus, OECs are potentially very promising seed cells. Obviously, OEC transplantation for SCI is one of the focuses in the field. However, there is no bibliometric analysis of the literature in the field. Therefore, this study aimed to evaluate the distribution characteristics of all the literature and to assess global research on OEC transplantation for SCI.

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## DATA SOURCES AND METHODOLOGY

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### Data retrieval

All literature in this study originated from the Web of Science, including SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED and IC. Based on a previous study<sup>[10]</sup>, the Institute for Scientific Information's Web of Science was searched using the keywords "olfactory ensheathing cells" or "OECs" or "olfactory ensheathing glia" or "OEG" or "olfactory ensheathing glial cells" or "OEGs" and "spinal cord injury" or "SCI" or "spinal injury" or "spinal transection", for literature published from 1898 to May 2012. All data were downloaded on June 6<sup>th</sup>, 2012 in the library of Xi'an Jiaotong University, China.

### Inclusion criteria

- (1) Original articles, reviews, proceedings papers, meeting abstracts, editorial materials and book chapters on OEC transplantation for SCI; (2) basic experiments, animal experiments and clinical trials.

## Exclusion criteria

(1) Unpublished literature; (2) literature for which manual information retrieval was required.

## Data analysis

The analyses were performed using the analysis functions in the Web of Science data and statistics in Microsoft Office Excel 2007 (12.0.6665.5003) SP2 MSO (12.0.6662.5000). All selected literature was evaluated for the following aspects: (1) publication year, (2) document type, (3) language, (4) author, (5) institution, (6) times cited, (7) Web of Science category, (8) source title, (9) countries/territories and funding agency. Furthermore, the results of the analyses are displayed in figures and tables (supplementary information online).

## RESULTS

### Distribution by publication year of literature on OEC transplantation in the Web of Science from 1995 to 2012

A total of 523 publications were finally searched, among which 415 publications were associated with OEC transplantation for SCI and selected for analyses. The output data showed that the earliest literature in the Web of Science on OEC transplantation for SCI was published in 1995, written by Doucette<sup>[11]</sup>. Up to June 6<sup>th</sup>, 2012, it was cited 67 times, with 3.72 citations per year on average. However, there was no related literature record in 1996 or 1997. In 1998, one article<sup>[3]</sup> and one review<sup>[12]</sup> were indexed in the Web of Science. In addition, there was only one review<sup>[13]</sup> in 1999. The literature records from 2000 to May 2012 are displayed in Figure 1.

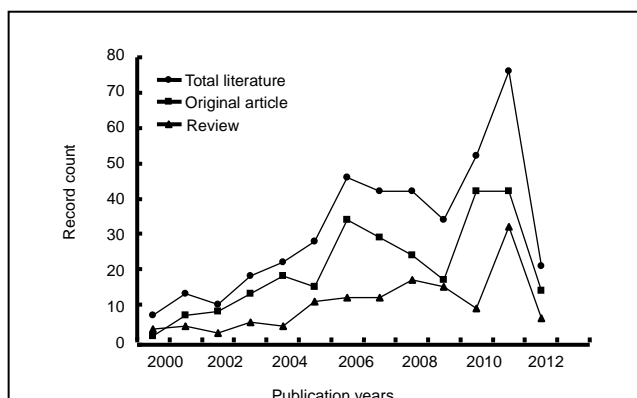


Figure 1 Annual publication count of literature on olfactory ensheathing cell (OEC) transplantation for spinal cord injury (2000–2012).

The literature comprises articles, reviews, proceedings papers, meeting abstracts, editorial materials and book chapters on OEC transplantation for spinal cord injury.

As shown in Figure 1, the number of publications on OEC transplantation for SCI in the database exhibits a rising trend over the past decade, with only a slight decrease in 2009. The record count was seven in 2000, while it was 76 in 2011, which was 11 times the former. The number of original articles also increased. In particular, up to the date that the data were downloaded, the number of publications published in the first 5 months of 2012 was almost equal to that in the whole of 2004, which indicated that this field was attracting more and more attention.

### Distribution by document type and language for OEC transplantation in the Web of Science from 1995 to 2012

The analysis of document types showed that original articles (259 records) and reviews (141 records) made up the majority of the literature. The other document styles included book chapter, proceedings paper, editorial material, meeting abstract, letter and book. The analysis indicated that 97% of the literature in the field was in English. The remaining publications were in French (five; 1.2%), Korean (four; 0.96%) and German (one; 0.24%). Obviously, English was the preferred language among the Science Citation Index papers. Scholars<sup>[14-15]</sup> obtained a similar conclusion that English was the dominant language, comprising 90–95% of all SCI-indexed papers. As an international language, English helps researchers to best share their research results with peers.

### Distribution by category for OEC transplantation in the Web of Science from 1995 to 2012

In the Web of Science, retrieval showed that the 415 publications were widely distributed over 43 research fields. As exhibited in Figure 2, the greatest number of publication records was in the Neuroscience category, followed by the Clinical Neurology category. As a whole, the distribution of Web of Science categories showed that the OEC transplantation for SCI papers mainly covered basic scientific research, with some clinical research.

### Distribution by author of publications in OEC transplantation in the Web of Science from 1995 to 2012

In all, there were 1 295 authors for the 415 documents, with three authors per publication on average. The 10 most productive authors and their institutions are listed in Table 1. There was no significant difference between the record counts in the top 10, which indicates a relative balance in the distribution of authors. The top 10 were the main international cooperation teams in the field.

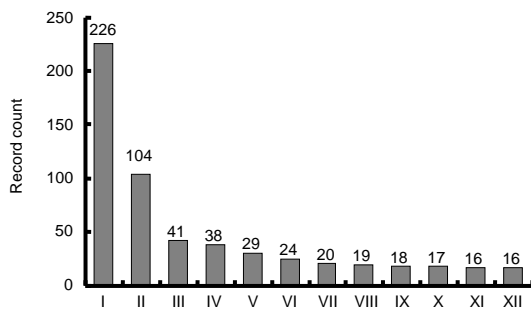


Figure 2 Distribution of Web of Science categories on olfactory ensheathing cell transplantation for spinal cord injury (1995–2012).

I: Neurosciences; II: clinical neurology; III: cell biology; IV: experimental medicine research; V: cell tissue engineering; VI: surgery; VII: biomedical engineering; VIII: critical care medicine; IX: pharmacology and pharmacy; X: rehabilitation; XI: biochemistry and molecular biology; XII: biotechnology and applied microbiology.

Table 1 The top 10 authors with 10 or more papers on olfactory ensheathing cell transplantation in the Web of Science from 1995 to 2012

Author	Institution	Record count (% of total literatures)	Rank
Kocsis JD	Yale University	13(3.133)	1
Radtke C	Yale University	13(3.133)	1
Barnett SC	Glasgow University	12(2.892)	3
Mackay-Sim A	Griffith University	12(2.892)	3
Raisman G	National Institution Medical Research	12(2.892)	3
Tetzlaff W	British Columbia University	12(2.892)	3
Wewetzer K	Vet Med Hannover University	12(2.892)	3
Bunge MB	Miami University	11(2.651)	8
Avila J	Autonoma Madrid University	10(2.410)	9
Ramon-Cueto A	Autonoma Madrid University	10(2.410)	9

### Distribution by institution in studies on OEC transplantation in the Web of Science from 1995 to 2012

Three hundred and ninety-eight research institutes worldwide were giving their best efforts to study OEC transplantation for SCI. As shown in Figure 3, nine institutions can be considered to be on the leading edge of research in the field. All of the top nine were from developed countries. Furthermore, publications from the nine institutions were cited relatively more frequently, and were of high quality.

In the Web of Science, literature in this field from Yale University was cited relatively more times, as follows:

Remyelination of the spinal cord following intravenous delivery of bone marrow cells<sup>[16]</sup>. Authors: Akiyama Y,

Radtke C, Honmou O and Kocsis JD; cited 147 times; published in 2002 in the Journal *Glia*.

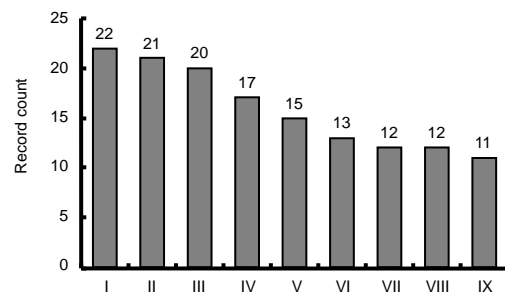


Figure 3 The top nine institutions on olfactory ensheathing cell transplantation for spinal cord injury (1995–2012).

I: Yale University; II: University of British Columbia; III: University of Miami; IV: Cambridge University; V: Hannover Medical School; VI: University of Glasgow; VII: Griffith University; VIII: Autonoma Madrid University; IX: University of Toronto.

Transplantation of OECs or Schwann cells restores rapid and secure conduction across the transected spinal cord<sup>[17]</sup>. Authors: Imaizumi T, Lankford KL and Kocsis JD; cited 121 times; published in 2000 in the Journal *Brain Research*.

Can regenerating axons recapitulate developmental guidance during recovery from SCI?<sup>[18]</sup> Authors: Harel NY and Strittmatter SM; cited 86 times; published in 2006 in the Journal *Nature Reviews Neuroscience*.

Molecular reconstruction of nodes of Ranvier after remyelination by transplanted OECs in the demyelinated spinal cord<sup>[19]</sup>. Authors: Sasaki M, Black JA, Lankford KL, Tokuno HA, Waxman SG and Kocsis JD; cited 61 times; published in 2006 in the *Journal of Neuroscience*.

OECs: bridging the gap in SCI<sup>[4]</sup>. Authors: Bartolomei JC and Greer CA; cited 56 times; published in 2000 in the Journal *Neurosurgery*.

In the Web of Science, literature in this field from the University of British Columbia was cited relatively more times, as follows:

Peripheral OECs reduce scar and cavity formation and promote regeneration after SCI<sup>[6]</sup>. Authors: Ramer LM, Au E, Richter MW, Liu J, Tetzlaff W and Roskams AJ; cited 128 times; published in 2004 in the *Journal of Comparative Neurology*.

OECs of the lamina propria *in vivo* and *in vitro*<sup>[20]</sup>.

Authors: Au E and Roskams AJ; cited 97 times; published in 2003 in the Journal *Glia*.

Cellular transplants in China: observational study from the largest human experiment in chronic SCI<sup>[21]</sup>. Authors: Dobkin BH, Curt A and Guest J; cited 95 times; published in 2006 in the Journal *Neurorehabilitation and Neural Repair*.

Lamina propria and olfactory bulb ensheathing cells exhibit differential integration and migration and promote differential axon sprouting in the lesioned spinal cord<sup>[22]</sup>. Authors: Richter MW, Fletcher PA, Liu J, Tetzlaff W and Roskams AJ; cited 75 times; published in 2005 in the *Journal of Neuroscience*.

Setting the stage for functional repair of spinal cord injuries: a cast of thousands<sup>[23]</sup>. Authors: Ramer LM, Ramer MS and Steeves JD; cited 72 times; published in 2005 in the journal *Spinal Cord*.

In the Web of Science, literature in this field from the University of Miami was cited relatively more times, as follows:

Long-distance axonal regeneration in the transected adult rat spinal cord is promoted by olfactory ensheathing glia transplants<sup>[3]</sup>. Authors: Ramón-Cueto A, Plant GW, Avila J and Bunge MB; cited 401 times; published in 1998 in the *Journal of Neuroscience*.

Schwann cell but not olfactory ensheathing glia transplants improve hindlimb locomotor performance in the moderately contused adult rat thoracic spinal cord<sup>[24]</sup>. Authors: Takami T, Oudega M, Bates ML, Wood PM, Kleitman N and Bunge MB; cited 234 times; published in 2002 in the *Journal of Neuroscience*.

Combining Schwann cell bridges and olfactory ensheathing glia grafts with chondroitinase promotes locomotor recovery after complete transection of the spinal cord<sup>[25]</sup>. Authors: Fouad K, Schnell L, Bunge MB, Schwab ME, Liebscher T and Pearse DD; cited 204 times; published in 2005 in the *Journal of Neuroscience*.

Delayed transplantation of olfactory ensheathing glia promotes sparing/regeneration of supraspinal axons in the contused adult rat spinal cord<sup>[26]</sup>. Authors: Plant GW, Christensen CL, Oudega M and Bunge MB; cited 110 times; published in 2003 in the *Journal of Neurotrauma*.

Bridging areas of injury in the spinal cord<sup>[27]</sup>. Authors:

Bunge MB; cited 107 times; published in 2001 in the *Journal Neuroscientist*.

### **Distribution by number of citations of literature on OEC transplantation in the Web of Science from 1995 to 2012**

#### ***Distribution of articles by number of citations***

According to bibliometric principles, if an article is cited more times than others, its quality can be considered higher. Scientometrics has demonstrated that references can be considered as “classical references” once an article is cited four or more times<sup>[28]</sup>. From the distribution of document type, 259 publications were articles. Literature in Table 2 represents the top 30 articles that were cited more than 55 times by the downloading date. Each of the top 10 articles was cited 10 times or more per year, on average. By definition, they are classical references in this field.

#### ***Distribution of reviews by number of citations***

In the analysis, 141 records were reviews on OEC transplantation for SCI. Literature listed in Table 3 are the top 20 reviews, according to the number of times they were cited up to the downloading date.

### **Distribution by source title of OEC transplantation literature in the Web of Science from 1995 to 2012**

According to Bradford's law, the core scientific source titles/journals in the subject publish 33% of all documents on the subject<sup>[28]</sup>. The output of the analysis showed that 415 papers were published in 181 journals. Table 4 shows that the top 10 source titles were the core journals in which 143 papers were published, comprising 34.5% of all records. Six journals were published in the United States, indicative of that country's advanced research and leading position. *Neural Regeneration Research* is the only one from China.

### **Distribution by country/territory of studies on OEC transplantation in the Web of Science from 1995 to 2012**

Eleven countries/territories were the most productive, with more than 10 papers each. The other 25 countries/territories are not displayed in Figure 4. Beyond doubt, the United States, with 127 publications, was the key player in the field. Although China ranked second, the number of publications was only 53, which indicates the disparity in research on OEC transplantation for SCI between the two countries. As shown in Figure 4, six countries/territories (England, Spain, Germany, France, Netherlands and Scotland) are in Europe.

Table 2 The top 30 articles cited more than 55 times in the Web of Science from 1995 to 2012

Rank	Title	Author	Source title	Publication year	Total citation
1	Long-distance axonal regeneration in the transected adult rat spinal cord is promoted by olfactory ensheathing glia transplants <sup>[3]</sup>	Ramón-Cueto A, Plant GW, Avila J, et al	<i>Journal of Neuroscience</i>	1998	401
2	Schwann cell but not olfactory ensheathing glia transplants improve hindlimb locomotor performance in the moderately contused adult rat thoracic spinal cord <sup>[24]</sup>	Takami T, Oudega M, Bates ML, et al	<i>Journal of Neuroscience</i>	2002	234
3	Combining Schwann cell bridges and olfactory-ensheathing glia grafts with chondroitinase promotes locomotor recovery after complete transection of the spinal cord <sup>[25]</sup>	Fouad K, Schnell L, Bunge MB, et al	<i>Journal of Neuroscience</i>	2005	204
4	Olfactory ensheathing cells promote locomotor recovery after delayed transplantation into transected spinal cord <sup>[29]</sup>	Lu J, Féron F, Mackay-Sim A, et al	<i>Brain</i>	2002	181
5	Guidance of glial cell migration and axonal growth on electrospun nanofibers of poly-epsilon-caprolactone and a collagen/poly-epsilon-caprolactone blend <sup>[30]</sup>	Schnell E, Klinkhammer K, Balzer S, et al	<i>Biomaterials</i>	2007	174
6	Autologous olfactory ensheathing cell transplantation in human spinal cord injury <sup>[7]</sup>	Féron F, Perry C, Cochrane J, et al	<i>Brain</i>	2005	159
7	Remyelination of the spinal cord following intravenous delivery of bone marrow cells <sup>[16]</sup>	Akiyama Y, Radtke C, Honmou O, et al	<i>Glia</i>	2002	147
8	Transplantation of nasal olfactory tissue promotes partial recovery in paraplegic adult rats <sup>[31]</sup>	Lu J, Féron F, Ho SM, et al	<i>Brain Research</i>	2001	141
9	Peripheral olfactory ensheathing cells reduce scar and cavity formation and promote regeneration after spinal cord injury <sup>[6]</sup>	Ramer LM, Au E, Richter MW, et al	<i>Journal of Comparative Neurology</i>	2004	128
10	Transplantation of olfactory ensheathing cells or Schwann cells restores rapid and secure conduction across the transected spinal cord <sup>[17]</sup>	Imaizumi T, Lankford KL, Kocsis JD	<i>Brain Research</i>	2000	121
11	Olfactory mucosa autografts in human spinal cord injury: A pilot clinical study <sup>[32]</sup>	Lima C, Pratas-Vital J, Escada P, et al	<i>Journal of Spinal Cord Medicine</i>	2006	112
12	Delayed transplantation of olfactory ensheathing glia promotes sparing/regeneration of supraspinal axons in the contused adult rat spinal cord <sup>[26]</sup>	Plant GW, Christensen CL, Oudega M, et al	<i>Journal of Neurotrauma</i>	2003	110
13	<i>Ex vivo</i> adenoviral vector-mediated neurotrophin gene transfer to olfactory ensheathing glia: effects on rubrospinal tract regeneration, lesion size, and functional recovery after implantation in the injured rat spinal cord <sup>[33]</sup>	Ruitenber MJ, Plant GW, Hamers FP, et al	<i>Journal of Neuroscience</i>	2003	105
14	Olfactory ensheathing cells of the lamina propria <i>in vivo</i> and <i>in vitro</i> <sup>[20]</sup>	Au E, Roskams AJ	<i>Glia</i>	2003	97
15	Neurotrophic and migratory properties of an olfactory ensheathing cell line <sup>[34]</sup>	Boruch AV, Conners JJ, Pipitone M, et al	<i>Glia</i>	2001	96
16	Cellular transplants in China: observational study from the largest human experiment in chronic spinal cord injury <sup>[21]</sup>	Dobkin BH, Curt A, Guest J	<i>Neurorehabilitation and Neural Repair</i>	2006	95
17	Neurotrophic properties of olfactory ensheathing glia <sup>[35]</sup>	Lipson AC, Widenfalk J, Lindqvist E, et al	<i>Experimental Neurology</i>	2003	90
18	Influence of patients' age on functional recovery after transplantation of olfactory ensheathing cells into injured spinal cord injury <sup>[36]</sup>	Huang H, Chen L, Wang H, et al	<i>Chinese Medical Journal</i>	2003	88
19	Autologous olfactory ensheathing cell transplantation in human paraplegia: a 3-year clinical trial <sup>[37]</sup>	Mackay-Sim A, Féron F, Cochrane J, et al	<i>Brain</i>	2008	84
20	Olfactory ensheathing cells induce less host astrocyte response and chondroitin sulphate proteoglycan expression than Schwann cells following transplantation into adult CNS white matter <sup>[38]</sup>	Lakatos A, Barnett SC, Franklin RJ	<i>Experimental Neurology</i>	2003	83
21	Update on the treatment of spinal cord injury <sup>[39]</sup>	Baptiste DC, Fehlings MG	<i>Neurotrauma: New Insights into Pathology and Treatment</i>	2007	78
22	Lamina propria and olfactory bulb ensheathing cells exhibit differential integration and migration and promote differential axon sprouting in the lesioned spinal cord <sup>[22]</sup>	Richter MW, Fletcher PA, Liu J, et al	<i>Journal of Neuroscience</i>	2005	75
23	Viral vector-mediated gene expression in olfactory ensheathing glia implants in the lesioned rat spinal cord <sup>[40]</sup>	Ruitenber MJ, Plant GW, Christensen CL, et al	<i>Gene Therapy</i>	2002	72
24	Olfactory ensheathing cells genetically modified to secrete GDNF to promote spinal cord repair <sup>[41]</sup>	Cao L, Liu L, Chen ZY, et al	<i>Brain</i>	2004	69

Table 2 Continued

Rank	Title	Author	Source title	Publication year	Total citation
25	Transplantation of Schwann cells and olfactory ensheathing glia after spinal cord injury: does pretreatment with methylprednisolone and interleukin-10 enhance recovery? <sup>[42]</sup>	Pearse DD, Marcillo AE, Oudega M, et al	<i>Journal of Neurotrauma</i>	2004	68
26	Molecular reconstruction of nodes of Ranvier after remyelination by transplanted olfactory ensheathing cells in the demyelinated spinal cord <sup>[19]</sup>	Sasaki M, Black JA, Lankford KL, et al	<i>Journal of Neuroscience</i>	2006	61
27	Viral vector-mediated gene transfer of neurotrophins to promote regeneration of the injured spinal cord <sup>[43]</sup>	Hendriks WT, Ruitenber MJ, Blits B, et al	<i>Ngf and Related Molecules in Health and Disease</i>	2004	58
27	LacZ-expressing olfactory ensheathing cells do not associate with myelinated axons after implantation into the compressed spinal cord <sup>[44]</sup>	Boyd JG, Lee J, Skihar V, et al	<i>Proceedings of the National Academy of Sciences of the United States of America</i>	2004	58
29	Survival, integration, and axon growth support of glia transplanted into the chronically contused spinal cord <sup>[45]</sup>	Barakat DJ, Gaglani SM, Neravetla SR, et al	<i>Cell Transplantation</i>	2005	57
29	Olfactory ensheathing cells do not exhibit unique migratory or axonal growth-promoting properties after spinal cord injury <sup>[46]</sup>	Lu P, Yang H, Culbertson M, et al	<i>Journal of Neuroscience</i>	2006	57

Table 3 The top 20 reviews cited more than 55 times in the Web of Science

Rank	Title	Author	Journal	Publication year	Total citation
1	Neural tissue engineering: strategies for repair and regeneration <sup>[47]</sup>	Schmidt CE, Leach JB	<i>Annual Review of Biomedical Engineering</i>	2003	338
2	Therapeutic interventions after spinal cord injury <sup>[48]</sup>	Thuret S, Moon LD, Gage FH	<i>Nature Reviews Neuroscience</i>	2006	176
3	Bridging areas of injury in the spinal cord <sup>[27]</sup>	Bunge MB	<i>Neuroscientist</i>	2001	107
4	Spinal cord repair strategies: why do they work? <sup>[49]</sup>	Bradbury EJ, McMahon SB	<i>Nature Reviews Neuroscience</i>	2006	95
5	Can regenerating axons recapitulate developmental guidance during recovery from spinal cord injury? <sup>[16]</sup>	Harel NY, Strittmatter SM	<i>Nature Reviews Neuroscience</i>	2006	86
6	Experimental strategies to promote spinal cord regeneration – an integrative perspective <sup>[50]</sup>	Schwab JM, Brechtel K, Mueller CA, et al	<i>Progress in Neurobiology</i>	2006	84
7	Transplantation of Schwann cells and/or olfactory ensheathing glia into the contused spinal cord: survival, migration, axon association, and functional recovery <sup>[51]</sup>	Pearse DD, Sanchez AR, Pereira FC, et al	<i>Glia</i>	2007	82
8	Review of treatment trials in human spinal cord injury: issues, difficulties, and recommendations <sup>[52]</sup>	Tator CH	<i>Neurosurgery</i>	2006	81
9	Repair of neural pathways by olfactory ensheathing cells <sup>[9]</sup>	Raisman G, Li Y	<i>Nature Reviews Neuroscience</i>	2007	74
10	Setting the stage for functional repair of spinal cord injuries: a cast of thousands <sup>[23]</sup>	Ramer LM, Ramer MS, Steeves JD	<i>Spinal Cord</i>	2005	72
11	Olfactory ensheathing cells: potential for glial cell transplantation into areas of CNS injury <sup>[11]</sup>	Doucette R	<i>Histology and Histopathology</i>	1995	67
11	Bioengineered strategies for spinal cord repair <sup>[53]</sup>	Nomura H, Tator CH, Shoichet MS	<i>Journal of Neurotrauma</i>	2006	67
13	Tissue-engineering approaches for axonal guidance <sup>[54]</sup>	Zhang N, Yan H, Wen X	<i>Brain Research Reviews</i>	2005	62
14	Neuregulins: versatile growth and differentiation factors in nervous system development and human disease <sup>[55]</sup>	Esper RM, Pankonin MS, Loeb JA	<i>Brain Research Reviews</i>	2006	60
15	Repair of chronic spinal cord injury <sup>[11]</sup>	Houle JD, Tessler A	<i>Experimental Neurology</i>	2003	57
15	Current status of acute spinal cord injury pathophysiology and emerging therapies: promise on the horizon <sup>[56]</sup>	Rowland JW, Hawryluk GW, Kwon B, et al	<i>Neurosurgical Focus</i>	2008	57
17	Olfactory ensheathing cells: bridging the gap in spinal cord injury <sup>[4]</sup>	Bartolomei JC, Greer CA	<i>Neurosurgery</i>	2000	56
18	Defining the role of olfactory ensheathing cells in facilitating axon remyelination following damage to the spinal cord <sup>[57]</sup>	Boyd JG, Doucette R, Kawaja MD	<i>Faseb Journal</i>	2005	56
19	Olfactory ensheathing glia: their contribution to primary olfactory nervous system regeneration and their regenerative potential following transplantation into the injured spinal cord <sup>[58]</sup>	Franssen EH, de Bree FM, Verhaagen J	<i>Brain Research Reviews</i>	2007	55
20	Olfactory ensheathing cell transplantation following spinal cord injury: hype or hope? <sup>[59]</sup>	Richter MW, Roskams AJ	<i>Experimental Neurology</i>	2008	54

Table 4 Distribution of core sources in studies on olfactory ensheathing cell transplantation in the Web of Science from 1995 to 2012

Source	ISSN	Country	Issues/year	Impact factor in 2011	Records
<i>Experimental Neurology</i>	0014-4886	United States	12	4.699	32
<i>Glia</i>	0894-1491	United States	12	4.820	22
<i>Journal of Neurotrauma</i>	0897-7151	United States	12	3.654	19
<i>Journal of Neuroscience</i>	0270-6474	United States	50	7.115	13
<i>Neural Regeneration Research</i>	1673-5374	China	36	0.216	12
<i>Brain Research</i>	0006-8993	Netherlands	60	2.728	11
<i>Cell Transplantation</i>	0963-6897	United States	8	6.204*	10
<i>Brain</i>	0006-8950	England	12	9.457	8
<i>Journal of Comparative Neurology</i>	0021-9967	United States	24	3.808	8
<i>Spinal Cord</i>	1362-4393	England	12	1.805	8

\*6.204 was the impact factor of *Cell Transplantation* in 2010.

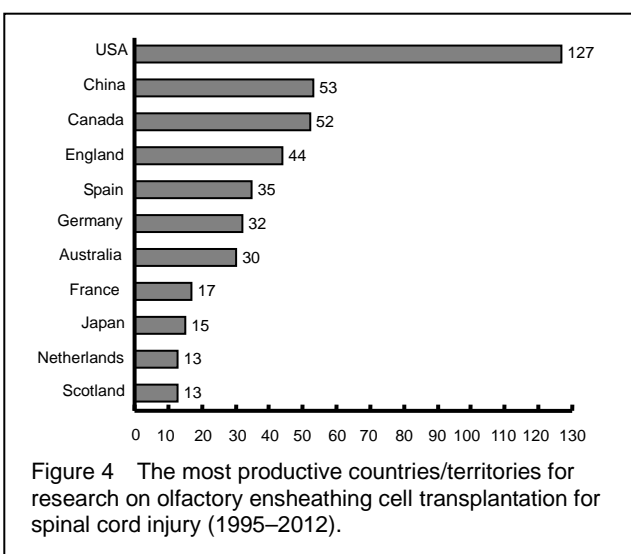


Figure 4 The most productive countries/territories for research on olfactory ensheathing cell transplantation for spinal cord injury (1995–2012).

The United States has made great contributions to research on OEC transplantation for SCI. Further analyses indicated that Yale University, the University of Miami and the University of California, Los Angeles were the main research institutions, having published 52 papers in total. Yale University ranked first in the distribution of institutions, with the University of Miami ranking third in the world. In the United States, Kocsis JD (13 records, Yale University), Radtke C (12 records, Yale University) and Bunge MB (11 records, Miami University) were the most productive authors. Authors in the United States preferred to publish their research results in *Experimental Neurology* (15 records), *Journal of Neurotrauma* (11 records) and *Journal of Neuroscience* (nine records).

In the past decade, China also devoted herself to research on OEC transplantation for SCI. Similar to American literature, further analyses demonstrated that The Second Military Medical University, Chinese Academy of Sciences and Soochow University were the main research institutions, having published 19 papers in total. In China, Cao L (six records), He C (six records) and Su ZD (six

records) were the most productive authors, and were all from The Second Military Medical University. Authors in China preferred to publish their research results in *Neural Regeneration Research* (12 records), *Brain Research* (four records) and *Cell Transplantation* (four records). Nevertheless, the quality and impact of Chinese literature were still not high enough. There is obviously a long way to go before China catches up to the United States in this research field.

In the Web of Science, publications in this field from China that were cited relatively more times were as follows:

Influence of patients' age on functional recovery after transplantation of OECs into injured spinal cord injury<sup>[36]</sup>. Authors: Huang H, Chen L, Wang H, Xiu B, Li B, Wang R, Zhang J, Zhang F, Gu Z, Li Y, Song Y, Hao W, Pang S and Sun J; cited 88 times; published in 2003 in the *Chinese Medical Journal*.

OECs genetically modified to secrete GDNF to promote spinal cord repair<sup>[41]</sup>. Authors: Cao L, Liu L, Chen ZY, Wang LM, Ye JL, Qiu HY, Lu CL and He C; cited 69 times; published in 2004 in the journal *Brain*.

Tissue-engineering approaches for axonal guidance<sup>[54]</sup>. Authors: Zhang N, Yan H and Wen X; cited 62 times; published in 2005 in the Journal *Brain Research Reviews*.

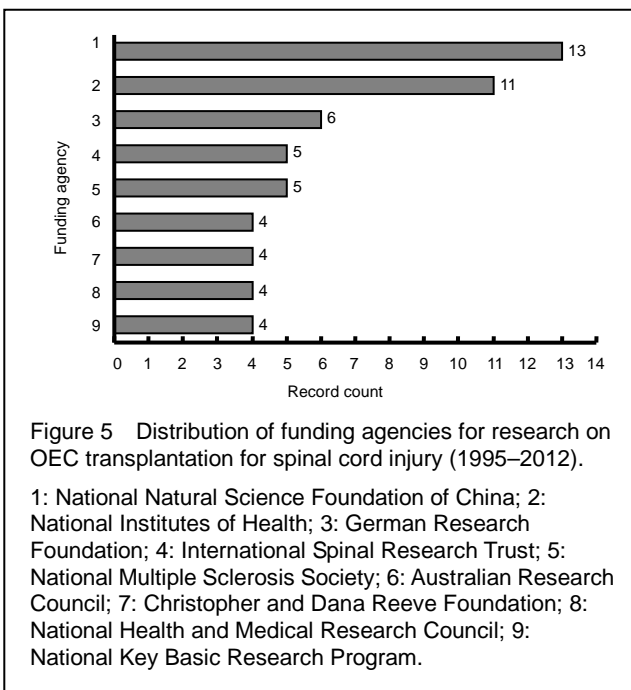
Actions of neurotrophic factors and their signaling pathways in neuronal survival and axonal regeneration<sup>[60]</sup>. Authors: Cui Q; cited 39 times; published in 2006 in the Journal *Molecular Neurobiology*.

Glial cell line-derived neurotrophic factor promotes OEC migration<sup>[61]</sup>. Authors: Cao L, Su Z, Zhou Q, Lv B, Liu X, Jiao L, Li Z, Zhu Y, Huang Z, Huang A and He C; cited 28 times; published in 2006 in the Journal *Glia*.



### Distribution by funding agency of studies on OEC transplantation in the Web of Science from 1995 to 2012

The results show that there were 278 funding agencies for the 415 publications. Each of the 11 agencies in Figure 5 had funded four or more papers. Among these agencies, there were two (National Natural Science Foundation of China and National Key Basic Research Program) from China funding 17 papers, and two (National Institutes of Health and National Multiple Sclerosis Society) from the United States funding 16 papers. Good research and publications were based on funding support.



## DISCUSSION

SCI patients suffer to such a great extent that the quality of their lives is rather low. Unfortunately, treatments for SCI cannot satisfactorily alleviate their symptoms. Sadly, most experimental research is restricted to animal experiments or pre-clinical trials, except in a few institutions such as Second Affiliated Hospital, College of Medicine, Xi'an Jiaotong University. We are doing our best to advance translational medicine in OEC transplantation for SCI, which means we translate basic research results to clinical trials to benefit patients. OEC transplantation is one of the hottest research fields in tissue engineering and cell transplantation. The use of bibliometric analytical techniques for examining OEC transplantation for SCI research was hitherto not presented in the literature.

The objective of the present study was to perform a bibliometric analysis of all the related publications in the Science Citation Index. Bibliometrics is a series of analyses for evaluating or quantifying literature and information. It is a scientific method widely used in many fields, and is based on a number of laws, including Bradford's law. This analysis was performed using the Web of Science published by the Institute for Scientific Information. All the Science Citation Index papers were analyzed for various factors. Through this analysis, we were able to gain insight into the current state of research and trends in the field of OEC transplantation for SCI.

The analyses of the distributions of authors and institutions could, to some degree, help encourage global cooperation and teamwork in the field. This should help researchers make the best use of available resources to increase efficiency and accelerate progress. For better international communication, English is our first choice as the publication language. The analysis of the core publication journals could help scholars select the appropriate journal for paper submission, thereby increasing the chance of acceptance. Among the core journals, *Experimental Neurology*, *Glia*, *Journal of Neurotrauma*, *Journal of Neuroscience* and *Neural Regeneration Research* are the key journals in this field. Among these, *Neural Regeneration Research* is quite popular in China. The highly cited articles and reviews are classical papers that students and primary researchers should read carefully, particularly if they plan to devote themselves to OEC transplantation for SCI. The analysis of the distribution of countries shows that China is a productive country. However, the average number of citations is not high; the most-cited paper was cited only 88 times (up to the date the data were downloaded). This demonstrates that innovation in the field in China needs to be improved. Chinese scholars should strive to innovate in the field, either through independent research or through international collaboration. With this approach, Chinese scientists can expect to play a leading role in the field in the near future.

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**Supplementary information:** Supplementary data associated with this article can be found in the online version, by visiting [www.nrronline.org](http://www.nrronline.org).

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