



# Bibliometric Analysis of Research Development in the Field of Science Cartilage Regeneration Using Adipose-Derived Stem Cells

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**Abstract.** In order to analyze trends of development bibliometric analysis of researches development in major of science cartilage regeneration using adipose-derived stem cells that conducted in 2013–2022, wished could help other researches to comprehend latest information of this trend. This study is directed to determine: (1) The development of the number of international publications in the major of cartilage regeneration in Scopus database from 2013–2022; (2) core journals in international publications in the major of cartilage regeneration; (3) researches productivity in major of cartilage regeneration; (4) the number of publications build upon collaboration of institutions in international publications in the field of cartilage regeneration; (5) development of international publications on cartilage regeneration’s research upon the use of stem cells. Method done by collecting data which searching through Scopus with the keyword cartilage repair using adipose-derived stem cells, cartilage regeneration, cartilage repair, cartilage repair adipose stem cells by categories article titles, abstracts, and keywords, in range 2013–2022 and analyzed using Publish or Perish software. The results performed that development of major in cartilage repair in 2013–2022 indexed in Scopus is 13 publications. The most active country done research about cartilage repair is China following by Japan and Korea. The Chinese People’s Liberation Army General Hospital is the institution that publish the most research in major of cartilage repair as many as 3 publications and Guo is the most productive writer in major of cartilage repair.

**Keywords:** Adipose · Bibliometric · Cartilage Repair · Publish or Perish · Regeneration · Stem cells

## 1 Introduction

Many researches about cartilage regeneration using adipose-derived stem cells reported to be written in various scientific article database, either is Scopus. This research has done so many studies about potential of adipose-derived stem cells as supported base of cartilage repair. Cartilage is one of specific connective tissue quiet dense but not firm as bone. Cartilage’s matrix arranged by glycoprotein and collagen fiber produced by

chondrocyte. Proteoglycan and aggregate proteoglycan in cartilage conducts solid bond in matrix. This bond gathers interstitial liquid and configure strong intrinsic mechanism. By that, about 65–80% the net weight of cartilage's matrix is fluid and bonded into a complex internal structure of matrix's cartilage. It what makes cartilage's tissue not bonded and firmed as compact bone tissue [1].

Cartilage doesn't have blood vessels or any other vessels such as nerve and lymph so that all nutrition, oxygen and respiration's result need to be secreted through matrix. There are no adequate supportive cells that forms differentiation in cartilage. If blood supply around tissue are deficit, the cells will be perishing. This is causing metabolism or recovery of injury becomes hampered [2].

Stem cells is a unique, potentials, regenerative and well-to-do to differentiate into various cells. A perfect solution for specific illness. Stem cells divided into 4 groups first is totipotent stem cells, supporting embryo's growth and development, second is pluripotent embryonic stem cells, third is multipotent stem cells that capable to differentiate into specific cell for example an adult stem cells and last, unipotent stem cells which only has single various of growth into epidermal stem cells. From these various stem cells, adipose tissue is one of the best basic to produce stem cells by reason of easy to find which from medical waste, liposuction [3].

In sight of the characteristic and capability, stem cells have potential to be cartilage's repair alternative alongside with the development of science. Moreover, basic of the cartilage's matrix is fat content proteoglycan so adipose-derived stem cells compatible as an alternative of cartilage's repair [3]. Many factors interfere the process of differentiate such as nutrition, circumstance around tissue even physiology condition of it cells. By that, done many researches determine to explore capability of stem cells maximum. This study purposed to collecting data of publication development about cartilage's repair using adipose-derived stem cells in 2013–2022.

## **2 Methods**

### **2.1 Research Procedures**

This research based in international data publication about cartilage's repair using adipose derived stem cells from Scopus database. Data collected by searching of issue in Scopus using keywords cartilage repair using adipose-derived stem cells, cartilage repair, cartilage regeneration, cartilage adipose stem cells with title and keyword's category in 2013–2022.

### **2.2 Data Analysis**

Collected data being reviewed and performed using Microsoft Excel software.

## **3 Result and Discussion**

There were 13 articles that complied the criteria stated about adipose-derived stem cell for cartilage repair were indexed in Scopus database in 2013–2022. Mostly publications are research articles (12; 93%), alongside with the review article (1; 7%). Eighty-six

percent of the articles were published in English, other language that appear is Chinese (2 articles; 14%). There are more than 10 scholarly journals that published about ADSCs research. The most active journals to be presented is Chinese Journal of Tissue Engineering Research, Arthroscopy Journal and Journal of Tissue Engineering and Regenerative Medicine. CJTER published 15 articles, Arthroscopy Journal published 105 articles and JTERM published 206 articles regarding to the criteria stated. The most active institution done ADSCs research is Chinese PLA General Hospital which published 2 publications and has one author, Guo Quan Yi known as the most active author to write articles about criteria mentioned. Apparently ADSCs issue that has been indexed into Scopus only 13 publications. These 13 mostly from 3 countries which all is Asia. The top country with the most publications is China with 10 total publications, and followed by Japan with 1 total publication, South Korea with 1 publication and Taiwan with 1 publication.

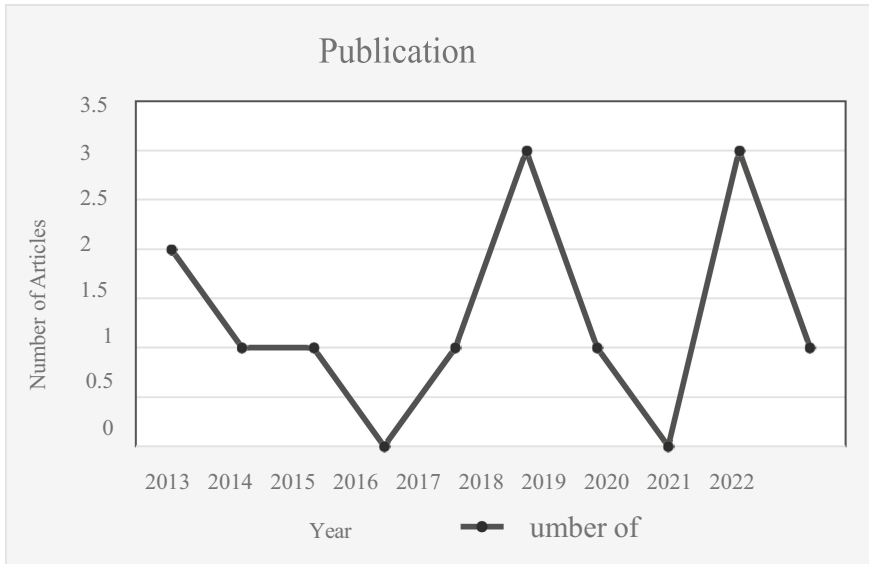
### 3.1 Trends in ADSCs for Cartilage Repair Publication

The amount of publications (Fig. 1) indicated the development of the trend research about ADSCs used as cartilage repair is up and down over time. Reported in 2013 there are 2 publications, in 2014, 2015, 2017, 2019 and 2022 appeared has 2 publications, 2016 and 2020 no publication and the year that has the most publications is 2018 and 2021 which are 3 publications.

(Fig. 1) appearing publication trends of articles searched by keyword “adipose derived stem cells” and “cartilage repair” in category title, abstract, and keyword. These years, more articles about adipose-derived stem cells for cartilage repair already published but the keywords are not always match in the titles. Amount of articles avails via Scopus and the amount of articles with needed keywords other than in the front page of the article were not same. The amount of published articles has been risen after 2016 can be indicated as innovation of adipose-derived stem cells research. In 2017, Muttigi et al. from Chung-Ang University of South Korea initiate research of ADSCs after 1 year no publications about this research reported (Table 1), with entitled “Matrilin-3 codelivery with adipose-derived mesenchymal stem cells promotes articular cartilage regeneration in a rat osteochondral defect model” and a year ahead, appears 3 publications such as “Hyaluronan microenvironment enhances cartilage regeneration of human adipose-derived stem cells in a chondral defect model” by Wu et al., from Kaohsiung Med University of Taiwan, “Effect of TGF- $\beta$ 3 transfected with adipose derived stem cells and OGP-HA-chondroitin sulfate scaffold on repair of condylar cartilage in rabbits” by Guo et al. from Jining and Jinan Hospital of Stomatology China and last “Polylactic acid/polyglycolic acid copolymer scaffolds carrying bone morphogenetic protein 2 gene enhanced adipose-derived stem cells promote cartilage defect repair” by Ruan et al. from China. These 13 articles were published by more than 15 research institutions.

### 3.2 Articles Results Regarding to Criteria Stated

These 13 articles likely to discuss about the feasibility of ADSCs as an alternative way to repair cartilage damaged, with many treatments added in aim to boosted the potential of ADSCs for cartilage repair (Table 1). These researches mostly done in rabbit model



**Fig. 1.** Publication trends of ADSCs during 2013–2022

followed by pig and rat. Mostly treatment added is transfusion of protein either hyaluronic or glucose category.

### 3.3 Frequently Cited Articles

Articles with many citations cannot be guarantee to have impeccable quality, but it can be a measurement to showing that article is well-known and giving a good recommendation to society especially in science group. Articles that mostly cited can be seen in Table 2. The articles with the highest cited can be conceived as the most famous articles in last 10 years. Averagely, only Kang and Wu seen to have gradually increase citation since their publication years which is more than 100 citations. First rank of highest cited article published in 2014 while the second rank published in 2013, this is shown the trend of ADSCs were recognized among scientist gradually.

### 3.4 Publication by Country

Research performance based on country assessed using total number of articles, either it is independently written or cooperate with other articles. In current years, there are five indicators that used to assessed research performance by country. Including total, independent, collaborative, first author and corresponding author articles.

The contribution given by various countries and was conjectured from the affiliation of at least one author correlated to the articles. All of 13 articles (100%) on Scopus reported with addresses and 2 of total (15,3%) were international collaborative articles. Those countries were ranked by amount of articles, as well as percentage of collaborative articles. China became first ranked (Fig. 2) as the country who has the most research and

**Table 1.** Results of Appeared Articles

|  | <b>Year</b> | <b>Title</b>  | <b>Aim</b>  | <b>Results</b>  |
|--|-------------|---|---|---|
| Li, S., Liu, J., Liu, S., Jiao, W., & Wang, X.   | 2021        | Chitosan oligosaccharides packaged into rat adipose mesenchymal stem cells-derived extracellular vesicles facilitating cartilage injury repair and alleviating osteoarthritis | This study aims to analyze mesenchymal stem cell (AMSC)-derived extracellular vesicles (EVs)'s utility bonded with chitosan oligosaccharides (COS) in cartilage injury.   | Conjugation of extracellular vesicles and chitosan oligosaccharides able to functioned as a new free biomaterial cell to aid cartilage's repair and improve osteoarthritis. |
| Xie, A., Peng, Y., Yao, Z., Lu, L., Ni, Tao  | 2021        | Effect of a subset of adipose-derived stem cells isolated with liposome magnetic beads to promote cartilage repair  | This study purposed to analyze the capability of CD146* as a substance of ADSCs to heal cartilage damage  | CD146*LMB fully capable isolate the CD146 *ADSCs and heal damaged of articular cartilage which could lead into new tissue engineering                                       |
| Guo, Y, W., & Yang, S, M   | 2018        | Effect of TGF- $\beta$ 3 transfected with adipose derived stem cells and OGP-HA-chondroitin sulfate scaffold on repair of condylar cartilage in rabbits                       | This study is aiming to analyze the chance of ADSC transfused by specify protein collaborated with scaffold consists of osteogenesis peptide, hyaluronic acid and chondroitin sulfate for cartilage repair in rabbit condylar | OGP-HA-ChS scaffold and transfused ADSCs own capability on repairing cartilage damaged  |
| Kang, H., Peng, J., Lu, S., Liu, S., Zhang, L., Huang, J., Sui, X., Zhao, B., Wang, A., Xu, W., Luo, Z., & Guo, Q. | 2014        | In vivo cartilage repair using adipose-derived stem cell-loaded decellularized cartilage ECM scaffolds  | This study purposed to exploring more the chance of cell-loaded scaffolds application, using autologous adipose-derived stem cells for cartilage repair in rabbit model.  | Damaged cartilage tissue induced by ECM scaffold from ADSC-loaded is compatible regarding to biochemical components and mechanical properties as ordinary cartilage.        |

*(continued)*

**Table 1.** (continued)

|   | <b>Year</b> | <b>Title</b>   | <b>Aim</b>  | <b>Results</b>   |
|---|-------------|--|---|--|
| Shi, J., Zhang, X., Zhu, J., Zhou, C. Hu, X., & Ao, Y | 2013        | Nanoparticle delivery of the Bone Morphogenetic Protein 4 Gene to Adipose- Derived Stem Cells Promotes Articular Cartilage in Vitro and In Vivo                      | This study determines is to assess the effectiveness of poly lactic-co-glycolic acid (PLGA) and poly L-lactic co-glycolic acid (PLLGA) delivers EGF protein plasmid into ADSCs in vitro | Protein plasmid injected into ADSCs supported by PLGA nanoparticles significantly support chondrogenesis. By that, nanoparticles and BMP-4 capable used as therapy in chondral defects of knee |
| Ruan, S.Q., Deng, J., Yang, L., & Huang, W.L          | 2018        | Polylactic acid/polyglycolic acid copolymer scaffolds carrying bone morphogenetic protein 2 gene enhanced adipose-derived stem cells promote cartilage defect repair | This study aims is to examine regeneration of damaged osteochondral done by ADSCs that transfused by bone morphogenetic protein-2 (BMP-2) which growth on PLGA copolymer scaffold       | BMP-2 supported by ADSCs and PLGA copolymer scaffold is very valuable to facilitate the Regeneration of damaged osteochondral  |
| Ruan, S.Q., Deng, J., Yang, L., & Huang, W.L          | 2018        | Polylactic acid/polyglycolic acid copolymer scaffolds carrying bone morphogenetic protein 2 gene enhanced adipose-derived stem cells promote cartilage defect repair | This study aims is to examine regeneration of damaged osteochondral done by ADSCs that transfused by bone morphogenetic protein-2 (BMP-2) which growth on PLGA copolymer scaffold       | BMP-2 supported by ADSCs and PLGA copolymer scaffold is very valuable to facilitate the Regeneration of damaged osteochondral  |
| Numata, H., Nakase, J., Oshima, T., & Tsuchiya, H     | 2019        | Effectiveness of Adhering adipose-derived stem cells to defective cartilage in promoting cartilage regeneration in a rabbit model                                    | This study aims is to figure capability of local adherent technique and the therapeutic effect as it transplanted ADSCs for cartilage regenerations that endures osteochondritis        | Local adhesion of ADSCs helps Cartilage repair better than injection of intra-articular and surely facilitate the osteochondral damage to regenerate   |

(continued)

**Table 1.** (continued)

|   | <b>Year</b> | <b>Title</b>   | <b>Aim</b>  | <b>Results</b>   |
|---|-------------|--|---|--|
| Wu, S.C., Huang, P.Y., Chen, C.H., Teong, B., Chen, J.W., Wu, C.W., Chang, J.K., Ho, M.L.                                 | 2018        | Hyaluronan microenvironment enhances cartilage regeneration of human adipose-derived stem cells in a chondral defect model                       | This study purposes is to examine the capability of Hyaluronan microenvironment for human ADSCs that used for articular cartilage repair          | Hyaluronic microenvironment facilitate and extend human ADSCs to repair damaged cartilage and has potential as a Foundation of articular cartilage tissue discipline                                     |
| Liao, S., Meng, H., Zhao, J., Lin, W., Liu, X., Tian, Z., Lan, L., Yang, H., Zou, Y., Xu, Y., Gao, X., Lu, S., & Peng, J. | 2022        | Injectable adipose-derived stem cells-embedded alginate-gelatin microspheres prepared by Electrospray for cartilage tissue regeneration          | This study aimed to examined the effectiveness of ADSCs that Embedded by alginate gelatin microspheres (Alg-Gel-MSs) for heals damaged cartilage. | Alg-Gel-ADSCs-MSs extend and facilitate proliferation in Component of cartilage matrix. It also performed the capability to repair cartilage tissue applications   |
| Muttigi, M.S., Kim, B.J., Choi, B.G., Yoshie, A., Kumar, H., Han, Inbo., Park, H.S., & Lee, S.H.                          | 2017        | Matrilin-3 codelivery with adipose-derived mesenchymal stem cells promotes articular cartilage regeneration in a rat osteochondral defect model  | This study purposed to examine the capability of ADSCs combined with matrilin 3 for articular cartilage repair                                    | Matrilin-3 combined with ADSCs perfectly impressed repairing of articular cartilage, and has potential as a stem cell therapy  |
| Wu, L., Cai, X., Zhang, S., Karperien, M., & Lin, Y.  | 2013        | Regeneration of articular cartilage by adipose tissue derived mesenchymal stem cells: Perspectives from stem cell biology and molecular medicine | This article is verifying an up-to-date research that has done adipose stem cells for cartilage repair.   | Articles shows that research about adipose derived stem cells for chondrocytes has improve alongside with the trend and pushing other research as gene manipulation to gain chondrocytes differentiation |

(continued)

**Table 1.** (continued)

|                                   | Year | Title  | Aim   | Results  |
|-----------------------------------|------|--|---|--|
| Ma, H. B., Li, Y. X, & Wang, M. L | 2015 | Adipose-derived stem cells transfected with adenovirus carrying bone morphogenetic protein 14 for repair of articular cartilage injury | This study aims to analyze the capability of BMP-14 combined with ADSCs transfused by adenovirus in process repair of cartilage damaged | The ADSCs almost able to restore cartilage tissue that injured and Strengthen by transfusion of BMP-14 |

**Table 2.** Five most frequently cited cartilage repair using adipose derived-stem cells research articles in Scopus database

| Rank | Cited | Article  |
|------|-------|--|
| 1    | (106) | In vivo cartilage repair using adipose-derived stem cell-loaded decellularized cartilage ECM scaffolds   |
| 2    | (101) | Regeneration of articular cartilage by adipose tissue derived mesenchymal stem cells: Perspectives from stem cell biology and molecular medicine |
| 3    | (41)  | Nanoparticle delivery of the Bone Morphogenetic Protein 4 Gene to Adipose-Derived Stem Cells Promotes Articular Cartilage in Vitro and In Vivo   |
| 4    | (16)  | Matrilin-3 codelivery with adipose-derived mesenchymal stem cells promotes articular cartilage regeneration in a rat osteochondral defect model  |
| 5    | (13)  | Hyaluronan microenvironment enhances cartilage regeneration of human adipose-derived stem cells in a chondral defect model                       |

publication about adipose stem cell and cartilage repair. Other countries such as Japan, Korea, and Taiwan appear as the next rank due to amount of articles reportedly indexed to Scopus database. For UK and Netherlands also reported to has publication criteria mentioned before with a total of 1 article (Table 3), as a correspondence article.

### 3.5 Most Productive Author

Productivity of author assessed on how many articles that published either as first author or as correspondence author. Articles with criteria mentioned that reportedly indexed in Scopus at least written by two authors (13%) and most widely by ten (76,9%) collaborations of authors (Table 1). According to the collected data, Guo Quan Yi wrote two articles about adipose-derived stem cells for cartilage repair, “In vivo cartilage repair using adipose-derived stem cell-loaded decellularized cartilage ECM scaffolds” and “Repair of Articular cartilage defect using adipose-derived stem cell-loaded scaffold derived from native cartilage extracellular matrix” which in those two articles Guo roles



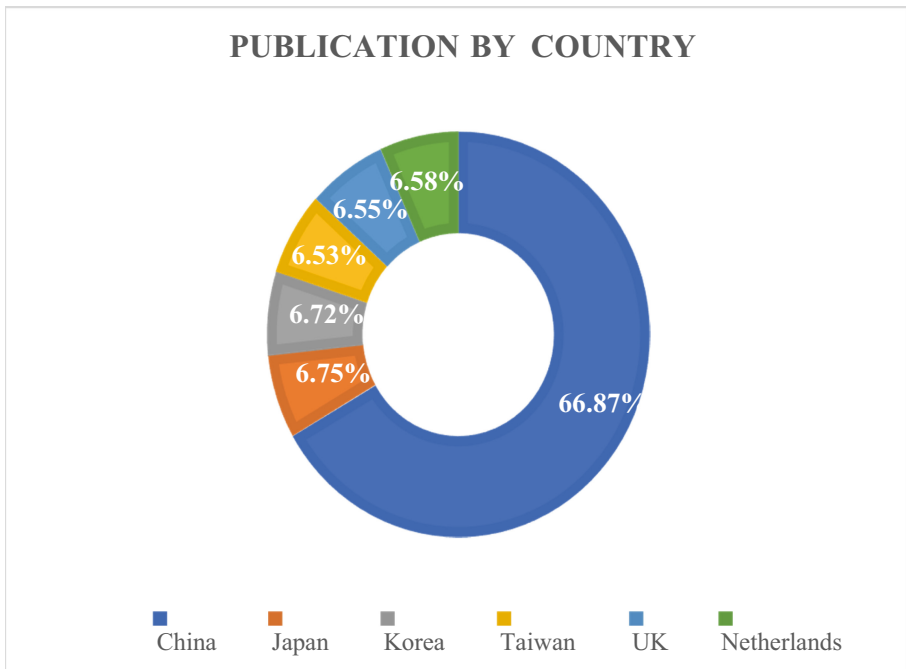
**Table 3.** Articles based on country and institution

| <b>Country</b> | <b>Institution</b>                                       | <b>Title</b>   |
|----------------|--|--|
| China          | Peking University Third Hospital                         | Nanoparticle delivery of the Bone Morphogenetic Protein 4 Gene to Adipose- Derived Stem Cells Promotes Articular Cartilage in Vitro and In Vivo                      |
| China          | Sichuan University and University of Twente, Netherlands | Regeneration of articular cartilage by adipose tissue derived mesenchymal stem cells: Perspectives from stem cell biology and molecular medicine                     |
| China          | Chinese PLA General Hospital and University of Leeds, UK | In vivo cartilage repair using adipose-derived stem cell-loaded decellularized cartilage ECM scaffolds   |
| China          | Mengyin County Hospital                                  | Adipose-derived stem cells transfected with adenovirus carrying bone morphogenetic protein 14 for repair of articular cartilage injury                               |
| Korea          | Chung Ang University                                     | Matrilin-3 codelivery with adipose-derived mesenchymal stem cells promotes articular cartilage regeneration in a rat osteochondral defect model                      |
| China          | Jining Hospital of Stomatology                           | Effect of TGF- $\beta$ 3 transfected with adipose derived stem cells and OGP-HA-chondroitin sulfate scaffold on repair of condylar cartilage in rabbits              |
| China          | Hospital of Zunyi  | Polylactic acid/polyglycolic acid copolymer scaffolds carrying bone morphogenetic protein 2 gene enhanced adipose-derived stem cells promote cartilage defect repair |
| Taiwan         | Kaohsiung Medical University Hospital                    | Hyaluronan microenvironment enhances cartilage regeneration of human adipose-derived stem cells in a chondral defect model   |
| Japan          | Kanazawa University                                      | Effectiveness of Adhering adipose-derived stem cells to defective cartilage in promoting cartilage regeneration in a rabbit model                                    |

*(continued)*

**Table 3.** (continued)

| Country | Institution  | Title   |
|---------|--|---|
| China   | China Medical University   | Chitosan oligosaccharides packaged into rat adipose mesenchymal stem cells-derived extracellular vesicles facilitating cartilage injury repair and alleviating osteoarthritis |
| China   | Shanghai Jiao Tong University School of Medicine   | Effect of a subset of adipose-derived stem cells isolated with liposome magnetic beads to promote cartilage repair  |
| China   | University of Science and Technology of China, Nanjing Drum Tower Hospital and The Chinese People's Liberation Army General Hospital | Repair of Articular cartilage defect using adipose-derived stem cell-loaded scaffold derived from native cartilage extracellular matrix                                       |
| China   | Chinese PLA General Hospital and Guangzhou Medical University  | Injectable adipose-derived stem cells-embedded alginate-gelatin microspheres prepared by electrospray for cartilage tissue regeneration                                       |

**Fig. 2.** Articles indexed on Scopus based on country

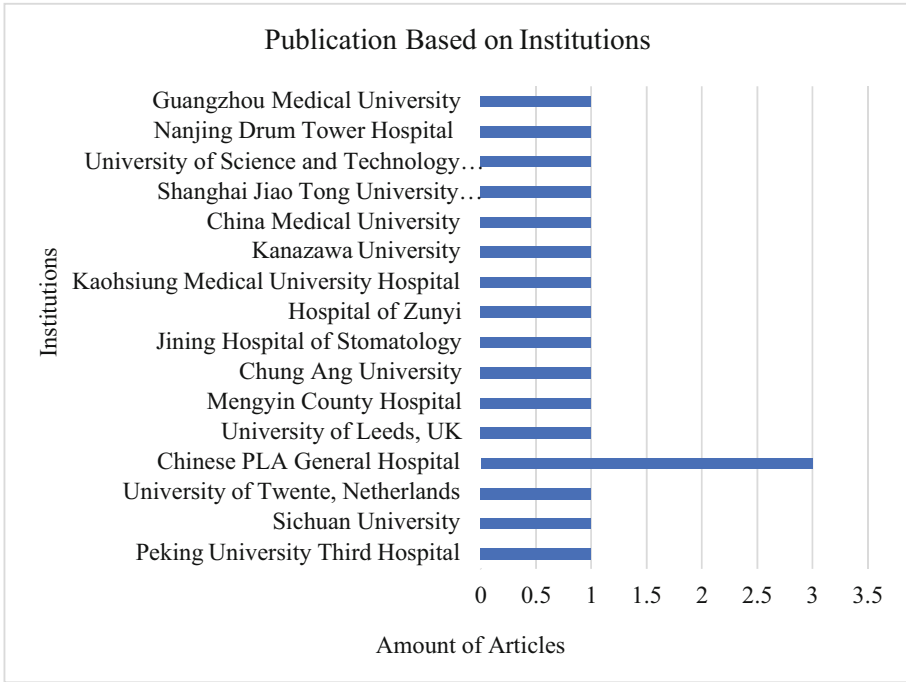


Fig. 3. Articles published regarding to institution

as correspondence author (Table 1). The rest of authors reported only has single publication either as first author or collaborative author. By that, it can tell that Guo is the most productive author to publish an article about ADSCs. Based on collected data, it is also noticed that Guo originated from Chinese People’s Liberation Army Hospital. Then it can be concluded that Chinese PLA General Hospital is the most institutions done research about ADSC build upon Scopus database (Fig. 3).

#### 4 Conclusion

This bibliometric analyze of articles for adipose-derived stem cell for cartilage repair research depict there are 13 articles found and published in Scopus database in range 2013–2022. The most active country to produce ADSCs research is in Asia continental which is China followed by Japan, Korea and Taiwan. UK and Netherlands showed up as a correspondence institute. Even though China became the most active country, however articles that has the most cited entitled “In vivo cartilage repair using adipose-derived stem cell-loaded decellularized cartilage ECM scaffolds” is from Chung-Ang University, an institution from Korea which published in 2013. But this research trend just reaches the peak at 2018 and 2021 which there are 3 publications reported. Meaning that articles published earlier is having opportunity to improve more citation rather than article that has just published recently. Studies and researches about cartilage repair using adipose-derived stem cells has been quiet famous these years. Many research done in

various country in order to gain the knowledge and the potential of adipose-derived stem cells, especially for cartilage damaged therapy. It has big advantage especially for elder community, and obviously trend of the research must keep go on.

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