

Publication Status of Mouse Embryonic Fibroblast Cells in Scientific Journals

Ahmet Sarper Bozkurt 

Department of Physiology, Gaziantep University Faculty of Medicine, Gaziantep, Turkey

ABSTRACT

Objective: A bibliometric analysis was performed to investigate trends in mouse embryonic fibroblast (MEF) cells as a topic and also to compare the contributions of countries, journals, authors, keywords and citations. The elaboration of a strategic plan for the development of scientific research in stem cells and especially MEF as a research topic was analyzed.

Methods: A bibliometric study was carried out on Web of Science (WOS) and Scopus databases comprising the period between 1991 and 2020. These papers were analyzed and evaluated in terms of all years, field parameters (authors, keywords, affiliations, funding agencies, authors' nationalities, article type, networks, h-index of journals and authors) and citations.

Results: As a result of the conducted research, it was found that the WOS and Scopus had published 1,255 and 6,562 papers, respectively, on 'Mouse Embryonic Fibroblast' as topic and article title, abstract and keywords. The articles are analyzed by bibliometric techniques in this study.

Conclusion: On analysis of papers related to the main parameters of MEF, it has been ascertained that the MEF-related articles published in the journals within the scope of Science Citation Index (SCI)/Science Citation Index Expanded (SCI-E) was quite high and is growing rapidly. The medical publication feature has been characterized by international visibility and extensive networking with many foreign research structures. The number of citations was increasing significantly. The publishing patterns were different depending on the area of interest. These data are useful in studying the dynamical nature of science and can help in planning newer studies for researchers.

Keywords: Mouse, embryonic, fibroblast, bibliometric

INTRODUCTION

With increased life expectancy, the researchers are exploring new methods for diagnosed people. Stem cell technology has a great potential for the treatment of infarction tissues. Stem cell technologies and gene editing techniques are two of the most promising developments in a variety of fields. Primitively, the research based on fibroblast cells was described at the end of the 19th century. These cells are the most common type of cell from the connective tissue in animals, presenting an elongated morphology and extended cellular processes, with a fusiform shape.^{1,2} Fibroblasts are mesenchymal-derived cell types, important and major cell types in extracellular matrix, epithelial differentiation, and wound healing. A fibroblast is the most common cells of connective tissue and synthesizes the extracellular matrix and collagen.^{3,4} Practically, fibroblasts were more effective in cell therapy than mesenchymal stem cells, as they may not require isolation of specific subtypes of cells.⁵ The first mouse embryonic fibroblast (MEF) publications are found in 1986⁶ and 1956⁷ in Web of Science and Scopus, respectively. MEF cells have a structure similar to stem cells, which are frequently used as feeder cells because they harbor various growth factors to promote the self-renewal of embryonic stem cells as well as their undifferentiated growth.⁸ The MEF encompasses significant opportunities for both basic research and clinical applications in the areas of regenerative medicine and

tissue engineering. Fibroblast growth factors (FGF) have been identified in mice. It is named FGF1-FGF23. FGFs are mostly found in developing and adult tissues. FGFs have various biological activities both in vivo and in vitro conditions such as angiogenesis, cell migration and tissue wound healing. Another effect of the FGF family has been stated to be important for neuronal signal transmission in the central and peripheral nervous systems.⁹ The establishment of MEF from large animals that model human diseases is significant.¹⁰ Many cell types remodel the extracellular matrix; osteoblasts,¹¹ astrocytes,¹² vascular endothelium,¹³ macrophages,¹⁴ and pericytes.¹⁵ Today, studies related to tumor and the development of some diseases and cell programming research in humans are strongly influenced by mouse models. The laboratory mice with their ease of genetic manipulation have been used in biomedical research for understanding the complexity of different human pathogenesis. But there are both similarities and discrepancies between mouse and human studies.¹⁶ In this study, the MEF topic is investigated to understand and plan a new study. The originality, creativity, curiosity, novelty, potentiality, and capacity of wondering and questioning with respect to unusual observations, capacity to interact, and to create favorable scientific environment are steps of research plan. The bibliometric analysis of MEF was considered cautiously at this stage. The qualitative bibliometric analyses of the topic decreased the

How to cite: Bozkurt AS. Publication Status of Mouse Embryonic Fibroblast Cells in Scientific Journals. Eur J Ther 2021; 27(2): 135–141.

ORCID ID of the author: A.S.B. 0000-0002-7293-0974.

Corresponding Author: Ahmet Sarper Bozkurt E-mail: asbozkurt@gantep.edu.tr

Received: 18.11.2020 • **Accepted:** 19.06.2021

Table 1. Main Statistical Information of MEF Articles in WOS and Scopus

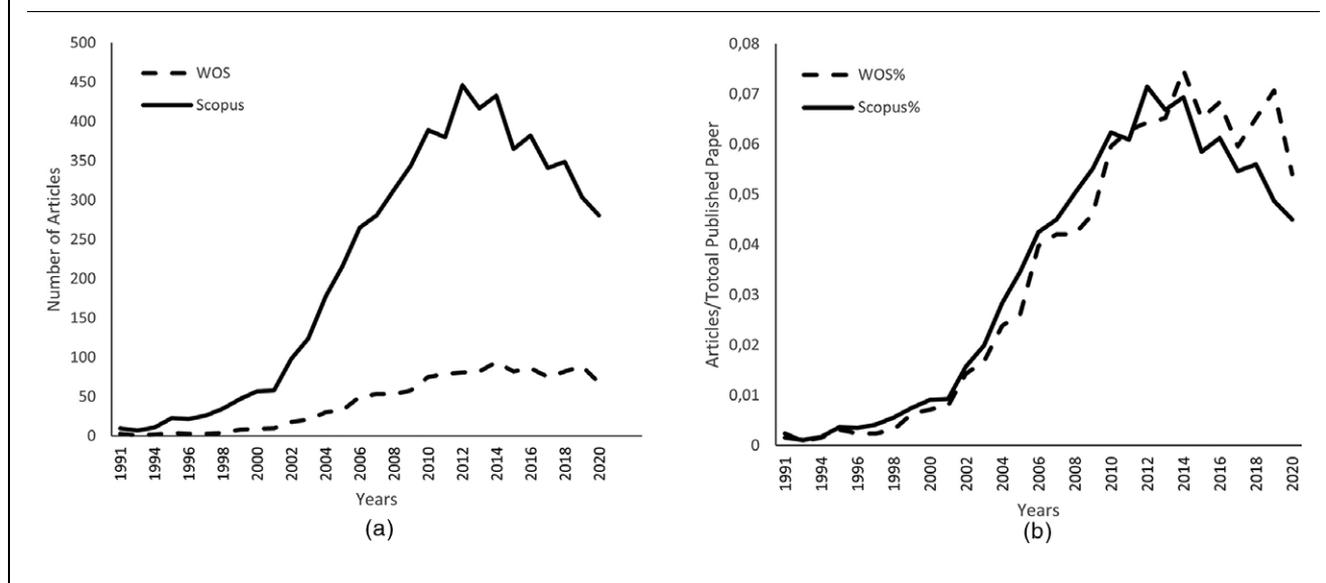
Description	WOS	Scopus
Timespan	1991:2020	1997:2020
Sources (journals, books, etc.)	567	1,179
Documents	1,255	6,000
Average years from publication	7.89	8.26
Average citations per documents	32.14	44.29
Average citations per year per doc	3.032	4.035
<i>Document types</i>		
Article	1,171	5,766
Article: book chapter	15	57
Article: proceedings paper	15	67
Correction	1	7
Review	5	71
<i>Document contents</i>		
Keywords plus (ID)	4,618	28,688
Author's keywords (DE)	3,050	9,004
<i>Authors</i>		
Authors	5,879	26,898
Author appearances	7,733	42,297
Authors of single-authored documents	9	57
Authors of multiauthored documents	5,870	26,841
<i>Authors collaboration</i>		
Documents per author	0.213	0.223
Authors per document	4.68	4.48
Coauthors per documents	6.16	7.05
Collaboration index	4.71	4.52

Main Point

- Such studies open a variety of new areas for scientists and manifest health-informatics importance.
- The publications on MEF as topic has shown an increasing trend.
- This study is expected to contribute to the preparation of more original studies on the related subjects, besides preventing repetitive studies relating MEF cells.

risks in research. The paucity or absence of significant publications, global productivity of a researcher, repetition of articles, impact factor, h-index, citation index of papers, the best journals of the discipline were analyzed carefully by this method. The impact factors of papers published in international journals indexed in WOS and Scopus, rank of scientists, associated coauthors were analyzed. The use of artificial intelligence and big data in medicine is growing rapidly in recent years. The bibliometric and phrase frequency analysis that covered the popularity of authors, journals and organizations, publication properties, and the frequency of words and phrases in title keywords and abstracts appeared in the literature. To the best of

Figure 1. The increase in (a) the number and (b) ratio of articles in WOS (dashed line) and Scopus (straight line) databases.



our knowledge, this is the first study aimed at investigating the research on MEF originating on a global basis. The aim of this study was to provide a primer point of scientific results for high-quality research and highlight possible potentials in this field, thereby promising future collaborations for catalyzing the scientific innovation.

METHODS

In order to understand the work done with MEF cells from the repetitive publications, also to determine the international limits of the work done with these cells and to guide future studies, the bibliometric method is used. The bibliometric analysis provides more objective and reliable statistical results,¹⁷ by having the analyses of documentation related to the field of interest.¹⁸ Through the evolution of the digital age, the scientific community has been investigating and representing a huge number of papers in all fields. Many online scientific databases such as Web of Science, Science Direct, Scopus, Researchgate, and Google Scholar were the sources of article information. Precisely, the Web of Science and the Scopus are the two most extensive databases chosen for this analysis. A new research paper is published every 30 seconds, and there are 10,000 updates to PubMed every day. WOS is maintained by Clarivate Analytics to explore the systematic literature reviews of different scientific domains. It includes different citation databases with journal conference proceedings and books. Scopus, an another alternative database for retrieving bibliometric datasets, considers wider timespan than WOS. The well-known and widely used databases of WOS and Scopus are advantaged for searching the literature on different scientific fields.¹⁹ WOS had been the only citation database which covered all domains of science for many years. Other widespread used database of Scopus database in Elsevier Science started at 2004. As previously explained, the disadvantages of these databases are higher rate of duplicated citation, self-citation records, and certain lack of standardization procedures. WOS is considered the source of bibliometric data with the highest quality of informa-

tion. The WOS database was used to search for documents containing the 'Mouse Embryonic Fibroblast' as a topic with quotes. To collect the MEF-related articles, we queried the WOS indexing database on September 20, 2020. A bibliometric analysis was conducted to look into the article's publication date, journal's name, authors' institutions, organizations, article and author's citations and the related countries. The number of publications is currently increasing, and it is becoming increasingly infeasible to remain updated with everything that is being published. We searched for all the documents in WOS including MEF as topic, obtaining 1,255 entries. We performed bibliometric analysis by using main information about publication and its citation performance parameters for productivity and research performance. The inappropriate data of some journals and irrelevant articles were eliminated and the dataset was rearranged for bibliometric analyses. This set covers documents published until September 2020, since the WOS Core Collection indexes only those MEF publications which appeared after 1991. This is a well-known limit because the keywords of the documents published before the nineties are generally not indexed.²⁰ The number of articles related to MEF was 1,255, including 1,171 articles, 15 proceedings papers, and five reviews in this reference interval. The limitation of this study is mainly related to the used tools and methods of bibliometric analysis. We included articles from WOS and Scopus, but the most common medical database PubMed is not included. The analyses and results in this study provide significant insights into the evolving trends over the last decades.

Statistical Analysis

Data were collected and exported into bibliometric R-package for generating descriptive analyses, statistical graphs, and science maps²¹

RESULTS AND DISCUSSION

Towards the end of 1990s, the volume of documents increased annually, with an average production equal to 7.92 documents

Table 2. The Impact of Authors in MEF Topic in WOS

Author	h-index	TC	NP	PY
Zhang Y	11	472	23	2006
Li Y	11	453	16	2008
Wang Y	9	217	15	2011
Li X	9	358	14	2008
Wang L	9	446	13	2004
Zhang J	8	281	17	2005
Liu Y	8	289	12	2006
Batiha Ges	7	106	11	2019
Beshbishy Am	7	106	11	2019
Wang Z	6	122	13	2008
Özdemir A	5	175	17	2015
Kaplancikli Za	5	133	13	2015
Zhang	5	142	11	2009
Atli O	5	146	11	2014
Sever B	4	48	12	2017

TC, total citations; NP, number of publication; PY, publication year.

Table 3. Country Scientific Production in Scopus

Country	Frequency	Country	Frequency
USA	7,200	Australia	344
China	2,251	India	268
Japan	2,224	Netherlands	253
South Korea	1,047	Sweden	227
Germany	1,021	Iran	208
Canada	793	Switzerland	206
UK	742	Turkey	205
France	572	Singapore	199
Spain	488	Belgium	152
Italy	461	Austria	144

per year. The main information and statistics of analyzed articles are reported in [Table 1](#). A number of publications increase and reach at least 50 documents per year in WOS. The total number of papers in Scopus is higher than WOS. But the increase in the ratio of articles to the total published docu-

Table 4. Most Cited Countries in WOS

Country	Total citations	Average article citations
USA	19,705	57.28
Japan	3,821	31.07
China	2,762	14.93
Korea	1,976	16.2
United Kingdom	1,767	49.08
India	963	16.05
Israel	962	160.33
Singapore	918	76.5
Canada	866	26.24
Spain	786	34.17
Sweden	713	64.82
Germany	659	21.97
Australia	594	37.12
France	513	34.2

ments is similar to WOS as shown in [Figure 1](#). The main factors for the growth in the number of articles are the increasing number of researchers and the development of laboratory opportunities. When searching for MEF, we found that there was only one document before 1991 in WOS. The number of articles on WOS and Scopus database is compared in years between 1991 and 2020 in [Figure 1](#). The search results revealed 1,255 articles in WOS and 6,562 articles in Scopus. The articles in WOS showed an average citation of 32.14 per article in the period between 1991 and 2020 and were written by 4.68 authors with a mean of 0.212 articles per author as shown in [Figure 1](#). The articles in Scopus showed an average citation of 44.29 per article in the period between 2007 and 2020 (latest 6,000 papers were selected) and were written by 4.48 authors with a mean of 0.223 articles per author. In [Table 2](#), the impact of authors with h-index and publications data are shown. There were five Turkish authors in the author's impact list of WOS in MEF topic. The authors' Hirsch index (h-index) is an author-level publication metric that attempts to measure both the productivity and citation impact of a scientist or scholar.^{22,23} The h-index of the following scientists with citations is given in [Table 2](#). The most productive countries were analyzed using Scopus database and are tabulated in [Table 3](#). The generated citations were used to find the frequency of the most cited references or the most cited first authors or the countries. The most cited countries sorted by total citations in WOS are shown in [Table 4](#). The total citations should increase with the increase in the number of publications, in general; however, a high number of publications do not represent high citation numbers in this study. The cited references have problems in the format due to nonstandardized format in databases. In [Figure 2](#), the

Figure 2. Most relevant journals of MEF.

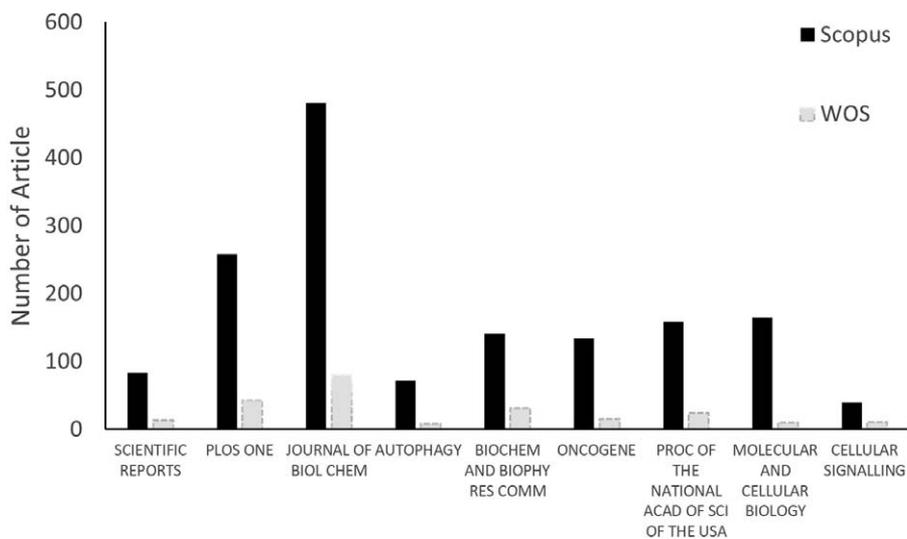


Table 5. Most Global Cited Documents in Scopus

Author, paper	Total citations	TC/year
Stambolic V, 1998, Cell	1,945	84.56
Zinszner H, 1998, Genes Dev	1,558	67.73
Okita K, 2008, Science	1,494	114.92
Xu C, 2001, Nat Biotechnol	1,492	74.60
De Brito Om, 2008, Nature	1,341	103.15
Burma S, 2001, J Biol Chem	1,268	63.40
Jacobs JI, 1999, Nature	1,266	57.545
Scorrano L, 2003, Science	1,147	63.72
Wang JI, 2000, Proc Natl Acad Sci USA	1,059	50.42
Zhao T, 2011, Nature	992	99.20

most productive source was the “Journal of Biological Chemistry” in WOS and Scopus. The number of articles on MEF in journals is comparatively given in Figure 2. WOS and Scopus databases are permanently improving. The significant advantage of choosing one of these two sources depends on the subject’s area. Among the most cited articles, countries are given in Table 5. The first ranked article is “Stambolic V, 1998, Cell” with 1,945, followed by “Zinszner H, 1998, Genes Dev” with 1,558 global citations. The various most frequent keywords and their importance within the collection of articles are given in Table 6. As expected, the most frequent phrases (common keywords) in the WOS and Scopus database results were cytotoxicity, MEF, apoptosis, and autophagy, as that MEF was also the main search term. The keywords in articles could reflect the change of hot spots and concerns in databases with their own

priorities. The thematic evolution due to authors’ keyword is given in Figure 3. From the analysis of publications and the publishing profile, the thematic evolution due to authors’ keyword is presented. And Interestingly, the keywords and the trend were given in current research. After analyzing each sub-period, it is possible to trace the temporal evolution of MEF research keywords. The diagram is used to show profiles, connections, and developments of the themes in this time interval.

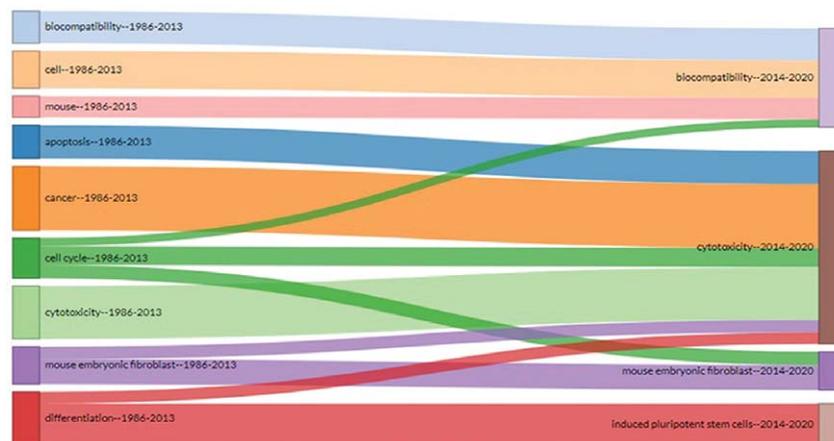
CONCLUSION

This paper focused at presenting a systematic analysis of MEF topic-related articles published on WOS and Scopus databases through a bibliometric approach. In this study, the bibliometric profile of MEF in scientific publications was documented in two

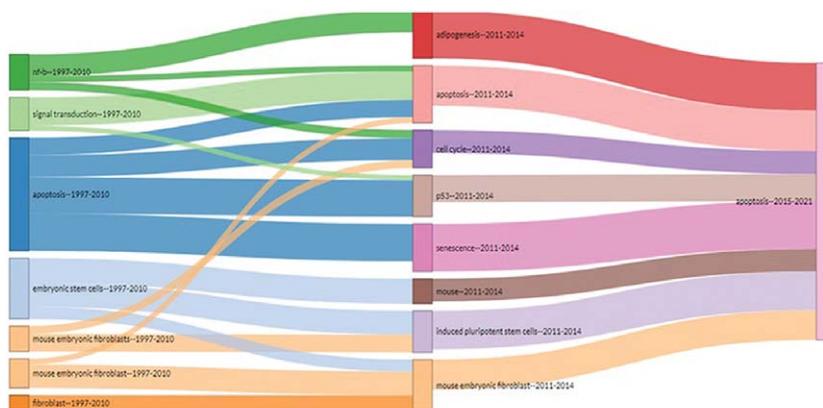
Table 6. Most Frequent and Most Important Phrases (Most Frequent Keywords)

WOS			Scopus		
Item	Freq	Year	Item	Freq	Year
Cytotoxicity	58	2016	Apoptosis	88	2018
Mouse embryonic broblast	37	2012	Autophagy	87	2018
Autophagy	35	2015	Mouse embryonic broblasts	67	2018
P53	27	2012	Cytotoxicity	59	2017
Differentiation	23	2009	Mitochondria	49	2018
Embryonic stem cells	23	2009	Cancer	34	2017
Mouse	21	2013	Induced pluripotent stem cells	33	2018
Biocompatibility	19	2016	Reprogramming	33	2018
Embryonic stem cell	19	2009	Senescence	25	2019
Fibroblast	16	2016	Mtor	23	2017
DNA damage	16	2010	P53	22	2017
Cell	16	2013	Cell proliferation	20	2016

Figure 3. The thematic evolution due to authors' keyword (a) in WOS and (b) in Scopus.



(a)



(b)

databases. The indicators were used to describe the comprehensive picture of the documents, the scientific activity, capacity, and orientation. The results drawn are salient as they provide requisite suggestions for scholars and publishers. The number of articles on MEF as a topic has shown an increasing trend in this period. The most frequently used keywords are apoptosis, mouse embryonic fibroblast, autophagy, P53, differentiation, and embryonic stem cells. In summary, both the articles and reviews in this research are an excellent source of information on the current knowledge in the fibroblast growth factor signaling pathway in metabolic regulation, development, disease, and repair after injury field. An analysis on the other textual information could be considered to enrich our findings on MEF. A large amount of research indicate several features of MEF, and furthermore, in order to understand the fibroblast and especially MEF, several additional in vitro and in vivo experiments are needed. This study provided significant insights into the evolution of the topics discussed throughout the years. These types of methodological practices will greatly contribute to the research fields.

Ethics Committee Approval: N/A

Informed Consent: N/A

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author has no conflicts of interest to declare.

Financial Disclosure: The author declared that this study has received no financial support.

REFERENCES

- Duval M. *Atlas d'embryologie*. Paris: G. Masson, 1889.
- Virchow R. *Genauere Geschichte der Fettmetamorphose*. Virchow R. Die Cellularpathologie in ihrer Begründung auf physiologische und pathologische Gewebelehre. Berlin, Germany: Verlag von August Hirschwald, 1858:312-333.
- Croft C. Ultrastructural features of wound healing in mouse skin. *J Anat*. 1969;105:189-190.
- Lynch MD, Watt FM. Fibroblast heterogeneity: Implications for human disease. *J Clin Invest*. 2018;128(1):26-35. [\[CrossRef\]](#)
- Ichim TE, O'Heeron P, Kesari S. Fibroblasts as a practical alternative to mesenchymal stem cells. *J Trans Med*. 2018;16(1):212. [\[Cross-Ref\]](#)
- Haarr L, Kleppe K, Lillehaug JR. Changes in polypeptide-synthesis and glycosylation in mouse embryonic fibroblast C3h/10t1/2-Cl-8 cells caused by the tumor promoter 12-O-tetradecanoylphorbol 13-acetate. *Biochim Biophys Acta*. 1986;889(3):334-345. [\[CrossRef\]](#)
- Tobioka M, Bieseke JJ. Mitochondria in living cells: An analysis of movements. *J Cell Biol*. 1956;2(4):319-324. [\[CrossRef\]](#)
- Qin Y, Shin JH, Yoon J-H, Park S-H. Embryonic fibroblasts promote antitumor cytotoxic effects of CD8+ T cells. *Front Immunol*. 2018;9:685. [\[CrossRef\]](#)
- Bozkurt AS. *An Investigation of the Effect of Extracellular Vesicles Isolated from Mouse Embryonic Fibroblasts on Wound Healing in an Experimental Diabetic Mouse Model* [PhD thesis]. Department of Physiology, University of Gaziantep, 2018:7-10.
- Kalluri R, Zeisberg M. Fibroblasts in cancer. *Nat Rev Cancer*. 2006;6(5):392-401. [\[CrossRef\]](#)
- Ortega N, Behonick DJ, Werb Z. Matrix remodeling during endochondral ossification. *Trends Cell Biol*. 2004;14(2):86-93. [\[CrossRef\]](#)
- Hernandez MR. The optic nerve head in glaucoma: Role of astrocytes in tissue remodeling. *Prog Retinal Eye Res*. 2000;19(3):297-321. [\[CrossRef\]](#)
- Davis GE, Senger DR. Endothelial extracellular matrix: Biosynthesis, remodeling, and functions during vascular morphogenesis and neovessel stabilization. *Circ Res*. 2005;97:1093-1107. [\[CrossRef\]](#)
- Shapiro SD, Senior RM. Matrix metalloproteinases: Matrix degradation and more. *Am J Respir Cell Mol Biol*. 1999;20(6):1100-1102. [\[CrossRef\]](#)
- Birbrair A, Zhang T, Files DK, et al. Type-1 pericytes accumulate after tissue injury and produce collagen in an organ-dependent manner. *Stem Cell Res Ther*. 2014;5(6):122. [\[CrossRef\]](#)
- Gabdoulline R, Kaisers W, Gasper A, et al. Differences in the early development of human and mouse embryonic stem cells. *PLoS One*. 2015;10(10):e0140803. [\[CrossRef\]](#)
- Diodato VP, Gellatly P. *Dictionary of Bibliometrics*. London: Routledge, 2013.
- McBurney MK, Novak PL. What is bibliometrics and why should you care? In *Proceedings of the IEEE International Professional Communication Conference*. 2002. IEEE. [\[CrossRef\]](#)
- Guz A, Rushchitsky J. Citation analysis of publications of NASU mechanicians in the database of the Thomson Reuters Institute for Scientific Information. *Int Appl Mech*. 2009;45(7):699. [\[Cross-Ref\]](#)
- Rousseau R, Egghe L, Guns R. *Becoming Metric-Wise: A Bibliometric Guide for Researchers*. Sawston, Cambridge: Chandos Publishing, 2018.
- Bibliometrix R Package. 2019. <https://www.bibliometrix.org>. Accessed 9 July 2020.
- Alonso S, Cabrerizo FJ, Herrera-Viedma E, Herrere F. h-Index: A review focused in its variants, computation and standardization for different scientific fields. *J Inform*. 2009;3(4):273-289. [\[CrossRef\]](#)
- Egghe L. The Hirsch index and related impact measures. *Ann Rev Inform Sci Technol*. 2010;44(1):65-114. [\[CrossRef\]](#)