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Global publication trends in ophthalmic genetics and gene therapy research: A Scientometric analysis

Tendências globais de publicação de pesquisas sobre genética oftálmica e terapia genética: uma análise cientométrica

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ABSTRACT

Objective: *A scientometric analysis produced in ophthalmic genetics and gene therapy research is lacking. The purpose of this study is to present a holistic analysis of ophthalmic genetics literature.* ***Methods:*** *The data used in this study were obtained from the Web of Science (WoS) Core Collection. All published documents between 1975-2019 were included. The data exported from WoS enabled the extensive details of ophthalmic genetics related literature including countries, institutions, authors, citations and keywords. Scientometric network maps of keywords and also country and institution co-authorships were created with free software. Global contributions of the countries to the ophthalmic genetics literature were shown by a graphic.* ***Results:*** *The search query revealed a total of 2322 documents. Most of the documents were original articles (75.75%). USA was the leading country by producing 45.39% of all documents in ophthalmic genetics research followed by UK, Germany, China and France. Pennsylvania University was the most contributing institution in the literature (5.25%) followed by University College London and Moorfields Eye Hospital. The average citations per item was 29.4. The most used keywords over a 40-year period were 'family', 'cell', 'photoreceptor' and 'expression'.* ***Conclusions:*** *USA and UK dominated the ophthalmic genetics research. A substantial increase in the number of published documents in this field were observed after 2010.*

Keywords: *Gene therapy; Retinal diseases; Eye diseases/genetics; Scientometrics; Altmetrics*

RESUMO

Objetivo: A literatura carece de análise cienciométrica produzida em genética oftálmica e de pesquisa em terapia genética. O objetivo deste estudo é apresentar uma análise holística da literatura genética oftálmica. **Métodos:** Os dados utilizados neste estudo foram obtidos na base de dados Web of Science (WoS) Core Collection. Todos os documentos publicados entre 1975 e 2019 foram incluídos na análise. Os dados exportados da WoS viabilizaram acesso a amplos detalhes da literatura relacionada à genética oftálmica, incluindo países, instituições, autores, citações e palavras-chave. Mapas de rede cienciométrica foram criados por meio de software gratuito, com base em palavras-chave e em coautorias de países e instituições. As contribuições globais dos países para a literatura sobre genética oftálmica foram apresentadas em gráfico. **Resultados:** a busca por pesquisas revelou um total de 2.322 documentos cuja maioria eram artigos originais (75,75%). Os EUA foram o país que mais produziu artigos sobre o tema, com 45,39% de todos os documentos em pesquisa genética oftálmica; ele foi seguido pelo Reino Unido, Alemanha, China e França. A Universidade da Pensilvânia foi a instituição que mais contribuiu para a literatura (5,25%), e foi seguida pela University College London e pelo Moorfields Eye Hospital. A média de citações por item foi de 29,4. As palavras-chave mais usadas em um período de 40 anos foram 'família', 'célula', 'fotorreceptor' e 'expressão'. **Conclusões:** Os EUA e o Reino Unido dominaram a pesquisa em genética oftálmica. Após 2010, observou-se um aumento substancial no número de documentos publicados nessa área.

Descritores: Terapia genética; Doenças retinianas; Oftalmopatias/genética; Cientometria; Almetria

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Introduction

Bibliometrics analyses publications generated in a specific discipline of academic literature and elucidates publication patterns and trends. Scientometrics also known as 'science of science' is a recent and popular statistical discipline explores all features of scientific literature.[1,2] Scientometric studies evaluate characteristics and features of the authors, organizations and countries of the documents in the literature.[1]

Although ophthalmic genetics and gene therapy in ophthalmology are the trend topics of the ophthalmology practice, there has been no recent scientometric analysis of publications published in ophthalmic genetics and gene therapy literature. This study aims to present a comprehensive analysis of academic literature about ophthalmic genetics and gene therapy in ophthalmology. To the best of our knowledge, this is the first report in this field.

Methods

All data of this study were obtained from Web of Science Core Collection (WoS; Thomson Reuters, New York, NY, USA) databases and carried out on 17 December 2019. A search question including keywords of ('ophthalmic genetics OR 'inherited retinal disease' OR 'gene therapy') AND ('ophthalmology'). All documents from the WoS database produced between 1975 and 2019 included in the analyses. Data were exported from WoS in "Full record and cited references" and "Tab-delimited for Mac" formats. A free web source titled GunnMap 2 application -a free web site-was used to create a world map informing publication production densities of world countries.[3] Scientometric network analysis was achieved by using VOS viewer freeware (Leiden University, Leiden, Netherlands).[4] Citation counts reflect all the documents obtained on 17 December 2019 when the WoS database search process for this study was conducted. Institutions were determined using the "Organizations-Enhanced" field. Documents from England, Wales, Scotland and Northern Ireland were combined under the United Kingdom (UK).

Results

General characteristics of the documents

A total of 2322 published documents were retrieved during the period 1975–2019, 75.75% of which were original articles. The most popular research areas of the literature were ophthalmology, genetics heredity, biochemistry molecular biology, experimental research medicine and neurosciences (39.36%, 27.73%, 13.52%, 9.99% and 8.22%, respectively). The first document about this field was published in 1982. The peak year of production was 2018 with 243 items. The predominant language of the literature was English (95.12%) followed by German, French, Spanish and Portuguese (2.65%, 1.32%, 0.40% and 0.16%, respectively) (Table 1).

The most contributing authors, journals, meetings and institutions

The most productive author was Moore AT with 58 articles in this area (Table 1). The most contributed source title was found to be Investigative Ophthalmology Visual Science with 181 articles followed by Human Molecular Genetics, Plos One, Molecular Vision, British Journal of Ophthalmology, Scientific Reports and Ophthalmic Genetics (n=181, 66, 62, 59, 52, 49 and 45 items, respectively; Table 1). The most contributing meetings were noted to be the Annual Meeting of The Association for Research in Vision and Ophthalmology-ARVO in this field. The most productive institutions in the world were from USA and UK. Pennsylvania University was the most contributing institution in the literature with 122 documents followed by University College London and Moorfields Eye Hospital (Table 2).

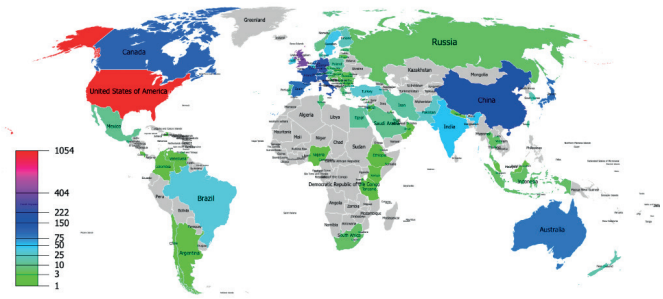

Figure 1: Publication density of world countries in ophthalmic genetics research

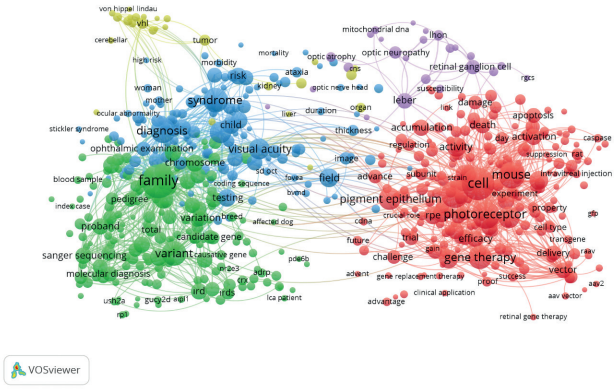

Figure 2: Scientometric network of the most used keywords in ophthalmic genetics literature

Global productivity

USA was the leading country in the ophthalmic genetics and gene therapy literature and covered 45.39% of all productivity with 1054 items. The UK was the second leading country with 404 documents followed by Germany, China and France (n=222, 181 and 163 items, respectively; Table 1). The North America and Europe dominated the publication density around the world but the least contribution to this field was observed in Africa (Figure 1).

Citations, keywords analysis and co-authorship network for countries and institutions

The h-index of the literature was 126 in this period and the total number of citations was 73040 (64094 without self-citations). The average citations per item was 29.4. The most cited document was an original article written by Maguire AM. Et al titled 'Safety and efficacy of gene transfer for Leber's congenital amaurosis' published in the New England Journal of Medicine in 2008 (Table 3). The most used keywords over a 40-year period were 'family', 'cell', 'photoreceptor' and 'expression' (Table 3). The scientometric network of keywords showed a 'dichotomous pattern' (Figure 2). USA was the most collaborative country with 1054 documents followed by the UK (Figure 3). Pennsylvania

Table 1
General characteristics of publications in ophthalmic genetics and gene theraphy research between 1975 and 2019

Document Types	**Record count**	**% of 2322**
Article	1759	75.754
Review	393	16.925
Meeting abstract	102	4.393
Proceedings paper	95	4.091
Book chapter	46	1.981
Editorial material	31	1.335
Early access	11	0.474
Correction	6	0.258
Letter	6	0.258
Note	5	0.215
Book	1	0.043
Item about an individual	1	0.043
Reprint	1	0.043
Retracted publication	1	0.043
Total	2322	100
Research Areas	**Record count**	**% of 2322**
Ophthalmology	914	39.363
Genetics heredity	528	22.739
Biochemistry molecular biology	314	13.523
Research experimental medicine	232	9.991
Neurosciences/neurology	191	8.226
Science tecnology/other topics	172	7.407
Cell biology	147	6.331
Biotechnology applied microbiology	108	4.651
General internal medicine	65	2.799
Pharmacology/pharmacy	57	2.455
Oncology	46	1.981
Veterinary sciences	39	1.680
Pediatrics	32	1.378
Pathology	30	1.292
Life sciences biomedicine/other topics	29	1.249
Endocrinology metabolism	24	1.034
Hematology	24	1.034
Chemistry	19	0.818
Biophysics	18	0.775
Physiology	16	0.689
The 20 most prolific authors	**Record count**	**% of 2322**
Moore AT	58	2.498
Michaelides M	49	2.110
Webster AR	47	2.024
Cremers FPM	40	1.723
Stone EM	38	1.637
Sahel JA	37	1.593
Bennett J	36	1.550
Bhattacharya SS	33	1.421
Jacobson SG	32	1.378
Sharon D	32	1.378
Aguirre GD	31	1.335
Banin E	30	1.292
Auricchio A	29	1.249
Pierce EA	29	1.249
Daiger SP	28	1.206
Inglehearn CF	25	1.077
Ayuso C	24	1.034
Chen R	24	1.034
Holder GE	24	1.034
Ali RR	23	0.991

The 10 most productive source titles	Country	Records	% Of 2322
Investigative Ophthalmology Visual Science	USA	181	7.795
Human Molecular Genetics	UK	66	2.842
Plos One	USA	62	2.670
Molecular Vision	USA	59	2.541
British Journal of Ophthalmology	UK	52	2.239
Scientific Reports	UK	49	2.110
Ophthalmic Genetics	UK	45	1.938
Proceedings of The National Academy of Sciences of The United States of America	USA	43	1.852
Experimental Eye Research	USA	36	1.550
American Journal of Human Genetics	USA	34	1.464
The top 20 countries		**Records**	**% Of 2322**
Usa		1054	45.392
England		404	17.399
Germany		222	9.561
China		181	7.795
France		163	7.020
Italy		147	6.331
Canada		111	4.780
Netherlands		101	4.350
Japan		100	4.307
Spain		95	4.091
Australia		87	3.747
Switzerland		74	3.187
Israel		59	2.541
India		52	2.239
Sweden		44	1.895
Belgium		40	1.723
Ireland		40	1.723
Scotland		38	1.637
Brazil		33	1.421
Turkey		29	1.249

Table 2
The 20 most productive institutions in ophthalmic genetics and gene therapy literature between 1975 and 2019

Organizations	Country	Records	% Of 2322
Pennsylvania University	USA	122	5.254
University College London	UK	117	5.039
Moorfields Eye Hospital	UK	100	4.307
University College London-The Institute of Ophthalmology	UK	76	3.273
Iowa University	USA	65	2.799
Radboud University	Netherlands	62	2.670
National Eye Institute	USA	61	2.627
Tubingen University	Germany	52	2.239
California University Los Angeles	USA	51	2.196
Baylor College of Medicine	USA	49	2.110
Columbia University	USA	46	1.981
Florida University	USA	45	1.938
California University San Francisco	USA	42	1.809
Cambridge University	UK	42	1.809
Harvard University	USA	41	1.766
Michigan University	USA	41	1.766
Johns Hopkins University	USA	38	1.637
French National Institute of Health and Medical Research	France	36	1.550
Oxford University	UK	35	1.507
Pierre and Marie Curie University	France	35	1.507

Table 3
Most cited articles and keywords in ophthalmic genetics and gene therapy literature between 1975-2019

Article	Author(s)	Journal	Year	Total citations	Average citations per Year
Safety and efficacy of gene transfer for Leber's congenital amaurosis	Maguire, Albert M.; Simonelli, Francesca; Pierce, Eric A. et al	New England Journal of Medicine	2008	1356	113
The human ATP-binding cassette (ABC) transporter superfamily	Dean, M; Rzhetsky, A; Allikmets, R.	Genome Research	2001	1159	61
Nuclear gene OPA1, encoding a mitochondrial dynamin-related protein, is mutated in dominant optic atrophy	Delettre, C; Lenaers, G; Griffoin, JM et al	Nature Genetics	2000	901	45.05
The ABC of APC	Fearnhead, NS; Britton, MP; Bodmer, WF	Human Molecular Genetics	2001	590	31.05
Multiple Growth-Factors, Cytokines, And Neurotrophins Rescue Photoreceptors from The Damaging Effects of Constant Light	Lavaıl, Mm; Unokı, K; Yasumura, D. et al	Proceedings of The National Academy of Sciences of The United States of America	1992	580	20.71
Therapeutic in vivo gene transfer for genetic disease using AAV: progress and challenges	Mingozzi, Federico; High, Katherine A.	Nature Reviews Genetics	2011	530	58.89
Age-dependent effects of RPE65 gene therapy for Leber's congenital amaurosis: a phase 1 dose-escalation trial	Maguire, Albert M.; High, Katherine A.; Auricchio, Alberta et al	Lancet	2009	520	47.27
Apoptotic Photoreceptor Cell-Death in Mouse Models of Retinitis-Pigmentosa	Porteracaılliau, C; Sung, Ch; Nathans, J. et al.	Proceedings of The National Academy of Sciences of The United States of America	1994	519	19.96
Mutations in RPE65 cause autosomal recessive childhood-onset severe retinal dystrophy	Gu, SM; Thompson, DA; Srikumari, CRS et al.	Nature Genetics	1997	450	19.57
Germline Mutations in The Von hippel-Lindau Disease Tumour-Suppressor Gene - Correlations with Phenotype	Chen, F; Kishida, T; Yao, M. et al.	Human Mutation	1995	414	16.56
Pharmacology of nucleoside and nucleotide reverse transcriptase inhibitor-induced mitochondrial toxicity	Kakuda, TN	Clinical Therapeutics	2000	409	20.45
Histopathology of the human retina in retinitis pigmentosa	Milam, AH; Li, ZY; Fariss, RN.	Progress in Retinal and Eye Research	1998	391	17.77
Gene Therapy for Leber's Congenital Amaurosis is Safe and Effective Through 1.5 Years After Vector Administration	Simonelli, Francesca; Maguire, Albert M.; Testa, Francesco et al.	Molecular Therapy	2010	359	35.9
Biodegradable polymers as non-viral carriers for plasmid DNA delivery	Luten, Jordy; van Nostruin, Cornelus F.et al.	Journal of Controlled Release	2008	356	29.67
Gene Therapy for Leber Congenital Amaurosis Caused by RPE65 Mutations Safety and Efficacy in 15 Children and Adults Followed Up to 3 Years	Jacobson, Samuel G.; Cideciyan, Artur V.; Ratnakaram, Ramakrishna et al.	Archives of Ophthalmology	2012	348	43.5
Retinal-specific guanylate cyclase gene mutations in Leber's congenital amaurosis	Perrault, I; Rozet, JM; Calvas, P. et al.	Nature Genetics	1996	344	14.33
Retinitis pigmentosa	Hamel, C.	Orphanet Journal of Rare Diseases	2006	340	24.29
Distribution of fundus autofluorescence with a scanning laser ophthalmoscope	Vonruckmann, A; Fitzke, FW; Bird, AC.	British Journal of Ophthalmology	1995	334	13.36

Expression in Cochlea and Retina of Myosin VIIA, The Gene-Product Defective in Usher Syndrome Type 1B	Hasson, T; Heintzelman, Mb; Santos--Sacchı, J. et al.	Proceedings of The National Academy of Sciences of The United States of America	1995	330	13.2
Photoreceptor degeneration: genetic and mechanistic dissection of a complex trait	Wright, Alan F.; Chakarova, Christina F.; El-Aziz, Mai M. et al.	Nature Reviews Genetics	2010	317	31.7

Keywords	Records
Family	451
Cell	414
Photoreceptor	340
Expression	293
Mouse	256
Diagnosis	236
Syndrome	236
Variant	229
Gene therapy	212
Pigment epithelium	200
Animal model	178
Visual acuity	178
Activity	153
Clinical trial	146
Exon	141
Mouse model	139
Child	124
Cohort	120
Risk	120
Chromosome	119

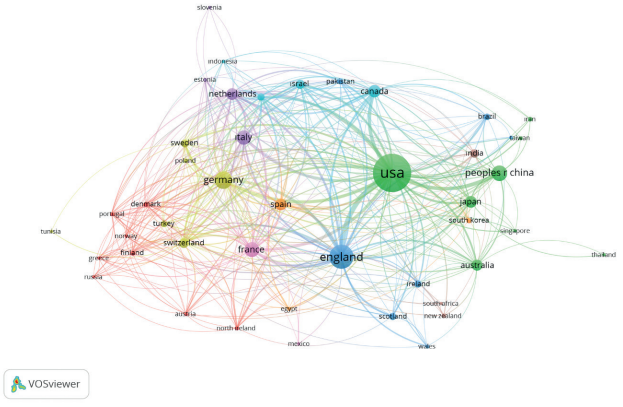

Figure 3: Scientometric network of the most collaborative countries in ophthalmic genetics literature

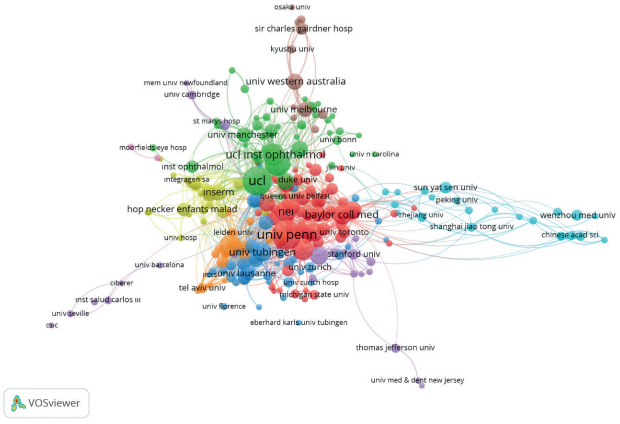

Figure 4: Scientometric network of the most collaborative institutions in ophthalmic genetics literature

University and University College London were the most collaborative institutions (Figure 4).

Discussion

Scientometric studies display publication trends and creativity of the countries, authors and organizations in a certain area.[1] Scientometrics enables the qualitative and quantitative assessment of academic literature and also provides the details of the most popular, active and trending fields.[5] In contrary to scientometrics' growing popularity, there have been scarce articles investigating ophthalmology field.

Fan et al. reported the citation analysis of the most influential authors and ophthalmology journals in the field of cataract and corneal refractive surgery between 2000–2004.[6] they used only Science Citation Index Expanded (SCI) to explore the citations of the authors and ophthalmology journals.[6] The network

analysis between authors, keywords, countries and institutions were lacking in their report. Recently, research productivity across different ophthalmic subspecialties in the USA were analyzed.[7] The authors found that uveitis was the most prolific subspecialty whereas cataract was the least fertile subspecialty within USA.[7] In a bibliometric analysis on dry eye disease, the authors reported 5522 documents were published about dry eye disease and they found that the most productive country was USA with 34.53% of the overall articles studied.[8] Different from this current study, only the journal articles and reviews were included in that mentioned report.[8]

In a scientometric analysis of glaucoma research between 1993 and 2013, the authors reported a trend was evident towards genomic research studies after 2010.[9] Similarly, a substantial increase in the amount of published documents were observed after 2010 in our study. Although a search query including the years between 1975 and 2019 was performed in this current study, the first report about ophthalmic genetics was published in 1982. Interestingly, available published data about ophthalmic genetics were under 100 documents/year until 2010.

Nearly about 90% of the global productivity in ophthalmic genetic documents were achieved by USA and a few European countries (UK, Germany, France, Italy and Netherlands). Except for China, all of the first 10 leading contributing countries in ophthalmic genetics were developed ones.

This current study has two main limitations. First, though WoS reflects more reliable data than other databases, only WoS database was used for analysis in this study.[10] A comparison with other studies could not be achieved due to the lack of a previous related bibliometric or scientometric study in ophthalmic genetics literature. Therefore, the results of this study were only compared with the published scientometric reports of ophthalmology. However, this is the first report focusing on ophthalmic genetics and gene therapy in ophthalmology by scientometric analysis.

Conclusions

The results of this study may assist health professionals interested in this field to better figure out ophthalmic genetics and gene therapy research worldwide. Beneficial information about dynamic and trending search topics in ophthalmic genetics field may be obtained by this study. Additionally, the results of this study may help fellows in choosing leading institutions and countries for education. Policy makers around the world could spend their resources accurately to improve and monitor the ophthalmic genetics research.

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