• Bibliometric Research •

Hotspots and frontiers of genetic research on pediatric cataracts from 2013 to 2022: a scientometric analysis

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Abstract

● **AIM:** To explore the hotspots and frontiers of genetic research on pediatric cataracts.

● **METHODS:** Global publications from 2013 to 2022 related to genes in pediatric cataracts were extracted from the Web of Science Core Collection, and were analyzed in terms of the publication counts, countries, journals, authors, keywords, cited references, subject categories, and the underlying hotspots and frontiers.

● **RESULTS:** Totally 699 publications were included in the final analysis. The predominant actors were identified, with China (*n*=240) and *PLoS One* (*n*=33) being the most productive country and journal respectively. The research hotspots extracted from keywords were crystallin gene mutations, pathogenicity evaluation, phenotypes of ocular and neurodevelopmental abnormalities, genes encoding membrane proteins, and diagnosis of multisystemic disorders. The co-cited articles formed 10 clusters of research topics, including *FYCO1* (56 items), mutation screening (43 items), gap junction (29 items), the Warburg Micro syndrome (29 items), ephrin-A5 (28 items), novel mutation (24 items), eye development and function (22 items), cholestanol (7 items), *OCRL* (6 items), and pathogenicity prediction (3 items). The research frontiers were *FYCO1*, ephrin-A5, and cholestanol. Cell biology showed the strongest bridging effects among different disciplines in the field (betweenness centrality=0.44).

● **CONCLUSION:** With the progress in next-generation sequencing and multidisciplinary collaboration, genetic research on pediatric cataracts broadens the knowledge scope of the crystalline lens, as well as other organs and systems, shedding light on the molecular mechanisms of systemic diseases. Cell biology may integrate multidisciplinary content to address cutting-edge issues in the field.

● **KEYWORDS:** gene; pediatric cataract; next generation sequencing; genotype phenotype association

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INTRODUCTION

Pediatric cataracts account for 5%-20% of the world's childhood blindness[1], bringing significant socioeconomic burdens, especially to developing countries[2]. Genetic factors were estimated to attribute to 10%-50% of pediatric cataracts, and the percentage was expected to climb with the popularization of sequencing technologies[3]. The scope and depth of research in the area of genes associated with pediatric cataracts have expanded quickly in recent years, generating complex networks of research information. It is, therefore, necessary to develop a more comprehensive understanding of the patterns of scientific publications on genes associated with pediatric cataracts, as well as to analyze the hotspots and frontiers in the field.

Over the past few years, several reviews have been published on the genetic etiology and prevalence of pediatric cataracts aiming at specific issues in basic sciences and/or clinical practices[2,4]. However, a more comprehensive, objective, and quantitative overview of the research development on genes associated with pediatric cataracts has yet to be put forward. The scientometric approaches enable the identification of research hotspots and frontiers in a research field by providing

Table 1 Search strategy

#	Search query	Database	Results
1	TS=(infan* NEAR/3 cataract*)	Web of Science Core Collection	392
2	TS=(adolescen* NEAR/3 cataract*)	Web of Science Core Collection	10
3	TS=(p$ediatric NEAR/3 cataract*)	Web of Science Core Collection	919
4	TS=(teenage* NEAR/3 cataract*)	Web of Science Core Collection	5
5	TS=(congenital NEAR/3 cataract*)	Web of Science Core Collection	3008
6	TS=(inherited NEAR/3 cataract*)	Web of Science Core Collection	175
7	TS=((young NEAR/3 people) NEAR/3 cataract*)	Web of Science Core Collection	2
8	TS=(juvenile* NEAR/3 cataract*)	Web of Science Core Collection	212
9	TS=(developmental NEAR/3 cataract*)	Web of Science Core Collection	231
10	TS=(infan* NEAR/3 (opaci* NEAR/3 lens*))	Web of Science Core Collection	6
11	TS=(p$ediatric NEAR/3 (opaci* NEAR/3 lens*))	Web of Science Core Collection	7
12	TS=(teenage* NEAR/3 (opaci* NEAR/3 lens*))	Web of Science Core Collection	1
13	TS=(congenital NEAR/3 (opaci* NEAR/3 lens*))	Web of Science Core Collection	21
14	TS=(inherited NEAR/3 (opaci* NEAR/3 lens*))	Web of Science Core Collection	4
15	TS=(juvenile* NEAR/3 (opaci* NEAR/3 lens*))	Web of Science Core Collection	1
16	TS=(developmental NEAR/3 (opaci* NEAR/3 lens*))	Web of Science Core Collection	6
17	#16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1	Web of Science Core Collection	3977
18	TS=(gene$)	Web of Science Core Collection	2882570
19	#18 AND #17	Web of Science Core Collection	1323
20	#19 Timespan: 2013-01-01 to 2022-12-30	Web of Science Core Collection	699

Two independent reviewers conducted a literature search in the Web of Science Core Collection (Clarivate Analytics, Philadelphia, PA, USA). Searches of the literature were conducted until 27 November 2022.

a quantitative study of the predominant actors and the dynamic shifts in a particular field using statistical and mathematical methods[5-6].

This scientometric study has been conducted to explore the hotspots and frontiers of genetic research on pediatric cataracts from 2013 to 2022, aiming to enable researchers to understand the main and cutting-edge content of research in this field, as well as the collaborations between different disciplines, as to provide a reference for exploring the future research directions and strategies.

MATERIALS AND METHODS

Literature Search and Selection Scientometric research typically requires the use of a single database to avoid duplicate acquisition of literature and maintain consistency in the definition of evaluation indicators[7-8]. The keywords covering genetic research on pediatric cataracts were searched in the Web of Science Core Collection (WoSCC; Clarivate Analytics, Philadelphia, PA, USA; Table 1). The WoSCC is a widely recognized and reliable resource that provides citation data and facilitates the examination of research frontiers. In this study, we utilized several sub-databases within the WoSCC to acquire comprehensive and diverse information in the field. These sub-databases included the Science Citation Index Expanded from 1999 to present, the Social Sciences Citation Index from 2002 to present, the Arts & Humanities Citation Index from 2002 to present, the Conference Proceedings Citation Index-Science from 2000 to present, the Conference Proceedings Citation Index-Social Sciences & Humanities from 1990 to present, the Emerging Sources Citation Index from 2018 to present, the Current Chemical Reactions from 1985 to present, and the Index Chemicus from 1993 to present. The search terms included variations of "infant", "adolescent", "pediatric", "teenage", "congenital", "inherited", "young people", "juvenile", and "developmental" in close proximity to "cataract" or "lens" and "opacity." Additionally, the search included the term "gene". All of the search terms were applied to the Title, Abstract, Author Keywords, and Keywords Plus fields. The time range was set from 2013 to 2022. The search was carried out on November 27, 2022. Therefore, the publication volume for 2022 is limited to a cut-off date of November 27, 2022 and does not include publications from the entire year. Figure 1 details the study selection and analysis procedures. Pediatric cataracts here refer to cataracts that occur in children with hereditary backgrounds.

Data Extraction and Collection Relevant data were downloaded to analyze annual publications, annual citations, countries, journals, authors and publication time. The full records of the selected publications including the cited references were collected for keyword analysis, cited reference analysis, and subject category analysis.

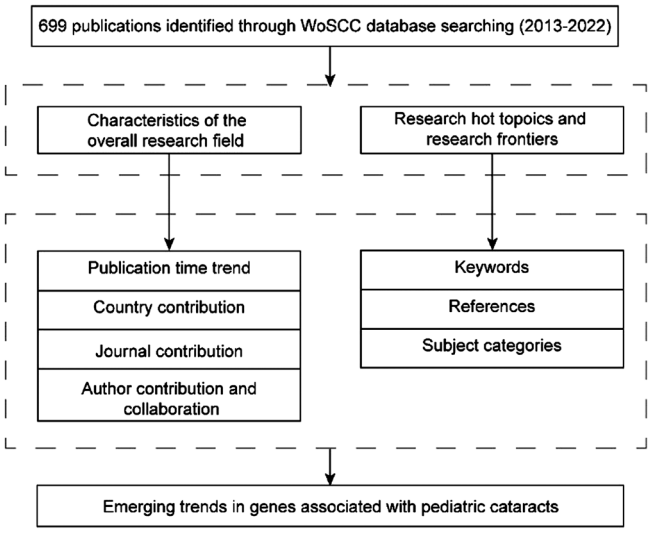

Figure 1 Flow chart of the literature selection and analysis procedures WoSCC: Web of Science Core Collection.

Analysis of Publication Attributes The publication volume and predominant actors, including countries, journals, and authors, were analyzed with Microsoft Excel 2019 (Microsoft Corporation, Redmond, WA, USA) and GraphPad Prism version 8.3.0 (GraphPad Software, La Jolla, CA, USA). In counting the country publication volume, the publication volume attributed to the United Kingdom represents the combined publication volume of Scotland, England, Wales, and Northern Ireland. The annual growth rate was calculated by dividing the value of the difference between publication counts in a given year and publication counts in the prior year by the publication counts in the prior year. The absence of growth was considered to be represented by a value of 0. A year with more than 100 publications and an annual growth rate of over 10% was defined as a year with remarkable publication activity[9].

The co-authorship analysis and the high-frequency keyword co-occurrence analysis were performed using VOSviewer 1.6.5 (Leiden University's Centre for Science and Studies, Leiden, the Netherlands). Through the co-authorship analysis, the collaboration networks were obtained. The association strength among authors was determined by the total link strength, which indicates the number of publications where two authors were present together[10]. The clusters in the co-author collaboration network analysis were named by the most collaborative authors in corresponding clusters.

Analysis of Research Hotspots In the keyword co-occurrence analysis, the keywords are weighted by their occurrence counts to form different keyword clusters according to the relevance between keywords by using VOSviewer. Both the frequency and the characteristics of the keywords in each cluster were taken into consideration for the identification of research hotspots that each cluster represented[11]. The clusters were named by the identified research hotspots.

Analysis of Research Trends We evaluated the total citation counts of articles to show the overview focus characteristics of the area because articles that were cited more frequently suggested more academic attention.

The co-citation analysis of cited references and co-occurrence analysis of networks of subject categories were performed using CiteSpace V version 6.1.4 (Drexel University, Philadelphia, PA, USA). To identify research frontiers, the cited references were clustered according to relevance and displayed in a timeline view, in which the clustered cited references were arranged on a horizontal timeline according to the publication time. The visualization of the timeline can provide an intuitive overview of the development of a certain cluster[6]. Clusters were labelled according to the subject content of the citing articles in corresponding clusters. Research frontiers were defined as clusters with the most recent mean publication year or the most recently recruited members, implying that they represented newly formed topics or topics with continual development. A significant betweenness centrality (BC), that is BC>0.1, of the cited references was used to identify the cited references that served as important turning points.

To determine the most involved subject categories in the field with ophthalmology, pediatrics, and genetics, all subject categories were analyzed. The significant BC of the subject categories were used to identify their bridging roles among disciplines.

RESULTS

Annual Global Output The annual global output and citations in the field of genes associated with pediatric cataracts from 2013 to 2022 are displayed in Figure 2A.There were 699 publications in the WoSCC, with the highest in 2021 (n=96; 13.73%) and the lowest in 2015 (n=58; 8.30%). The annual global output in 2021 was more than 1.5 times that of 2015. There were 7321 citations from 2013 to 2022, with an average of 10.47 citations per publication. The annual citations peaked in 2021 (n=1531). The years 2017, 2020, and 2021 were identified as years with remarkable publication activities.

Predominant Actors

Countries There were 67 countries that contributed to the publications in the field of genes associated with pediatric cataracts from 2013 to 2022 (Figure 2B). Among them, China had the most publications (n=240, 34.33%), followed by the USA (n=177, 25.32%), the UK (n=79, 11.30%), Germany (n=46, 6.58%), Japan (n=45, 6.44%), Italy (n=34, 4.86%), India (n=34, 4.86%), Canada (n=32, 4.58%), Turkey (n=29, 4.15%), and Spain (n=29, 4.15%).

Journals A total of 258 journals contributed to the publications on genes associated with pediatric cataracts during the study period. *PLoS One* had the most publications

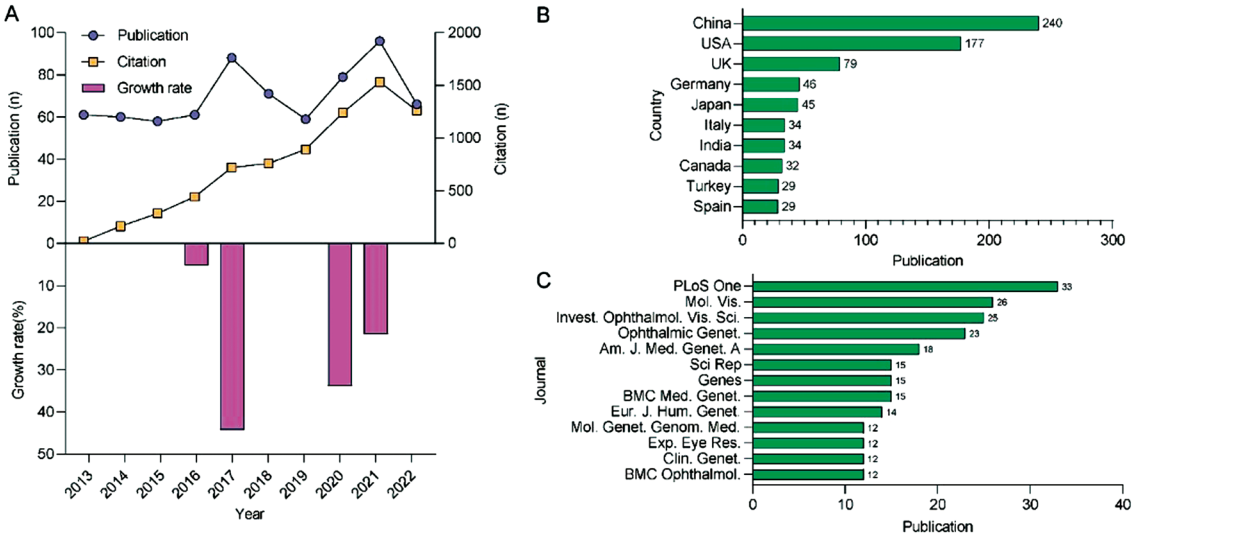

Figure 2 Overview of publication information on genes associated with pediatric cataracts from 2013-2022 A: The overall trends of publications and citations, and the annual publication growth rates; B: Top 10 countries by the number of publications; C: Top 13 journals by the number of publications.

(*n*=33, 4.72%), followed by *Molecular Vision* (*n*=26, 3.72%), *Investigative Ophthalmology Visual Science* (*n*=25, 3.58%), *Ophthalmic Genetics* (*n*=23, 3.29%) and *American Journal of Medical Genetics Part A* (*n*=18, 2.58%). The number of publications of the top 13 journals is displayed in Figure 2C.

Authors In general, 4629 authors participated in the publication of genes associated with pediatric cataracts, with an average of 6.62 authors per article. Ke Yao (18 publications; 2.58%) and J. Fielding Hejtmancik (16 publications; 2.29%) were the most prolific authors, followed by Kathryn P. Burdon (14 publications; 2.00%). Figure 3A shows the top 11 co-authors by the number of publications during the study period. The author collaboration network included 78 authors and 349 collaborations (Figure 3B). Prolific authors showed a tendency to form independent clusters and make collaborations with each other. Eight clusters were formed in the author collaboration analysis. The S. Amer Riazuddin and Sheikh Riazuddin cluster (17 authors), the Qiwei Wang cluster (15 authors), and the Ke Yao cluster (14 authors) were the three largest clusters.

Research Hotspots and Frontiers

Hot topics based on high-frequency keywords The hotspots of genes associated with pediatric cataracts were determined according to 93 high-frequency keywords (Figure 4). The research hotspots were: the crystallin gene mutations (26 items), pathogenicity evaluation (24 items), phenotypes of ocular and neurodevelopmental abnormalities (20 items), genes encoding membrane proteins (13 items), and diagnosis of multisystemic disorders (10 items).

Research frontiers based on co-cited articles We listed the top 20 cited articles on genetic research on pediatric cataracts (Table 2). Ten research topic clusters were formed in the cited

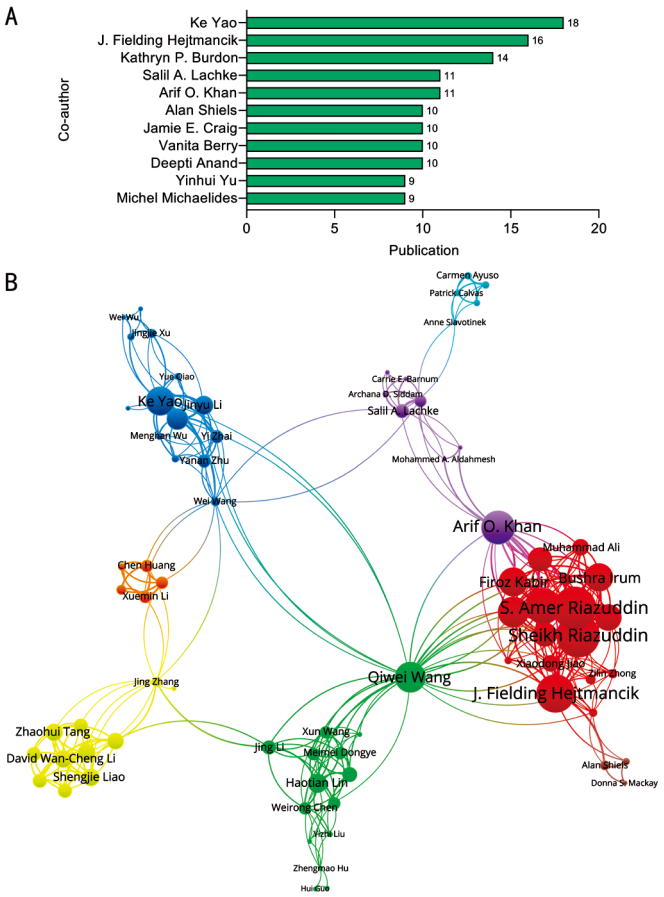

Figure 3 The most active authors in genetic research on pediatric cataracts A: Top 11 co-authors by the number of publications; B: Author collaboration network map.

reference analysis and were displayed in a timeline view as shown in Figure 5. The *FYCO1* (FYVE and coiled-coil domain autophagy adaptor 1) cluster (56 items, mean publication year=2017) was the largest cluster, as well as one of the most recently formed clusters. The mutation screening cluster (43

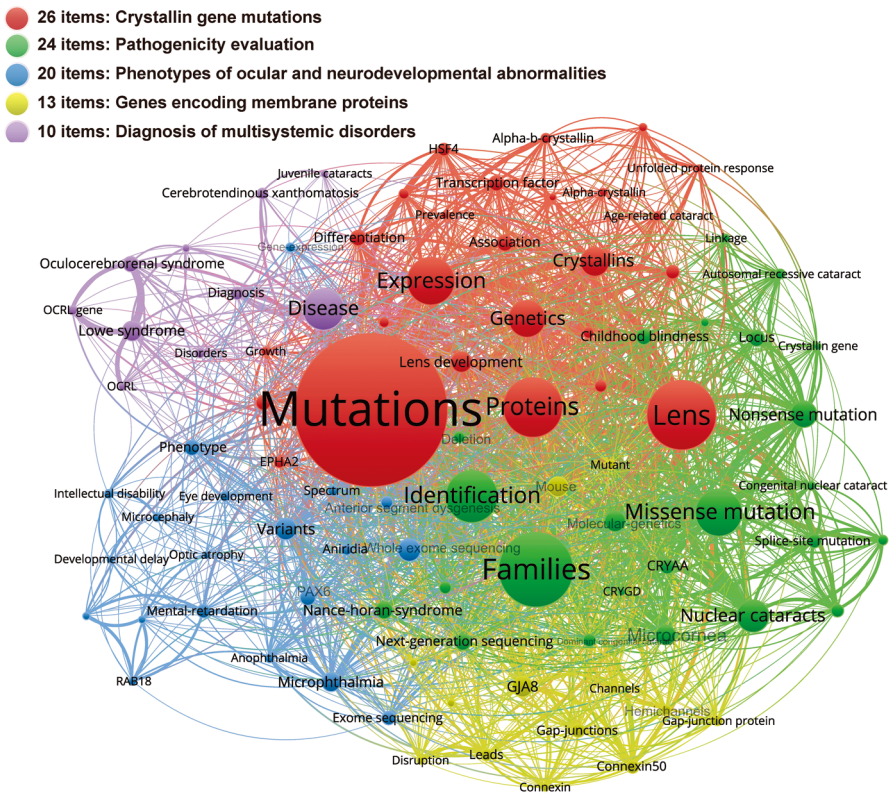

Figure 4 Keyword-based research hotspots of genetic research on pediatric cataracts A node represents a keyword. Larger nodes indicate more frequent keywords. Clusters are formed based on keyword co-occurrence analysis. Nodes that are closely related belong to the same cluster and are represented by the same color.

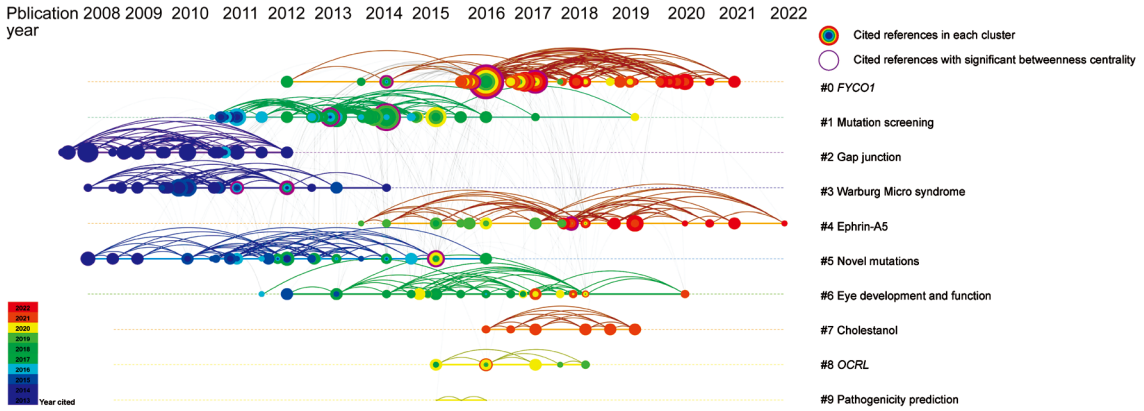

Figure 5 Reference-based research frontiers in genetic research on pediatric cataracts Each node represents a cited reference of included studies. Larger nodes indicate that higher citation frequency. All nodes are arranged in a timeline according to their publication time. The node color corresponds to the citation years. Nodes with a purple outer ring indicate they have a significant betweenness centrality (betweenness centrality>0.1), showing their role as a turning point in the shift of research direction. The main clusters are ordered by cluster size as clusters #0–9, with #0 containing the largest number of members. The labels of the clusters were derived from the citing articles in each cluster. *FYCO1*: FYVE and coiled-coil domain autophagy adaptor 1; *OCRL*: OCRL inositol polyphosphate-5-phosphatase.

items, mean publication year=2013) had no member that was cited after 2020. The gap junction cluster (29 items, mean publication year=2010), the Warburg Micro syndrome cluster (29 items, mean publication year=2010), and the novel mutation cluster (24 items, mean publication year=2012) formed before 2017. The ephrin-A5 cluster (28 items, mean publication year=2017) continuously recruited members as of 2022 and was one of the most recently formed clusters. There were 22 members in the eye development and function cluster (mean publication year=2015). The cholestanol cluster (7 items, mean publication year=2017) was one of the most recently formed clusters in the past decade. There were 6 members in the *OCRL* (OCRL inositol polyphosphate-5-phosphatase) cluster (mean publication year=2016). There were 3 members in the pathogenicity prediction cluster (mean publication year=2015). *FYCO1*, ephrin-A5, and cholestanol

Table 2 The 20 top-cited studies in genetic research on pediatric cataracts

Citations	Article title	Type	Year	Journal
139	Cerebrotendinous xanthomatosis: a comprehensive review of pathogenesis, clinical manifestations, diagnosis, and management	Review	2014	*Orphanet J Rare Dis*
111	Mutations and mechanisms in congenital and age-related cataracts	Article	2017	*Exp Eye Res*
109	Genetics of human cataract	Review	2013	*Clin Genet*
107	Personalized diagnosis and management of congenital cataract by next-generation sequencing	Article	2014	*Ophthalmology*
104	Deletion of autophagy-related 5 (Atg5) and Pik3c3 genes in the lens causes cataract independent of programmed organelle degradation	Article	2013	*J Biol Chem*
90	Mutation spectrum in RAB3GAP1, RAB3GAP2, and RAB18 and genotype-phenotype correlations in warburg micro syndrome and Martsolf syndrome	Article	2013	*Hum Mutat*
88	Loss-of-function mutations in TBC1D20 cause cataracts and male infertility in blind sterile mice and Warburg micro syndrome in humans	Article	2013	*Am J Hum Genet*
86	Sporadic and familial congenital cataracts: mutational spectrum and new diagnoses using next-generation sequencing	Article	2016	*Hum Mutat*
83	Primary cilia signaling mediates intraocular pressure sensation	Article	2014	*Proc Natl Acad Sci U S A*
81	A peroxisomal disorder of severe intellectual disability, epilepsy, and cataracts due to fatty acyl-CoA reductase 1 deficiency	Article	2014	*Am J Hum Genet*
79	Mutations impairing GSK3-mediated MAF phosphorylation cause cataract, deafness, intellectual disability, seizures, and a Down syndrome-like facies	Article	2015	*Am J Hum Genet*
76	Diagnostic exome sequencing in 266 Dutch patients with visual impairment	Article	2017	*Eur J Hum Genet*
72	The leukodystrophy protein FAM126A (hyccin) regulates PtdIns(4)P synthesis at the plasma membrane	Article	2016	*Nat Cell Biol*
70	Connexin mutants and cataracts	Review	2013	*Front Pharmacol*
70	The oculocerebrorenal syndrome of Lowe: an update	Review	2016	*Pediatr Nephrol*
66	Age-related cataracts: role of unfolded protein response, Ca^{2+} mobilization, epigenetic DNA modifications, and loss of Nrf2/Keap1 dependent cytoprotection	Review	2017	*Prog Retin Eye Res*
60	Whole exome sequencing in dominant cataract identifies a new causative factor, CRYBA2, and a variety of novel alleles in known genes	Article	2013	*Hum Genet*
59	Nystagmus in childhood	Review	2014	*Pediatr Neonatol*
56	Mutations in PIGY: expanding the phenotype of inherited glycosylphosphatidylinositol deficiencies	Article	2015	*Hum Mol Genet*
56	Molecular genetics of cataract	Review	2015	*Prog Molec Biol Transl Sci*

were listed as research frontiers in the research trends because they were relatively active in terms of corresponding members' recruitment time (Ephrin-A5 cluster) and cluster mean publication year (*FYCO1*, Ephrin-A5, and Cholestanol cluster; mean publication year=2017), respectively. Table 3 lists the top cited reference and citing article for each cluster in order of the mean cluster publication year to show the evolution of the clusters.

Frontiers in research subject categories To show the overall distribution of subject categories, we identified the top 12 subject categories in terms of their BC (Table 4). Cell biology (*n*=41, BC=0.44), biochemistry & molecular biology (*n*=108, BC=0.41), and medicine, research & experimental (*n*=54, BC=0.30) had the highest BC values, serving as bridging subject categories (Figure 6).

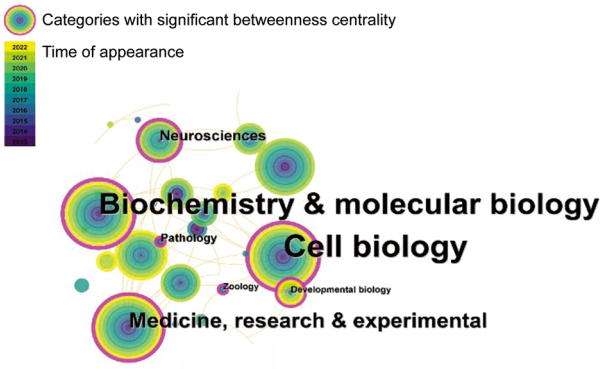

Figure 6 Subject categories of genetic research on pediatric cataracts The distribution map of subject categories. Seven bridging subject categories (betweenness centrality >0.1) indicated in a purple outer ring, were shown.

DISCUSSION

The research attributes and trends were identified according to 699 WoSCC articles on genes associated with pediatric cataracts in the past 10y, and the results showed that the crystallin gene mutations, pathogenicity evaluation, phenotypes of ocular and neurodevelopmental abnormalities, genes encoding membrane proteins, and diagnosis of multisystemic disorders were the research hotspots. *FYCO1*, ephrin-A5, and cholestanol were identified as research frontiers, with cell biology being a crucial bridging subject category among different disciplines.

The overall research profile of genes associated with pediatric cataracts suggests that this field is relatively condensed yet with a variety of sources. There were fluctuated annual publication counts and several identified years with remarkable

Table 3 The top cited reference and citing article for each cluster in order of the mean cluster publication year

Mean publication year	Frontier labels	Top cited reference with the highest citation in each cluster		Top citing article with the highest coverage in each cluster	
		Citations (*n*)	Author (y), title	Coverage (%)	Author (y), title
2010	#2 Gap junction	17	Hejtmancik (2008), Congenital cataracts and their molecular genetics	17	Deng (2014), Molecular genetics of congenital nuclear cataract
2010	#3 Warburg Micro syndrome	26	Shiels (2010), Cat-Map: putting cataract on the map	11	Gillespie (2014), The use of autozygosity mapping and next-generation sequencing in understanding anterior segment defects caused by an abnormal development of the lens
2012	#5 Novel mutations	23	Zhao (2015), Lanosterol reverses protein aggregation in cataracts	9	Hamada (2015), Role of carcinogenesis related mechanisms in cataractogenesis and its implications for ionizing radiation cataractogenesis
2013	#1 Mutation screening	31	Shiels (2013), Genetics of human cataract	25	Messina-Baas (2017), Inherited congenital cataract: a guide to suspect the genetic etiology in the cataract genesis
2015	#6 Eye development and function	9	Anand (2018), RNA sequencing-based transcriptomic profiles of embryonic lens development for cataract gene discovery	6	Kakrana (2018), iSyTE 2.0: a database for expression-based gene discovery in the eye
2015	#9 Pathogenicity prediction	3	Savojardo (2016), INPS-MD: a web server to predict stability of protein variants from sequence and structure	3	Zhang (2020), In silico analysis of non-synonymous single nucleotide polymorphisms (nssnps) in the human gja3 gene associated with congenital cataract
2016	#8 OCRL	17	Bökenkamp (2016), The oculocerebrorenal syndrome of Lowe: an update	3	Liu (2020), Transcriptome analysis of neural progenitor cells derived from lowe syndrome induced pluripotent stem cells: identification of candidate genes for the neurodevelopmental and eye manifestations
2017	#0 FYCO1	47	Ma (2016), Sporadic and familial congenital cataracts: mutational spectrum and new diagnoses using next-generation sequencing	23	Li (2020), Molecular genetics of congenital cataracts
2017	#4 Ephrin-A5	16	Anand (2018), Mutation update of transcription factor genes FOXE3, HSF4, MAF, and PITX3 causing cataracts and other developmental ocular defects	8	Vu (2022), Mapping the universe of eph receptor and ephrin ligand transcripts in epithelial and fiber cells of the eye lens
2017	#7 Cholestanol	5	Freedman (2019), Prevalence of cerebrotendinous xanthomatosis among patients diagnosed with acquired juvenile-onset idiopathic bilateral cataracts	7	Koyama (2021), Cerebrotendinous xanthomatosis: molecular pathogenesis, clinical spectrum, diagnosis, and disease-modifying treatments

Table 4 Betweenness centrality based top 12 subject categories

Subject category	Betweenness centrality	Occurrence
Cell biology	0.44	41
Biochemistry & molecular biology	0.41	108
Medicine, research & experimental	0.30	54
Neurosciences	0.20	22
Pathology	0.16	5
Developmental biology	0.13	12
Zoology	0.13	6
Clinical neurology	0.07	22
Endocrinology & metabolism	0.07	22
Biology	0.07	7
Veterinary sciences	0.07	6
Immunology	0.07	3

publication activities during a decade, indicating instability in a relatively small research field, but the engagement of numerous geographical countries, journals focused on different topics, and various closely collaborating authors suggested the diversity of research topics in this field. The potential impact of socioeconomic factors on the accessibility of healthcare services for pediatric cataract patients was undefined and could contribute to variations in publication activities[1-2,12]. In this study, we did not analyse research institutions. Future research could build upon our work by incorporating an analysis of research institutions.

Five research hotspots in the study of genes associated with pediatric cataracts during the last decade were identified. Hot topics in molecular genetics included the study of membrane protein-coding genes and crystallin genes, suggesting that as genes encode key structural proteins in the crystalline lens, membrane protein-coding genes and crystallin genes are receiving continuous attention. Second, the evaluation of the pathogenicity of sequence variants remained a research hotspot due to the heterogeneity of pediatric cataracts in molecular genetics and clinical manifestations[13-15]. Third,

the developmental abnormalities associated with pediatric cataracts were intensely studied, especially in ocular structure as well as the nervous system. It was reported that about 14.5% of congenital cataract cases involve additional ocular aberrant phenotypes[16]. Furthermore, pediatric cataracts and neurodevelopmental abnormalities often coexist, typical examples include Lowe syndrome caused by *OCRL* mutations, and in recent years, several other related genes have been identified, such as *RIC1* (RIC1 homolog, RAB6A GEF complex partner 1) and *FOSL2* (FOS like 2, AP-1 transcription factor subunit)[15,17-18]. Last but not least, great efforts had been made to identify novel cataract-related syndromes for accurate diagnosis and targeted treatment[19]. To date, more than 150 genetic loci related to syndromic pediatric cataracts have been identified[20]. According to our findings, the field of pediatric cataract genetics had focused attention on the clinical diagnosis and relevant evaluation of the pathogenicity of gene variants. Our knowledge of pathogenic genes and the patterns of gene mutations that cause disease was limited[3]. Furthermore, little was known about multisystem triggers because systemic conditions were rarely evaluated in the majority of the evidence collected from pediatric cataract genetic research[4]. Exploration of possible mechanisms of multi-system manifestations was still ongoing.

In terms of research frontiers, the roles of *FYCO1*, ephrin-A5, and cholestanol in lens development and transparency maintenance were found to attract great attention in recent years. Chen *et al*[21] discovered that mutations in *FYCO1* can cause autosomal recessive congenital cataracts. And the protein encoded by *FYCO1* plays a role in the autophagic process. In 2022, Khan *et al*[22] demonstrated that loss of *FYCO1* function had caused decreased autophagic flux, impaired organelle clearance, and cataractogenesis. However, whether impaired organelle removal dependent on the loss of function of *FYCO1* directly leads to cataracts warrants further study. Ephrin-A5 is a ligand for the Eph receptor. In different species, the disruption of Eph-ephrin signaling was found to be cataractogenesis[23-25]. Vu and Cheng[26] extracted and sequenced Eph receptor and ephrin ligand transcripts in adult mice and discovered that practically all Ephs and ephrins were expressed in the adult mouse lens. The spatiotemporal specificity of the expression of other receptor-ligand pairs and their role in the lens, and whether they are affected in the ephrin-A5 mutant lens remain to be elucidated. Cholestanol was recognized as a research frontier in the field, highlighting the potential role of lens opacity as a screening marker for multisystemic disorders for pediatric patients. Mutations in *CYP27A1* (cytochrome P450 family 27 subfamily A member 1), the gene encoding sterol 27-hydroxylase, cause cerebrotendinous xanthomatosis, a multisystemic disorder characterized by elevated levels of cholestanol[27]. A previous study showed that when genetic testing was unavailable or the results were inconclusive, ocular examinations were especially useful in diagnosing specific syndromes[28]. Specifically, Freedman *et al*[27] demonstrated that pediatric cataracts may be utilized as a screening marker for cerebrotendinous xanthomatosis, which is 500 times more likely to be detected in the pediatric cataract group than in the general population.

Our result showed that cell biology played the most prominent bridging role among multiple disciplines. In the field of genes associated with pediatric cataracts, cell biology may serve as the glue that integrates biological disciplines such as genetics for systematic research, and other related scientific fields such as neuroscience to address cutting-edge scientific questions. For example, congenital cataracts, a form of cataract in children, are generally characterized by defects in the structure or function of lens proteins and/or their coding genes, which can lead to lens opacity[12]. Utilizing cell biology research methods, we can investigate the pathogenic genes, the abnormalities in the structure of the encoded proteins, and their consequences[15,26]. For instance, changes in isoelectric point or local hydrophobicity/hydrophilicity can cause abnormal aggregation of crystallin, leading to a loss of solubility of high concentrations of intracellular proteins and resulting in lens opacity[12]. Additionally, abnormalities in ion pumps on the lens cell membrane, such as aquaporin and calcium channels, can disrupt metabolic homeostasis and cause lens opacity[25]. Furthermore, cell biology research methods can be used to explore the role of developmental biology in pediatric cataract genes, including the involvement of heat shock factor 4 as an eye development-related gene in cataract autophagy-related pathogenesis research[29]. It is also important to note that children with cataracts can exhibit abnormalities in the nervous system[15,18]. The integrative nature of cell biology enables researchers to explore interactions between ocular structures and the nervous system at the cellular level, promoting interdisciplinary research between pediatric cataracts and neuroscience and providing a deeper understanding of disease development mechanisms.

The study nature of a scientometric analysis brought some limitations to this study. Although PubMed is a commonly used database, it does not provide citation data. For this reason, we limited our literature selection for our research to the WoSCC, which does provide citation data for citation analysis. As a result, our research results cannot be generalized to literature not included in WoSCC. A literature search was conducted to ensure the research was specific to pediatric cataracts, and genetic studies in pediatric cataracts were selected. This allowed us to primarily investigate congenital, developmental, and hereditary types of pediatric cataracts.

However, it was possible that some literature had included a mix of congenital, developmental, hereditary, and traumatic cataracts in children. As a result, there may be some bias in the types of cataracts represented in our findings, and they should be interpreted with caution. The analysis conducted with VOSviewer and CiteSpace, which generated keyword co-occurrence and co-citation networks, had its limitations. It only took into account single factors such as keywords and citations, while overlooking the potential influence of the author's contributions and the contributions of the journals. This means that the results should be interpreted with caution and within the context of this research. Moreover, only English-language articles can be analyzed by VOSviewer and CiteSpace, which wouldn't affect the results of annual global output and predominant actors' output. However, the results of research hotspots and research frontiers might be subject to language bias. To address this issue, future scientometric research should focus on the landscape, hotspots, and frontiers of genetic research on pediatric cataracts in different regions and languages to provide a more refined analysis. It should be acknowledged that there may be a delay in the updating of information in the database, resulting in the potential omission of newly indexed articles during the data collection process. Conducting literature searches at a more recently updated time would likely yield a larger volume of data. For this study, the search was conducted until November 27, 2022. One limitation of this study is that the publication volume for 2022 does not encompass the entire year and is limited to a specific cut-off date of November 27, 2022. As a result, the annual publication volume for 2022 is underestimated in this study. However, given that our study covered a substantial majority of articles published between 2013 and 2022, it is unlikely that the inclusion of newly published articles would significantly alter our conclusions about the research hotspots and frontiers. Additionally, the results of this study may not comprehensively represent the barriers encountered by academics working in this field. This suggests that further research, such as a scoping review, may be necessary to fully understand these barriers.

In summary, researchers from different regions and countries paid continuous attention to genetic research on pediatric cataracts in the past decade. This field focused on the roles of key structural proteins in lens development and transparency maintenance, and on the molecular mechanism of ocular or systemic syndromes that presents with lens opacity. The application of next-generation sequencing and other new technologies, as well as multidisciplinary cooperation, played an important role in deepening and advancing the research in genes associated with pediatric cataracts.

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