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Review

A scientometric review of glycocalyx research (2007–2016)

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Abstract

The glycocalyx is a carbohydrate-rich layer that lines the luminal side of the epithelial cells in mammals. This structure is not just a barrier for vascular permeability but also contributes to various functions including the signal sensing and transmission of heamodynamic forces to the endothelium, the regulation of cell proliferation, differential and apoptosis. In this review, we conducted a scientometric analysis to summarize the panoramic network of the international research in the field of glycocalyx during the recent decades. With the help of Citespace software, a visual bibliometric analysis of references regarding glycocalyx research during years 2007-2016 was made. Finally, different visual maps were generated and a group of valuable conclusions were extracted from these maps, including prominent authors, critical articles, hot research topics, emerging trends and research front in the field of glycocalyx research, which is helpful for the comprehensive understanding of the advances in recent glycocalyx researches.

Key words: scientometric; glycocalyx; Citespace.

Introduction

The glycocalyx is a carbohydrate-rich layer that lines the luminal side of the mammalian epithelial cell such as vascular endothelium, which was first proposed by Danielli in 1940 [1]. It has become evident that the integrity of this structure is not just important for maintaining of vascular permeability but also has various critical contributions to cell functions including mechanotransduction of heamodynamic forces, regulation of cell progression, cell proliferation, angiogenesis, motility, and metastasis [2-9].

During the past years, many reviewers and analysts have summarized the research results of glycocalyx, in order to provide the readers with different kinds of information about glycocalyx research. For example, Reitsma S *et al.* [10] reviewed the composition and functions of the endothelial glycocalyx, and strengthened the roles of the glycocalyx in human diseases including diabetes, ischemia/reperfusion, and atherosclerosis. Moreover, the visualization methods of the endothelial glycocalyx including two-photon microscopic imaging are reviewed. Weinbaum S *et al.* [11] demonstrated the characteristic of endothelial glycocalyx layer and concluded that glycocalyx acts as a barrier of permeability in the transcapillary exchange of water, as a mechanosensor of fluid shear stress (FSS) to the endothelial cytoskeleton resulting biochemical responses, and as a regulator of the adhesion of white blood cell (WBC) to endothelial cell, with emphasis on the inflammatory response. Becker BF *et al.* [12] investigated the protection or the restoration of an already damaged glycocalyx by pharmacological blockers of radical production including the application of hydrocortisone, use of antithrombin III, direct inhibition of the cytokine tumour necrosis factor-alpha, and avoidance of the liberation of natriuretic peptides, which may be useful to diminish the oxygen radical stress. VanTeeffelen JWGE *et al.* [13] explored on the potential role of adenosine-induced modulation of glycocalyx exclusion properties in coupling increases in blood flow and circulating blood volume in the coronary circulation, and on how glycocalyx can be modulated by various agonists. Tuma M *et al.* [14] reviewed the role of the endothelial glycocalyx in the microcirculatory dysfunction associated with trauma. Tarbell JM *et al.* [5] focused on the roles of the glycocalyx in cancer and vascular diseases such as atherosclerosis, stroke, hypertension, kidney disease and sepsis.

Although each of these retrospective reviews offered an in-depth perspective, a holistic picture in the field of glycocalyx research should be helpful for the comprehensive understanding of the advances in recent glycocalyx researches. Scientometric review is a branch of information that quantitatively analyzes patterns in scientific literatures in order to understand emerging trends and the knowledge structure of a research field [15]. In this review, we conducted a scientometric review with Citespace software to make visual bibliometric analysis of research literatures on glycocalyx between January 2007 and November 2016 indexed in the Web of Science (WOS) core collection.

Method

Bibliographic Records

We collected the bibliographic records from the Web of Science Core Collection Citation Indexes (WOCCC), which include Science Citation Index Expanded, Social Sciences Citation Index, Arts & Humanities Citation Index, Conference Proceedings Citation Index—both Science, and Social Science & Humanities, and Emerging Sources Citation Index.

An initial topic search for "glycocal$x" resulted in 1583 records published between January 2007 and November 2016. The wild card "$" was used to capture the variations of the word, such as glycocalyx and glycocalix. We limited our study to records of the types of original articles, which are representative of original researches; and review articles, which are surveys of the literature. After filtering, the dataset was reduced to 1106 original research articles and 228 review articles. The whole bibliographic records were then exported to CiteSpaceV for subsequent analysis.

CiteSpace

CiteSpace is a scientific visualization software package programmed by Dr. Chaomei Chen at the College of Information Science and Technology of Drexel University (US) to facilitate the visual analysis of trends, patterns, and critical changes in a changeable information environment. It is freely available and requires the installation of the Java Runtime Environment (JRE) on the user's computer. By processing bibliographic data of scientific literature visually, CiteSpace identifies hotspots and fronts of a field based on the weight of connections, size of circles, and thickness of rings and diversity of colors. The CiteSpace 5.0.R1 SE was used in this study and the visual effects are improved by the combination of burst detection algorithm PFNETs and Kleinberg with middle measurement rule called Freeman [16-18].

Results

Co-authorship Analysis of the Important Research Community

To a certain extent, an author's level of productivity can be representative of the devoted efforts of that researcher. Co-authorship, a form of association in which two or more scientists jointly report their research results on some topic, is the most visible indicator of collaboration and has thus been frequently used to analyze scholarly communication and the status of individual researcher [19]. Figure 1 shows the co-authorship network. There are 771 nodes and 1114 links in the co-authorship network of glycocalyx research. Each node represents an author. The size of the circles indicates the numbers of publications of the author, and the links between the authors represent direct partnerships established through the co-authorship of papers. The different colors represent different years from 2007 to 2016.

Based on these co-author relationships, we can identify several important research communities in which indicate a close collaboration among authors.As shown in Figure 1, there are four major co-operative subnetworks were identified from the co-authorship network. One includes Vink H, van der Vlag J, Rabelink TJ, Ince C, etc. One includes Chappell D, Jacob M, Becker BF, Rehm M, and so on. The two author groups have a co-operative relationship with the work of Ince C. The other two author groups are the group of Johansson PI, Ostrowski SR, and so on, who focused on the role of glycocalyx in hemorrhagic shock; and the group of Tarbell JM, Fu BM, Dull RO, Zeng M, Zeng Y, etc, who focused on the role of the glycocalyx in vascular permeability, cardiovascular diseases, acute respiratory distress syndrome and cancer. Table 1 shows the top 10 most productive authors in the research field of glycocalyx with frequency and centrality.

Author Co-citation analysis of Commonly Cited Researchers

To evaluate an author's impact in terms of citations, we did the author co-citation analysis. In every field, authors with most citations tend to those who made a significant and basic effect on the development and evolution in the field. Different abbreviations for the name of each commonly cited author are eliminated. Table 2 lists the top 20 key cited authors in the field of glycocalyx research. Weinbaum S was one of the most important scholars in this field for his research work had been widely cited by other scholars in this field with the frequency 308 according to our Dataset. Additional highly cited authors include Nieuwdorp M (252), Pries AR (226), Reitsma S (224), Vink H (222), Chappell D (221), Rehm M (200), Van den Berg BM (171), Mulivor AW (157), Adamson RH (151), Henry CBS (147), Tarbell JM (146), and so on. It suggests that these researches had a big impact on current research and the future development of glycocalyx.

Table 1. Top 10 most productive authors in glycocalyx research

Freq	Centrality	Author	Year
40	0.02	Vink H	2007
37	0.02	Chappell D	2007
34	0	Jacob M	2007
31	0	Becker BF	2007
30	0	Rehm M	2007
29	0	Johansson PI	2011
28	0	Ostrowski SR	2011
26	0.01	Tarbell JM	2007
21	0	Conzen P	2007
15	0	van der Vlag J	2013

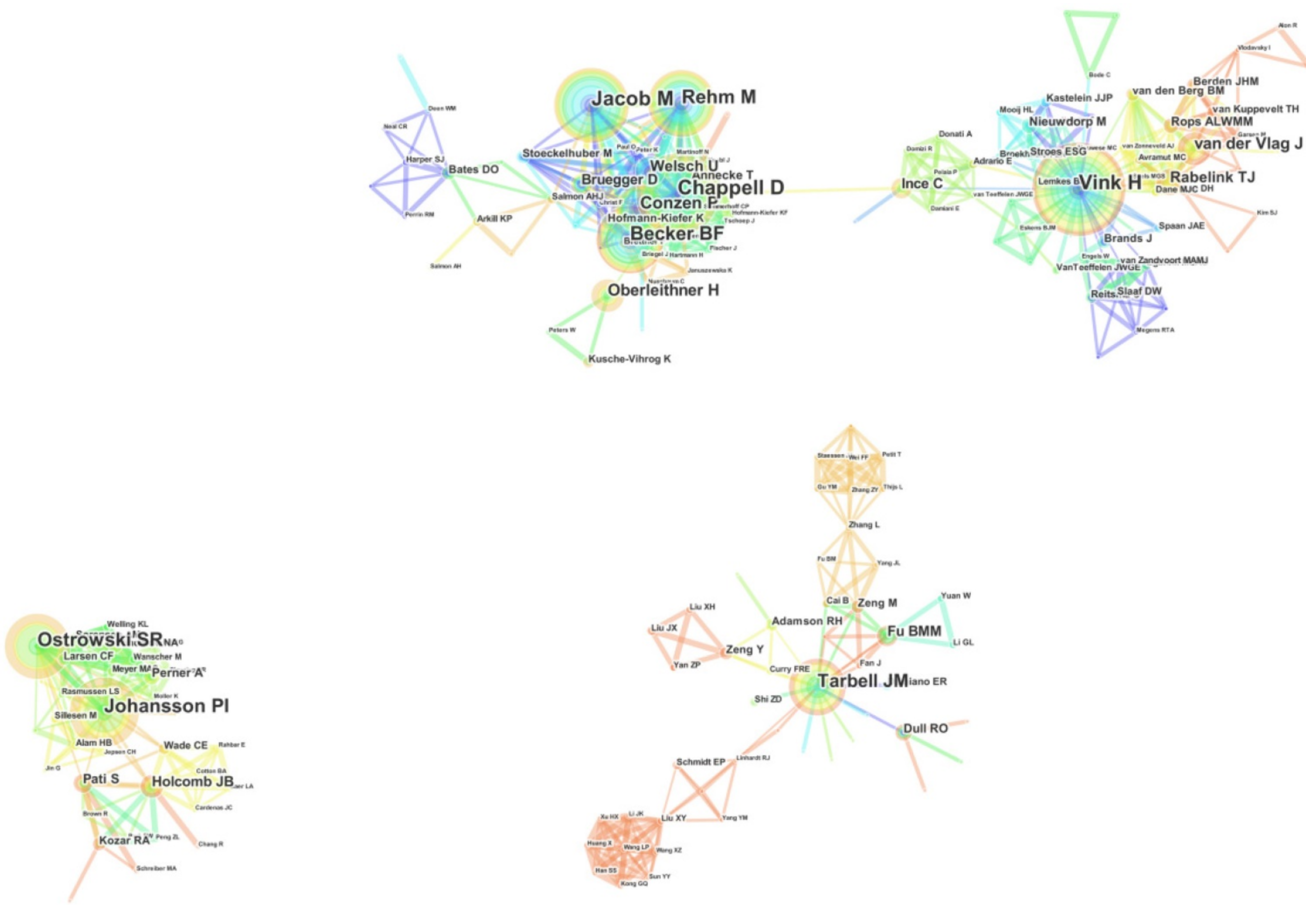

Figure 1. The co-authorship network of glycocalyx research Each node represents an author. The size of the circles indicates the numbers of publications of the author, and the links between the authors represent direct partnerships established through the co-authorship of papers. The different colors represent different years from 2007 to 2016. There are 771 nodes and 1114 links in the co-authorship network of glycocalyx research.

Table 2. The top 20 most cited authors of glycocalyx research

Freq	Centrality	Author	Year	Freq	Centrality	Author	Year
308	0	Weinbaum S	2007	147	0.01	Henry CBS	2007
252	0	Nieuwdorp M	2007	146	0.13	Tarbell JM	2007
226	0.04	Pries AR	2007	138	0.01	Constantinescu AA	2007
224	0	Reitsma S	2008	128	0.11	Florian JA	2007
222	0	Vink H	2007	122	0.33	Becker BF	2009
221	0.11	Chappell D	2008	114	0.01	Jacob M	2007
200	0.01	Rehm M	2007	97	0	Curry FE	2007
171	0.05	Van den Berg BM	2007	96	0.01	Johansson PI	2012
157	0	Mulivor AW	2007	94	0.01	Gouverneur M	2007
151	0.02	Adamson RH	2007	92	0.08	Bruegger D	2007

We analysed the betweenness centrality of cited-authors in order to figure out how vital they were for the cited author network. Centrality indicates the authors who act as bridges linking authors in different cited author networks. As shown in Table 2, Chappell D (0.11), Tarbell JM (0.13), Florian JA (0.11), Becker BF (0.33) have a betweenness centrality over 0.1, indicating that these authors have made significant contributions to the development of glycocalyx research. The analysis is limited by the lack of required data for all-author analysis, thus can not summarize the work published by different first author but from the same research group.

In a timezone model of author co-citation network as shown in Figure 2, each node represents one author, the size of each node represented their co-citation counts. A line connecting two nodes in this network represents a co-citation link. Figure 2 shows a timezone mode of author co-citation network of 367 authors and 428 co-citation links. Those authors who have strong influences on this field concentrated in earlier years from 2007 to 2010. Though some influential authors have been appeared after 2010 but there is a significant gap compared with formers. This might due to various reasons, for example, new studies were just released and have not received widely attention and reference yet.

Document Co-citation Analysis of Glycocalyx Research

The influential research references and hotspots in Glycocalyx Research

Figure 3 shows the document co-citation network of glycocalyx research. A document co-citation network represents a network of references that have been co-cited by a set of publications, and is useful in studies of the structure, dynamics, and paradigm developments of a given research field [20]. The highly cited and most influential research references in a specific research domain can be found by document co-citation analysis, and then researchers can easily track the hot aspect and obtain the references [21].

In the network, there are 529 unique nodes and 1092 links for a one-year time slice. Each node represents one cited reference. The citation history is visualized in terms of "tree rings" with different colors and thickness. The links in the network represent co-citation relationships. Each linked color corresponds directly to each time slice in which the co-citation link was first made. The oldest are in blue, and the newest are in red. Blue links describe two publications that were co-cited in 2007 and red links connect publications that were co-cited in 2016. The thickness of the circle is in proportion to the number of cited papers in the corresponding year. Nodes with citation bursts are visualized with rings in red. The larger node size implies that the article is an important one within the knowledge domain.

Table 3 presents the five top-cited articles associated with glycocalyx research between 2007 and 2016. The first one is a review by Weinbaum S *et al.* [11], which demonstrated the mechanical and biochemical properties of the endothelial glycocalyx layer and reviewed the studies on the interactions of this layer with WBCs. The second one is work from Reitsma S *et al*. [10], which is also a review provided basic insight into the composition and functions of the endothelial glycocalyx and gave an overview of the visualization methods of glycocalyx. The other three papers focused on the role of endothelial glycocalyx in different pathological states. For example, Rehm M *et al.* [22] provided the evidence for an acute destruction of the endothelial glycocalyx in patients with aortic surgery and global ischemia (DHCA) or regional ischemia (with and without CPB) by determining levels of syndecan-1 and heparan sulfate in blood at various phases of the procedure. Johansson PI *et al.* [23] investigated the markers of acute endothelial glycocalyx degradation, inflammation, coagulopathy and mortality after trauma, showing high circulating syndecan-1, a marker of endothelial glycocalyx degradation, is associated with inflammation, coagulopathy and increased mortality. Becker BF *et al.* [12] brought another review about the physiological role of the glycocalyx in reperfusion injury, inflammation, trauma, atherosclerosis, diabetes and hypervolaemia, and then gives some strategies aimed at preservation or resurrection of the endothelial glycocalyx layer. The highly cited papers can assist researchers to quickly collect the main advances in glycocalyx research.

The Trends in Annotation of Glycocalyx Research

Citespace divides the co-citation network into a number of clusters of co-cited references that are tightly connected within the same clusters, but are loosely connected with other clusters. In this instance, we get total 99 clusters in the glycocalyx research network, and Figure 4 shows the top 15 clusters (From cluster #0 to cluster #14). To characterize the nature of the clusters, CiteSpace can extract noun phrases to name the clusters automatically from the titles of articles that cited the cluster based on three specialized metrics-term frequency-inverse document frequency (TF-IDF), log-likelihood tests (LLR) and mutual information tests (MI). LLR usually gives the best result in terms of the uniqueness and coverage of themes associated with a cluster [21]. Table 4 details the top 15 clusters in rank order, all of the values of the silhouettes for each cluster are greater than 0.5, suggesting robust and meaningful results.

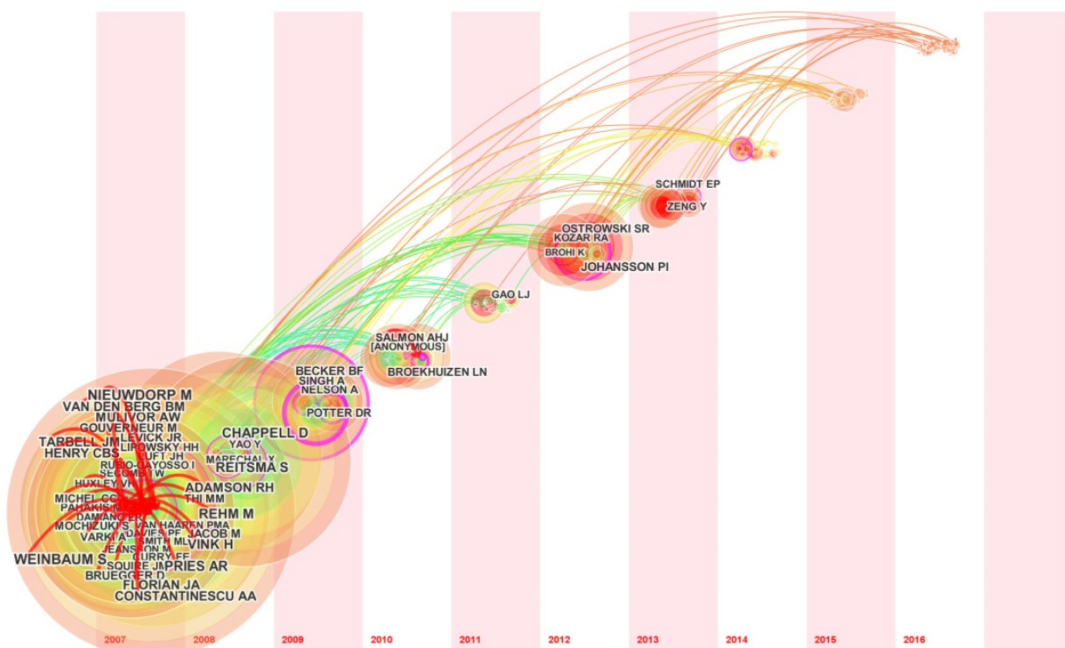

Figure 2. The timezone mode of author co-citation network of glycocalyx research Each node represented one author, the size of each node represented their co-citation counts. A line connecting two nodes in this network represents a co-citation link.

Table 3. Five critical articles in glycocalyx research

Citation Freq	Author	Centrality	Year	Title	Source	Vol	Page
123	Weinbaum S *et al.* [11]	0	2007	The structure and function of the endothelial glycocalyx layer.	ANNU REV BIOMED ENG	V9	P121
113	Reitsma S *et al.* [10]	0	2007	The endothelial glycocalyx: composition, functions, and visualization	PFLUG ARCH EUR J PHY	V454	P345
89	Rehm M *et al.* [22]	0.07	2007	Shedding of the endothelial glycocalyx in patients undergoing major vascular surgery with global and regional ischemia.	CIRCULATION	V116	P1896
88	Johansson PI *et al.* [23]	0.08	2011	A high admission syndecan-1 level, a marker of endothelial glycocalyx degradation, is associated with inflammation, protein C depletion, fibrinolysis, and increased mortality in trauma patients.	ANN SURG	V254	P194
75	Becker BF *et al.* [12]	0.02	2010	Therapeutic strategies targeting the endothelial glycocalyx: acute deficits, but great potential	CARDIOVASC RES	V87	P300

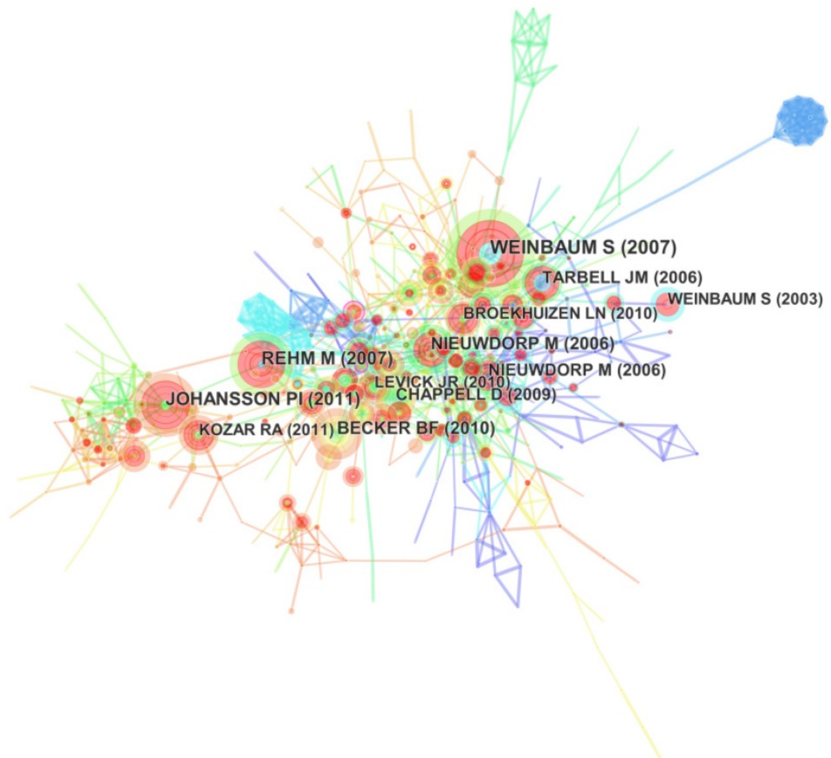

Figure 3. Document co-citation network of glycocalyx research Each node represents one cited reference. The citation history is visualized in terms of "tree rings" with different colors and thickness. The links in the network represent co-citation relationships. Each linked color corresponds directly to each time slice in which the co-citation link was first made. The oldest are in blue, and the newest are in red. Blue links describe two publications that were co-cited in 2007 and red links connect publications that were co-cited in 2016. The thickness of the circle is in proportion to the number of cited papers in the corresponding year. Nodes with citation bursts are visualized with rings in red. The larger node size implies that the article is an important one within the knowledge domain. In the network, there are 529 unique nodes and 1092 links for an one-year time slice.

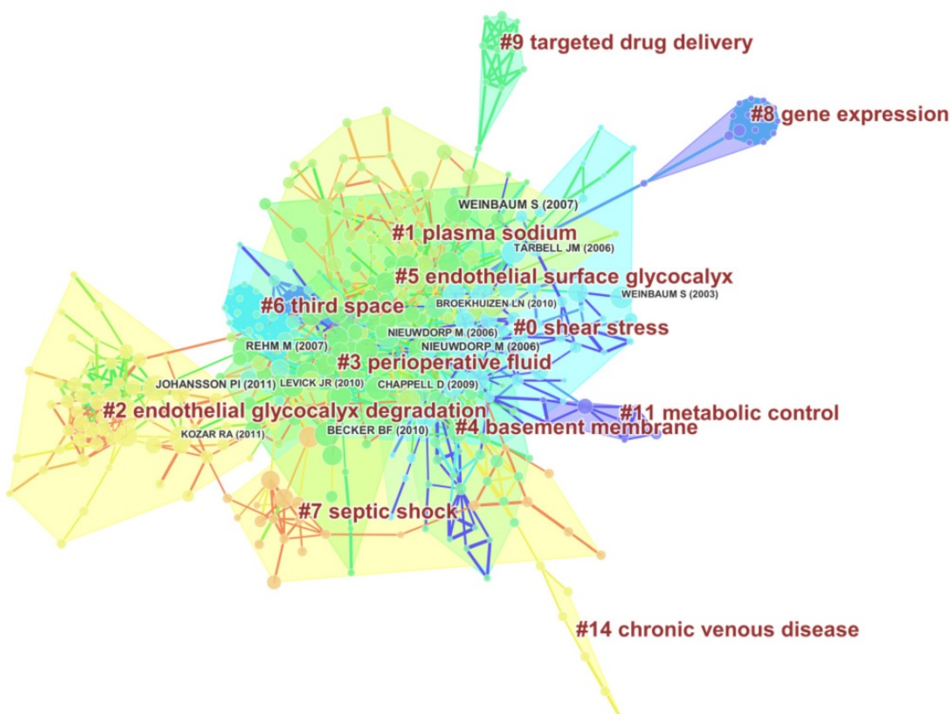

Figure 4. Clusters visualization based on a document co-citation network Citespace divides the co-citation network into a number of clusters of co-cited references that are tightly connected within the same clusters, but are loosely connected with other clusters. In this instance, we get total 99 clusters in the glycocalyx research network, and shows the top 15 clusters (From cluster #0 to cluster #14).

Table 4. Summary of the largest 15 clusters

Cluster ID	Size	Silhouette	Label (TF*IDF)	Label (LLR)	Label (MI)	Mean (Cited Year)
0	65	0.748	filtration rate	shear stress	venous pressure	2004
1	58	0.626	endothelial glycocalyx links albuminuria	plasma sodium	gold nanoparticle	2011
2	57	0.951	blunt liver injury	endothelial glycocalyx degradation	interference contrast microscopy	2011
3	49	0.759	renal dysfunction	perioperative fluid	glomerular capillary	2008
4	42	0.869	endothelialnitric oxide	basement membrane	articular cartilage	2007
5	34	0.751	perturbation	endothelial surface glycocalyx	atherosclerosis-resistant region	2010
6	25	0.905	inflammation	third space	hypervolemia increases release	2005
7	22	0.958	human albumin infusion	septic shock	hypervolemia increases release	2012
8	15	0.985	atherogenesis	gene expression	endothelial glycocalyx	2005
9	10	0.988	glutathione	targeted drug delivery	endothelial glycocalyx	2007
10	8	1	tissue engineering chromatography	sialic acid	sialic acid precursor	2006
11	7	0.981	streptozotocin-induced diabetic rats	metabolic control	endothelial glycocalyx	2004
12	7	1	inflammation	mesothelial cell	heparan sulfate	2003
13	6	1	pollendevelopment	pattern formation	pattern formation	2006
14	6	0.987	low density lipoprotein	chronic venous disease	endothelial glycocalyx	2012

Table 5. List of frequently cited references of cluster #0

Citation Freq	Author	Centrality	Year	Title	Source	Vol	Page
59	Tarbell JM *et al.* [24]	0.06	2006	Mechanotransduction and the glycocalyx	J INTERN MED	V259	P339
50	Weinbaum S *et al.* [28]	0	2003	Mechanotransduction and flow across the endothelial glycocalyx	P NATL ACAD SCI USA	V100	P7988
45	Pahakis MY *et al.* [38]	0.04	2007	The role of endothelial glycocalyx components in mechanotransduction of fluid shear stress	BIOCHEM BIOPH RES CO	V355	P228
42	Van den Berg BM *et al.* [29]	0.02	2003	The endothelial glycocalyx protects against myocardial edema	CIRC RES	V92	P592
38	Van den Berg BM *et al.* [39]	0.08	2006	Atherogenic region and diet diminish glycocalyx dimension and increase intima-to-media ratios at murine carotid artery bifurcation	AM J PHYSIOL-HEART C	V290	

The average year of publication of a cluster indicates its recentness. As shown in Table 3, *shear stress* is the largest and oldest cluster, consists of 65 members and a silhouette value of 0.748. It is labeled as *shear stress* by LLR, *filtration rate* by TF-IDF, and *venous pressure* by MI. We selected 5 major cited references in this cluster as shown in Table 5, in which Tarbell JM 2006 is the most cited article, which focused on mechanotransduction of shear stress by endothelial cells and presented the evidence in support of the surface glycocalyx acting as a mechanosensor [24]. The cluster was most actively cited by a review of VanTeeffelen, JWGE *et al.* (2010) [13].

Septic shock and *chronic venous disease* are the youngest clusters in recent (Table 4). *Septic shock* has 22 members and a silhouette value of 0.958. It is labeled as *septic shock* by LLR, *human albumin infusion* by TF-IDF, and *hypervolemia increases release* by MI. Table 6 lists five frequently cited references in this cluster, all the selected articles are published after 2012, indicating it is a recently formed cluster. The one that has the highest citation of 37 in this cluster is a review by Woodcock TE 2012, which attempted to reconcile clinical trial data and advances in clinical experience of therapy in microvascular physiology to improve the working paradigm for rational prescribing [25]. The cluster was most actively cited by a review of Vincent, JL *et al.* (2016) [26].

Chronic venous disease only has 6 members and a silhouette value of 0.987. It is labeled as *chronic venous disease* by LLR, *low density lipoprotein* by TFIDF, and *endothelial glycocalyx* by MI. The cluster was most actively cited by a review of Masola, V *et al.* (2014) [27], which focused on the therapeutic potential of heparins and GAGs in restoring a normal glycocalyx layer to physiological level.

The Ongoing Concern in Glycocalyx Research

Table 7 shows the top 20 references with the strongest citation bursts. Burst detection determines whether a given frequency function has statistically significant fluctuations during a short time interval within the overall time period. A citation burst indicates the likelihood that the scientific community has paid or is paying special attention towards the underlying contribution, and also is an indication of emerging thematic trends in a research field. Many members of Cluster #0 are found to have citation bursts, suggest #0 is indicated an important discovery in research field of glycocalyx. There is a list of references within Cluster #0 including WEINBAUM S et al., 2003 [28], VAN DEN BERG BM et al., 2003 [29], CONSTANTINESCU AA et al., 2003 [30], FLORIAN JA *et al.*, 2003[31], MOCHIZUKI S *et al.*, 2003 [32], MULIVOR AW *et al.*, 2004 [33], and THI MM *et al.*, 2004 [34]. These articles mostly focused on the role of glycocalyx in endothelial mechanotransduction [28, 31, 32], protection against myocardial edema [29] and modulation of immobilization of leukocytes at endothelial surface [30], and on its structural change during inflammation and ischemia [33]. The underlying mechanism is an important ongoing concern for decades [34].

Table 6. List of frequently cited references of cluster #7

Citation Freq	Author	Centrality	Year	Title	Source	Vol	Page
37	Woodcock TE *et al.* [25]	0.04	2012	Revised Starling equation and the glycocalyx model of transvascular fluid exchange: an improved paradigm for prescribing intravenous fluid therapy	BRIT J ANAESTH	V108	P384
28	Perner A *et al.* [40]	0.02	2012	Hydroxyethyl Starch 130/0.4 versus Ringer's Acetate in Severe Sepsis	NEW ENGL J MED	V367	P124
25	Myburgh JA *et al.* [41]	0.03	2012	Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care	NEW ENGL J MED	V367	P1901
11	Caironi P *et al.* [42]	0	2014	Albumin Replacement in Patients with Severe Sepsis or Septic Shock	NEW ENGL J MED	V370	P1412
10	Myburgh JA *et al.* [43]	0.02	2013	Resuscitation Fluids	NEW ENGL J MED	V369	P1243

Table 7. Top 20 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2007 - 2016	cluster #
WEINBAUM S *et al.*, 2003, P NATL ACAD SCI USA, V100, P7988 [28]	2003	23.0547	2007	2009		0
REITSMA S *et al.*, 2007, PFLUG ARCH EUR J PHY, V454, P345 [10]	2007	20.1888	2010	2013		61
VAN DEN BERG BM *et al.*, 2003, CIRC RES, V92, P592 [29]	2003	19.3231	2007	2009		0
WEINBAUM S *et al.*, 2007, ANNU REV BIOMED ENG, V9, P121 [11]	2007	17.4974	2010	2013		5
CONSTANTINESCU AA *et al.*, 2003, ARTERIOSCL THROM VAS, V23, P1541 [30]	2003	13.7566	2007	2009		0
REHM M *et al.*, 2007, CIRCULATION, V116, P1896 [22]	2007	12.8756	2009	2013		3
NIEUWDORP M *et al.*, 2006, DIABETES, V55, P480 [44]	2006	12.6286	2007	2011		3
FLORIAN JA *et al.*, 2003, CIRC RES, V93, P136 [31]	2003	12.3707	2007	2009		0
MOCHIZUKI S *et al.*, 2003, AM J PHYSIOL-HEART C, V285, P722 [32]	2003	12.3707	2007	2009		0
SCHMIDT EP *et al.*, 2012, NAT MED, V18, P1217 [35]	2012	11.7283	2014	2016		1
OSTROWSKI SR *et al.*, 2012, J TRAUMA ACUTE CARE, V73, P60 [36]	2012	11.7099	2014	2016		2
MULIVOR AW *et al.*, 2004, AM J PHYSIOL-HEART C, V286, P1672 [33]	2004	11.5848	2007	2010		0
REHM M *et al.*, 2004, ANESTHESIOLOGY, V100, P1211 [45]	2004	11.5848	2007	2010		3
ADAMSON RH *et al.*, 2004, J PHYSIOL-LONDON, V557, P889 [46]	2004	11.2197	2007	2010		3
THI MM *et al.*, 2004, P NATL ACAD SCI USA, V101, P16483 [34]	2004	11.2197	2007	2010		0
JOHANSSON PI *et al.*, 2011, ANN SURG, V254, P194 [23]	2011	10.9912	2013	2016		2
NIEUWDORP M *et al.*, 2005, CURR OPIN LIPIDOL, V16, P507 [47]	2005	10.3909	2007	2011		1
VLAHU CA *et al.*, 2012, J AM SOC NEPHROL, V23, P1900 [37]	2012	10.0097	2014	2016		1
NIEUWDORP M *et al.*, 2006, DIABETES, V55, P1127 [48]	2006	9.7548	2008	2012		4
GAO LJ *et al.*, 2010, MICROVASC RES, V80, P394 [49]	2010	8.9853	2012	2014		5

The most recent strongest burst articles started in 2014 are due to SCHMIDT EP 2012 *et al.* [35], OSTROWSKI SR 2012 *et al.* [36], and VLAHU CA 2012 *et al.* [37]. SCHMIDT EP *et al.* [35] elucidated the mechanisms by which glycocalyx loss occurs during inflammatory lung injury in sepsis and how this loss allows for neutrophil adhesion in the pulmonary circulation. OSTROWSKI SR *et al.* [36] evaluated degradation of the endothelial glycocalyx and ensuing release of its heparin-like substances induce auto heparinization and thereby contributes to trauma-induced coagulopathy. VLAHU CA *et al.* [37] used Sidestream Dark Field microscopy to detect changes in glycocalyx dimension in the sublingual microcirculation in dialysis patients.

Taken together, researches are focused on the regulatory factors involved in structural and function of glycocalyx, and the role of glycocalyx in human diseases such as sepsis-associated acute lung injury, severe injury and early traumatic coagulopathy and end stage renal disease. The precious regulatory molecular mechanisms and important roles in diagnosis, prevention and treatment of human diseases (such as cardiovascular diseases and cancer) are still remained to be elucidated, which is the future direction.

Limitations of the Analysis

It should be noted that the present study was limited to the database of WOSCC, and other databases were not included, especially studies written in non-English were not analyzed. Future researches might carry out studies with the data contained in PubMed, and Scopus. Furthermore, an expanded dataset will be supplemented to include the articles not contain any of the query terms in the topic search, which is a superset of the core dataset with extra bibliographic records obtained by association through citation links. The author co-citation analysis only uses the first author of a cited reference in our study due to the limitation of indexing practices of WOS citation databases. Further study might carry out to introduce a serial work of a group rather than a single work of the first-author. In addition, the citation analysis could not distinguish the inherent complexities of the literatures, for example, new researcher in the field or research from other field could not obtain information regarding the results in the highlighted literatures are related with each other or contradicted with each other, as well as the difference in their perspective. Nevertheless, our scientometric review has given a comprehensive understanding of the hotspots and advances in recent glycocalyx researches.

Conclusion

In summary, a comprehensive bibliometric analysis of research literatures in the field of glycocalyx from 2007 to 2016 was perform by Citespace software with the data source from the WOSCC, which led to a number of important findings.

In first, the close collaboration community and the most cited researchers in the research field of glycocalyx should be useful for support the new researchers to follow the research front of glycocalyx.

In secondary, we present the emerging trends and hotspots in the research field of glycocalyx during 2007-2016. Most recent investigation focused on the role of glycocalyx in endothelial mechanotransduction, and on its structural change and special role in pathological changes and human diseases, such as permeability dysfunction, inflammation, ischemia, cardiovascular diseases and cancer.

Finally, we attempted to show the research frontiers of glycocalyx research for decades. The precious regulatory molecular mechanisms and important roles in diagnosis, prevention and treatment of human diseases (such as cardiovascular diseases and cancer) are still remained to be elucidated, which is the future direction. The new innovation in glycocalyx involved in human diseases is a meaningful direction for future research.

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Competing Interests

The authors have declared that no competing interest exists.

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