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### Bibliometric analysis of the meibomian gland literature

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### The Ocular Surface

# Bibliometric analysis of the meibomian gland literature --Manuscript Draft--

Manuscript Number:	THEOCULARSURFACE-D-21-00011R3
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Keywords:	bibliometric analysis, citations, impact, meibomian gland, meibum, publication metrics
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Opposed Reviewers:	
Response to Reviewers:	THEOCULARSURFACE-D-21-00011-R3 March 10, 2021 The authors of the Research Correspondence submission entitled "Bibliometric analysis of the meibomian gland literature" are thankful to the editor/reviewer for their helpful suggestions to improve manuscript. Below are detailed comments that are included in the revision of the submission that we hope address the critiques raised. We have also condensed two paragraphs on authors, countries, affiliations, and journals and revised Figure 1 to summarize leaders in these areas (per the off-line suggestion of the Editor in Chief). Thank you again for these helpful comments.
	Editor and Reviewer comments: Thank you for resubmitting the manuscript. However, we need more insightful contents than just a list of facts. For example, we'd like ask you to provide the details of highly cited papers instead of highly cited institutions. We've requested it so far, but we need a perspective for the future research of MGD.
	RESPONSE: Thank you for this excellent idea. We have collapsed text in the manuscript regarding authors, institutions, countries, and journals and summarized top leaders along these lines in Figure 1. This allows for additional space to discuss in depth further details of highly cited and uncited papers (or trends along these lines as they relate to current and future MGD research). This has been revised in the manuscript as follows:
	"While citation analyses can be helpful in identifying trends in research, they do have limitations. For instance, older research is more likely to have higher citation counts than more recent research simply due to time, which itself allows for the accumulation of citations. Along these lines, it is clear from the very most current research in MGD that particularly over the very most recent years that therapeutic and diagnostic approaches are key areas of research in MGD. For instance, there is no doubt that innovations in imaging approaches (e.g., optical coherence tomography, meibography, confocal microscopy) are of vital importance to the field of MGD research, particularly

through their utility in diagnosis and follow-up, once treatment is initiated. Likewise, new diagnostic imaging approaches that are able to detect MGD absent of symptoms are of significant interest, as recent studies and reviews have suggested that asymptomatic MGD is much more frequent than is traditionally thought.[8] Further to this, newer understandings of the biochemical composition of the meibum and tear film lipids as key biomarkers or therapeutic targets are of substantial importance to the field going forward. In particular, the O-acyl-ω-hydroxy fatty acids (OAHFAs) have shown themselves recently to play major functional roles in allowing the tear film to structure itself properly as highly effective surfactants.[9, 10] While lipid emulsions are available for tear supplementation, most contain large, hydrophobic lipids such as mineral or caster oils, not present in human meibum otherwise. The OAHFAs could serve as potential therapeutic supplements along these lines, as they naturally occur in the meibum and tear film."

January 11, 2021

Dear Dr. Djalilian,

My coauthors and I wish to submit a new manuscript entitled "Bibliometric analysis of the meibomian gland literature" for consideration as a short Research Correspondence by *The Ocular Surface*. We confirm that this work is original and has not been published nor is it currently under consideration for publication elsewhere.

This paper reports on the important observations of the growing body of literature on meibomian glands in the context of ocular surface disease and reports on the most impactful articles, authors, journals, countries and affiliations.

We believe this work will be of interest and highly valuable to the ocular surface community who study dry eye and the meibomian glands. The appendix is intended to be supplementary material, available online to the readership.

Thank you for your consideration of this manuscript.

Sincerely,

/Min

**Corresponding Author** 

Jason J. Nichols, OD MPH PhD | Associate Vice President for Industry Research & Professor Office of the Vice President for Research Office of Industry Engagement UAB | The University of Alabama at Birmingham AB 714A | 1720 2<sup>nd</sup> Avenue South | Birmingham, AL 35294-0107

#### THEOCULARSURFACE-D-21-00011-R3

March 10, 2021

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### Editor and Reviewer comments:

Thank you for resubmitting the manuscript. However, we need more insightful contents than just a list of facts. For example, we'd like ask you to provide the details of highly cited papers instead of highly cited institutions. We've requested it so far, but we need a perspective for the future research of MGD.

**RESPONSE**: Thank you for this excellent idea. We have collapsed text in the manuscript regarding authors, institutions, countries, and journals and summarized top leaders along these lines in Figure 1. This allows for additional space to discuss in depth further details of highly cited and uncited papers (or trends along these lines as they relate to current and future MGD research). This has been revised in the manuscript as follows:

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### 1 RESEARCH CORRESPONDENCE

- 2 Bibliometric analysis of the meibomian gland literature
- 3 Jason J. Nichols, OD, MPH, PhD<sup>a</sup>
- 4 Lyndon W. Jones, DSc, FCOptom<sup>b</sup>
- 5 Philip B. Morgan, PhD<sup>c</sup>
- 6 Nathan Efron, AC, DSc, PhD<sup>d</sup>
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- 8 a. School of Optometry, The University of Alabama at Birmingham, Birmingham, Alabama,
- 9 United States.
- 10 b. Centre for Ocular Research & Education (CORE), School of Optometry and Vision
- 11 Science, University of Waterloo, Waterloo, Ontario, Canada and Centre for Eye and Vision
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- 14 Manchester, Manchester, United Kingdom
- 15 d. School of Optometry and Vision Science, Queensland University of Technology, Kelvin
- 16 Grove, Queensland, Australia
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- 18 Key Words: bibliometric analysis, citations, impact, meibomian gland, meibum,
- 19 publication metrics
- 20 Word Count (text only): 1,209
- 21 References: 11
- 22 Figures: 1
- 23 Supplementary Tables: 6
- 24
- 25 **Corresponding Author**: Jason J. Nichols OD MPH PhD, School of Optometry, University
- of Alabama at Birmingham, 1916 University Blvd, Birmingham, AL 35233, United States
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- 28
- 29 Financial support
- 30 This work did not receive any public or private extramural financial support.
- 31
- 32 Short title
- 33 Bibliometric analysis of the meibomian gland literature

There is a rich history of interest in the sebaceous glands located posterior to the tarsal plates in the eyelids, to which we refer today as the meibomian glands (MGs). Although there is acknowledgement of the MGs preceding the work of Johann Heinrich Meibom in the 1600's, he is credited with advancing our knowledge and study of these glands.[1]

39 The MGs produce a distinct lipid secretion ('meibum') made up of a variety of lipid classes. 40 mostly composed of nonpolar wax and cholesterol esters, although other nonpolar and 41 polar lipids are certainly known to exist in the meibum.[2] The normal function of meibum 42 is to make its way to the tear film lipid layer, ultimately forming a resistive barrier to evaporation of the aqueous component of the tear film. In disease, the MGs lose their 43 44 ability to secrete a normal meibum composition and/or are impeded due to factors such 45 as atrophy of the MGs, keratinization of the orifice of the gland from which the meibum is secreted onto the eyelid margin, or bacterial colonization of the eyelid, altering the 46 47 secretion itself once expressed.[3, 4] These conditions today are known as blepharitis. 48 including anterior and posterior blepharitis (which includes meibomian gland 49 dysfunction).[5]

50

51 Given the extensive study of MGs, a bibliometric analysis is warranted to acknowledge 52 and celebrate those contributing to this important part of ophthalmic research.

53

A bibliometric search was undertaken on January 5, 2021 of the titles of papers on the Scopus database. The goals of the search were to identify the most relevant meibomian gland-related documents published in peer-reviewed journals that are primarily meibomian gland driven, rather than to include secondary MG themes in this search; thus, only 'title' identifiers were used to capture this field of research with the highest sensitivity
 and specificity. To identify MG-related articles, the following search terms was used:

TITLE(meibum) OR TITLE(meibomian) OR TITLE(blepharitis) OR
 TITLE(meibomitis) OR TITLE(blepharon-conjunctivitis) OR TITLE(meibography\*)
 AND (LIMIT-TO(SRCTYPE, "j")) AND (LIMIT-TO(LANGUAGE, "English"))

64

The 25 most highly cited papers were determined from the total list of 1,462 papers found. The search term above was also limited to the last 10 years to determine the top contemporary articles in the field of meibomian gland research. A subject-specific meibomian gland-related h-index (h<sub>MG</sub>-index) was derived for authors, institutions, countries and journals to serve as a measure of impact in the field.[6] The top constituents of each category were ranked by h<sub>MG</sub>-index and tabulated for consideration.

71

The  $h_{MG}$ -index of the field was determined to be 85. The 1,462 papers have been cited a total of 32,657 times, and 18.2% of these papers have never been cited. The number of papers in the field published each year between 1849 and 2020 is shown in Figure 1, with a rapid increase evident from 2008.

76

The 25 most highly cited papers are listed in Table 1 of the Supplementary Data. Seven of the top 25 papers are affiliated with the International Workshop on Meibomian Gland Dysfunction conducted under the auspices of the Tear Film and Ocular Surface Society (TFOS), including the paper ranked #1 by first author Erik Knop ("anatomy, physiology, and pathophysiology of the meibomian glands").[7] Outside of this, six cover MG 82 physiology or pathophysiology, six relate to clinically oriented research (meibography,

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There is undoubtedly keen interest in defining and classifying MGD, as noted by the 85 86 number of Top 25 articles devoted to this topic and diagnostic criteria associated with the 87 condition. Further to this, another key theme of the Top 25 articles is that of the study of 88 MG physiology and pathophysiology, particularly as these relate to MG function and 89 meibum secretion. Several papers report on various basic science concepts, while others 90 describe clinical techniques (such as meibography) that are used to assess either MG 91 health and/or the lipid laver of the tear film. Others describe less common but important 92 related assessments such as evaporimetry. Further to this, several of these papers 93 address the apparent overlap between dry eye (aqueous deficiency) and evaporative diseases, such as MGD and blepharitis. It is clear that the TFOS International Workshop 94 95 on Meibomian Gland Dysfunction has had a substantial impact, in that 7 of the Top 25 96 articles are among the Top 25.

97

Table 2 shows the top 10 contemporary articles related to the study of the meibomian glands. It is clear that the top cited contemporary literature relates to the treatment of meibomian gland dysfunction (5 of 10 articles) and assessment of the meibomian glands and/or lipid layer (4 of 10 articles); the remaining (and top cited) article is focused on the pathophysiology of meibomian gland dysfunction.

103

While citation analyses can be helpful in identifying trends in research, they do have limitations. For instance, older research is more likely to have higher citation counts than more recent research simply due to time, which itself allows for the accumulation of 107 citations. Along these lines, it is clear from the most current research in MGD that, 108 particularly over the very most recent years, therapeutic and diagnostic approaches are 109 key areas of research in MGD. For instance, there is no doubt that innovations in imaging 110 approaches (e.g., optical coherence tomography, meibography, confocal microscopy) are 111 of vital importance to the field of MGD research, particularly through their utility in diagnosis and follow-up, once treatment is initiated. Likewise, new diagnostic imaging 112 113 approaches that are able to detect MGD absent of symptoms are of significant interest. 114 as recent studies and reviews have suggested that asymptomatic MGD is much more frequent than is traditionally thought.[8-10] Further to this, newer understandings of the 115 116 biochemical composition of the meibum and tear film lipids as key biomarkers or therapeutic targets are of substantial importance to the field going forward. In particular, 117 118 the O-acyl- $\omega$ -hydroxy fatty acids (OAHFAs) have shown themselves recently to play major 119 functional roles in allowing the tear film to structure itself properly as highly effective surfactants.[9, 11] While lipid emulsions are available for tear supplementation, most 120 121 contain large, hydrophobic lipids such as mineral or caster oils, not present in human meibum otherwise. The OAHFAs could serve as potential therapeutic supplements along 122 123 these lines, as they naturally occur in the meibum and tear film. There is much to be 124 considered along these lines for the future of research associated with MGD.

125

Tables 3, 4, 5, and 6 of the Supplementary Data lists the 10 most impactful authors, institutions, countries, and journals publishing meibomian gland-related articles, respectively. This is also summarized in Figure 1.

129

This bibliometric analysis has summarized the most important papers and themes in thefield of the study of the meibomian glands. It is clear that the TFOS International Workshop

132 on Meibomian Gland Dysfunction has had a substantial impact on the field of meibomian 133 gland research. Based on a prior bibliometric analysis of the entire dry eye field, it is clear 134 from the current bibliometric analysis of the MG-related literature that while there is some 135 overlap in content and top-ranked authors, the MG field is distinct in contributions and 136 growing perhaps at an equivalent rate to that of the entire dry eye literature.[12] 137 Notwithstanding the rich history of the study of MGs, current research activities appear to 138 be growing exponentially, so a re-analysis of this area of research in the years to come is 139 certainly warranted.

140

#### 141 FINANCIAL DISCLOSURES

142 Jason Nichols: In 2019 and 2020, Dr. Jason J. Nichols has received honoraria from 143 Paragon Vision Sciences and CooperVision. He has also received research funding from 144 Alcon, Bruder, Johnson and Johnson Vision, and Mallinckrodt over the last 3 years. Also, 145 Dr. Kelly Nichols is the spouse of Dr. Jason Nichols, extending her declarations to him. In 146 the past 12 months, Dr. Kelly Nichols has consulted for and received honorarium from: 147 Bruder, Dompe, Kala, Novartis/Shire (Medical Exchange International), Osmotica, Oyster 148 Point, Sight Sciences, Tear Film Innovations/Alcon/Acquiom, Thea, Tarsus, and TopiVert. 149 She has received research funding from: Allergan, Kala, and Tear Science.

150

151 Phillip Morgan: Nothing to declare.

152

Lyndon Jones: Over the past 3 years Dr Jones' research group (CORE) or he personally has received research support or lectureship honoraria from: Alcon, Allergan, CooperVision, GL Chemtec, iMed Pharma, J&J Vision, Lubris, Menicon, Nature's Way, Novartis, Ote, PS Therapy, Safilens, Santen, Shire, SightGlass and Visioneering. Dr Jones is also a consultant and/or serves on an advisory board for Alcon, CooperVision, J&J Vision, Novartis and Ophtecs.

159

160 Nathan Efron: Nothing to declare.

161

#### 162 **REFERENCES**

163 [1] Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on 164 meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and

pathophysiology of the meibomian gland. Invest Ophthalmol Vis Sci. 2011;52:1938-78.

166 [2] Chen J, Nichols KK, Wilson L, Barnes S, Nichols JJ. Untargeted lipidomic analysis of

167 human tears: A new approach for quantification of O-acyl-omega hydroxy fatty acids. Ocul

168 Surf. 2019;17:347-55.

169 [3] Jester JV, Parfitt GJ, Brown DJ. Meibomian gland dysfunction: hyperkeratinization or

atrophy? BMC Ophthalmol. 2015;15 Suppl 1:156.

- 171 [4] Suzuki T, Sutani T, Nakai H, Shirahige K, Kinoshita S. The Microbiome of the Meibum
- and Ocular Surface in Healthy Subjects. Invest Ophthalmol Vis Sci. 2020;61:18.
- 173 [5] Daniel Nelson J, Shimazaki J, Benitez-del-Castillo JM, Craig J, McCulley JP, Den S,
- 174 et al. The international workshop on meibomian gland dysfunction: Report of the definition
- and classification subcommittee. Invest Ophthalmol Vis Sci. 2011;52:1930-7.
- 176 [6] Hirsch JE. An index to quantify an individual's scientific research output. Proc Natl
- 177 Acad Sci U S A. 2005;102:16569-72.
- 178 [7] Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on
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- 181 [8] Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. TFOS DEWS
- 182 II Epidemiology Report. Ocul Surf. 2017;15:334-65.
- 183 [9] Bland HC, Moilanen JA, Ekholm FS, Paananen RO. Investigating the Role of Specific
- 184 Tear Film Lipids Connected to Dry Eye Syndrome: A Study on O-Acyl-ω-hydroxy Fatty
- Acids and Diesters. Langmuir. 2019;35:3545-52.
- 186 [10] Miyamoto M, Sassa T, Sawai M, Kihara A, Radhakrishnan A. Lipid polarity gradient
- 187 formed by  $\omega$  hydroxy lipids in tear film prevents dry eye disease. eLife. 2020;9.
- 188 [11] Schuett BS, Millar TJ. An investigation of the likely role of (O-acyl) ω-hydroxy fatty
- acids in meibomian lipid films using (O-oleyl)  $\omega$ -hydroxy palmitic acid as a model.
- 190 Experimental Eye Research. 2013;115:57-64.
- 191 [12] Nichols JJ. Citation analysis of the dry eye literature. Ocul Surf. 2013;11:35-46.

192

### 193 Figure Caption

194	Figure 1.	Number of publications and summary information in the field of meibomian
195		gland research published each year between 1849 and 2020. For brevity,
196		the Figure is truncated to works occurring on or after 1900.

1

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- 12 Research (CEVR), 17W Hong Kong Science Park, Hong Kong
- 13 c. Eurolens Research, Division of Pharmacy and Optometry, The University of
- 14 Manchester, Manchester, United Kingdom
- 15 d. School of Optometry and Vision Science, Queensland University of Technology, Kelvin
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   of Alabama at Birmingham, 1916 University Blvd, Birmingham, AL 35233, United States
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- 27 (e-mail: jjn@uab.edu). Tel: 205-975-3497
- 28
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150

151 Phillip Morgan: Nothing to declare.

152

Lyndon Jones: Over the past 3 years Dr Jones' research group (CORE) or he personally has received research support or lectureship honoraria from: Alcon, Allergan, CooperVision, GL Chemtec, iMed Pharma, J&J Vision, Lubris, Menicon, Nature's Way, Novartis, Ote, PS Therapy, Safilens, Santen, Shire, SightGlass and Visioneering. Dr Jones is also a consultant and/or serves on an advisory board for Alcon, CooperVision, J&J Vision, Novartis and Ophtecs.

159

160 Nathan Efron: Nothing to declare.

161

#### 162 **REFERENCES**

163 [1] Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on 164 meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and

- pathophysiology of the meibomian gland. Invest Ophthalmol Vis Sci. 2011;52:1938-78.
- 166 [2] Chen J, Nichols KK, Wilson L, Barnes S, Nichols JJ. Untargeted lipidomic analysis of
- 167 human tears: A new approach for quantification of O-acyl-omega hydroxy fatty acids. Ocul
- 168 Surf. 2019;17:347-55.
- 169 [3] Jester JV, Parfitt GJ, Brown DJ. Meibomian gland dysfunction: hyperkeratinization or
- atrophy? BMC Ophthalmol. 2015;15 Suppl 1:156.

- 171 [4] Suzuki T, Sutani T, Nakai H, Shirahige K, Kinoshita S. The Microbiome of the Meibum
- and Ocular Surface in Healthy Subjects. Invest Ophthalmol Vis Sci. 2020;61:18.
- 173 [5] Daniel Nelson J, Shimazaki J, Benitez-del-Castillo JM, Craig J, McCulley JP, Den S,
- 174 et al. The international workshop on meibomian gland dysfunction: Report of the definition
- and classification subcommittee. Invest Ophthalmol Vis Sci. 2011;52:1930-7.
- 176 [6] Hirsch JE. An index to quantify an individual's scientific research output. Proc Natl
- 177 Acad Sci U S A. 2005;102:16569-72.
- 178 [7] Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on
- 179 meibomian gland dysfunction: Report of the subcommittee on anatomy, physiology, and
- pathophysiology of the meibomian gland. Invest Ophthalmol Vis Sci. 2011;52:1938-78.
- 181 [8] Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. TFOS DEWS
- 182 II Epidemiology Report. Ocul Surf. 2017;15:334-65.
- 183 [9] Bland HC, Moilanen JA, Ekholm FS, Paananen RO. Investigating the Role of Specific
- 184 Tear Film Lipids Connected to Dry Eye Syndrome: A Study on O-Acyl-ω-hydroxy Fatty
- 185 Acids and Diesters. Langmuir. 2019;35:3545-52.
- 186 [10] Miyamoto M, Sassa T, Sawai M, Kihara A, Radhakrishnan A. Lipid polarity gradient
- 187 formed by  $\omega$  hydroxy lipids in tear film prevents dry eye disease. eLife. 2020;9.
- 188 [11] Schuett BS, Millar TJ. An investigation of the likely role of (O-acyl) ω-hydroxy fatty
- acids in meibomian lipid films using (O-oleyl)  $\omega$ -hydroxy palmitic acid as a model.
- 190 Experimental Eye Research. 2013;115:57-64.
- 191 [12] Nichols JJ. Citation analysis of the dry eye literature. Ocul Surf. 2013;11:35-46.

192

### 193 Figure Caption

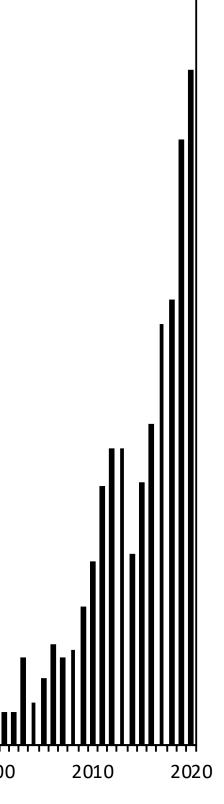
194	Figure 1.	Number of publications and summary information in the field of meibomian
195		gland research published each year between 1849 and 2020. For brevity,
196		the Figure is truncated to works occurring on or after 1900.

20 -				  1!u
40 -				
60 -				
80 -	<ul> <li>Most prolific country: United States (549 papers)</li> <li>Most impacful journal: Investigative Ophthalmology and Visual Science (h<sub>MG</sub> = 41)</li> <li>Most prolific journal: Cornea (130 papers)</li> </ul>			
100 -	<ul> <li>States) (81 papers)</li> <li>Most impactful country: United States (h<sub>MG</sub> = 71)</li> <li>Most prolific country: United States (549 papers)</li> </ul>			
	<ul> <li>Most impactful institution: UT Southwestern Medical School/Center (United States) (h<sub>MG</sub> = 32)</li> <li>Most prolific institution: Harvard University (United</li> </ul>			
120 -	<ul> <li>Most impactful author: James McCulley (h<sub>MG</sub> = 27)</li> <li>Most prolific author: Reiko Arita (48 papers)</li> </ul>			
140 -	Key metrics:			
160 -	h <sub>MG</sub> -index: 85 Publications with no citations: 18.2%			
	Total publications: 1,462 Total citations: 32,657			

Year published

Number of papers





### **Supplementary Material**

**Table 1**. Top 25 most highly cited meibomian gland-related articles ranked by number of citations.

Rank	Title	First Author	Journal	Year, Volume & Pages	Citations
1	The international workshop on meibomian gland dysfunction: Report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland	Erik Knop	Investigative Ophthalmology and Visual Science	2011 52; 1938-78	449
2	The international workshop on meibomian gland dysfunction: Executive summary	Kelly Nichols	Investigative Ophthalmology and Visual Science	2011 52; 1922-9	435
3	The international workshop on meibomian gland dysfunction: Report of the definition and classification subcommittee	Daniel Nelson	Investigative Ophthalmology and Visual Science	2011 52; 1930-7	368
4	Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population	Reiko Arita	Ophthalmology	2008 115; 911-5	352
5	The international workshop on meibomian gland dysfunction: Report of the diagnosis subcommittee	Alan Tomlinson	Investigative Ophthalmology and Visual Science	2011 52; 2006-49	333
6	Ocular surface changes and discomfort in patients with meibomian gland dysfunction	Jun Shimazaki	Archives of Ophthalmology	1995 113; 1266-70	321
7	Meibomian gland dysfunction: A clinical scheme for description, diagnosis, classification, and grading	Gary Foulks	The Ocular Surface	2003 1; 107-26	299
8	The international workshop on meibomian gland dysfunction: Report of the subcommittee on management and treatment of meibomian gland dysfunction	Gerd Geerling	Investigative Ophthalmology and Visual Science	2011 52; 2050-64	296
9	The international workshop on meibomian gland dysfunction: Report of the subcommittee on the epidemiology of, and associated risk factors for, MGD	Debra Schaumberg	Investigative Ophthalmology and Visual Science	2011 52; 1994-2005	265
10	Ocular evaporation in meibomian gland dysfunction and dry eye	William Mathers	Ophthalmology	1993 100; 347-51	231
11	Meibomian gland disease. Classification and grading of lid changes	Anthony Bron	Еуе	1991 5; 395-411	224
12	The contribution of meibomian disease to dry eye	Anthony Bron	The Ocular Surface	2004 2; 149-64	223
13	Meibomian gland dysfunction	Paul Driver	Survey of Ophthalmology	1996 40; 343-67	219
14	Classification of chronic blepharitis	James McCulley	Ophthalmology	1982 89; 1173-80	215
15	Meibomian gland studies: comparison of steer and human lipids	Nicholas Nicolaides	Investigative Ophthalmology and Visual Science	1981 20; 522-36	204

16	Targeted disruption of stearoyl-CoA desaturase1 gene in mice causes atrophy of sebaceous and meibomian glands and depletion of wax esters in the eyelid	Makoto Miyazaki	Journal of Nutrition	2001 131; 2260-8	198
17	Meibomian gland dysfunction in patients with Sjogren syndrome	Jun Shimazaki	Ophthalmology	1998 105; 1485-8	192
18	Effect of androgen deficiency on the human meibomian gland and ocular surface	Kathleen Krenzer	Journal of Clinical Endocrinology and Metabolism	2000 85; 4874-82	188
19	The international workshop on meibomian gland dysfunction: Report of the subcommittee on tear film lipids and lipid- protein interactions in health and disease	Kari Green-Church	Investigative Ophthalmology and Visual Science	2011 52; 1979-93	181
20	Contact lens wear is associated with decrease of meibomian glands	Reiko Arita	Ophthalmology	2009 116; 379-84	172
21	Meibomian gland dysfunction in chronic blepharitis	William Mathers	Cornea	1991 10; 277-285	172
22	Proposed diagnostic criteria for obstructive meibomian gland dysfunction	Reiko Arita	Ophthalmology	2009 116; 2058-64	161
23	Revisiting the vicious cycle of dry eye disease: A focus on the pathophysiology of meibomian gland dysfunction	Christophe Baudouin	British Journal of Ophthalmology	2016 100; 300-6	146
24	Pathogenic role of Demodex mites in blepharitis	Jingbo Liu	Current Opinion in Allergy and Clinical Immunology	2010 10; 505-10	144
25	Androgen influence on the meibomian gland	David Sullivan	Investigative Ophthalmology and Visual Science	2000 41;3732-42	143

**Table 2**. Top 10 most highly cited meibomian gland-related articles of the last 10 years ranked by number of citations.

Rank	Title	First Author	Journal	Year, Volume & Pages	Citations
1	Revisiting the vicious circle of dry eye disease: A focus on the pathophysiology of meibomian gland dysfunction	Christophe Baudouin	British Journal of Ophthalmology	2016 100; 300-6	147
2	A new system, the LipiFlow, for the treatment of meibomian gland dysfunction	Stephen Lane	Cornea	2012 31; 396-404	121
3	Evaluation of lipid layer thickness measurement of the tear film as a diagnostic tool for meibomian gland dysfunction	David Finis	Cornea	2013 32; 1549-53	108
4	Comparison of subjective grading and objective assessment in meibography	Heiko Pult	Contact Lens and Anterior Eye	2013 36; 22-7	102
5	Infrared imaging of the meibomian gland structure using a novel keratography	Sruthi Srinivasan	Optometry and Vision Science	2012 89; 788-94	102
6	Prospective trial of intense pulsed light for the treatment of meibomian gland dysfunction	Jennifer Craig	Investigative Ophthalmology and Visual Science	2015 56; 1965-70	101
7	Intense pulsed light treatment for dry eye disease due to meibomian gland dysfunction; a 3-year retrospective study	Rolando Toyos	Photomedicine and Laser Surgery	2015 33; 41-6	97
8	Correlation between quantitative measurements of the tear film lipid layer thickness and meibomian gland loss in patients with obstructive meibomian gland dysfunction and normal controls	Youngsub Eom	American Journal of Ophthalmology	2013 155; 1104-10	95
9	Interventions for chronic blepharitis	Kristina Lindsley	Cochrane database of systematic reviews	2012	88
10	Topical azithromycin and oral doxycycline therapy of meibomian gland dysfunction: A comparative clinical trial and spectroscopic pilot study	Gary Foulks	Cornea	2013 32; 44-53	85

Rank	Author	h <sub>MG</sub> -index	Paper count
1	James McCulley	27	34
2	David Sullivan	25	47
3	Reiko Arita	21	48
4	Kazuo Tsubota	21	31
5	lgor Butovich	20	29
6	Douglas Borchman	18	31
7	James Jester	18	30
8	Gary Foulks	18	21
9	Shiro Amano	17	23
10	Donald Korb	16	19
11	John Tiffany	16	17
12	Thomas Millar	15	17
13	Ward Shine	14	16
14	Marta Yappert	14	16
15	Kelly Nichols	13	28
16	Caroline Blackie	13	16
17	Anthony Bron	13	15
18	Jun Shimazaki	12	14
19	Nicholas Nicolaides	12	12
20	Tomo Suzuki	11	19

**Table 3.** Top authors of meibomian gland-related articles, ranked by author  $h_{MG}$ -index.

\*Authors with  $\leq$  11 papers and h<sub>MG</sub>  $\leq$  11: Louis Tong (11), Norihiko Yokoi (11), Donald Brown (10), Michael Dougherty (10), Murat Dogru (10), Wendy Kam (10), Poonam Mudgil (10), Ronald Smith (10), Yang Liu (9), Naoyuki Morishige (9), Jason Nichols (9), Frank Schirra (9), Rika Shirakawa (9), Jennifer Craig (8), Shima Fukuoka (8), Sruthi Srinivasan (8), Lyndon Jones (7), Ho-sik Hwang (5).

Rank	Institution	Country	H <sub>MG</sub> -index	Paper count
1	UT Southwestern Medical School/Center <sup>a</sup>	United States	32	55
2	Harvard University <sup>b</sup>	United States	31	81
3	Keio University/School of Medicine	Japan	24	37
4	University of Oxford <sup>c</sup>	United Kingdom	20	26
5	University of Louisville	United States	19	36
6	Ohio State University	United States	16	27
7	Western Sydney University	Australia	15	22
8	Keio University School of Medicine	Japan	14	22
9	Tokyo Dental College	Japan	14	19
10	Kyoto Prefectural University of Medicine	Japan	13	26

Table 4. Top institutions of meibomian gland-related articles, ranked by institution h<sub>mg</sub>-index.

\* Institutions with  $\leq$  13 papers and  $h_{MG} \leq$  13: Itoh Clinic (13), Korb Associated (13), University of California, Irvine (12), University of New South Wales (11), University of Southern California (11), National University of Singapore<sup>d</sup> (10), Fudan University/Eye ENT Hospital (9), Friedrich-Alexander-Universitat Erlangen-Nurnberg (9), University of Auckland (8), University of Waterloo (8), TearScience Inc (8), University of Alabama at Birmingham (7), University of Houston (7), Catholic University of Korea (5).

<sup>a</sup>Includes University of Texas at Dallas.

<sup>b</sup>Includes Harvard Medical School, Schepens Eye Research Institute, Mass Eye and Ear Infirmary, Brigham and Women's Hospital.

<sup>c</sup>Includes University of Oxford Medical Sciences Division.

<sup>d</sup>Includes National University of Singapore; Faculty of Medicine, Singapore Eye Research Institute; Singapore National Eye Centre; Duke-NUS Medical School Singapore; and Yong Loo Lin School of Medicine.

<b>Table 5.</b> Top countries of meibomian gland-related articles, ranked by country $h_{MG}$ -index.
-------------------------------------------------------------------------------------------------------

Rank	Country	h <sub>MG</sub> -index	Paper count
1	United States	71	549
2	Japan	39	149
3	United Kingdom	31	96
4	Germany	27	70
5	Australia	25	69
6	China	18	120
7	South Korea	18	68
8	Italy	18	46
9	Turkey	14	76
10	Spain	13	33

\*Countries with  $\leq$  13 papers but  $h_{MG}$  < 13: France (11), India (10), Canada (9), Singapore (11), Poland (10), Israel (8), New Zealand (8).

Rank	Journal	h <sub>MG</sub> -index	Paper count
1	Investigative Ophthalmology and Visual Science	41	117
2	Cornea	39	130
3	American Journal of Ophthalmology	20	55
4	Current Eye Research	20	43
5	British Journal of Ophthalmology	20	38
6	Experimental Eye Research	19	39
7	JAMA Ophthalmology <sup>a</sup>	19	35
8	Ophthalmology	19	30
9	The Ocular Surface	18	70
10	Eye and Contact Lens <sup>b</sup>	18	39

Table 6. Top journals for meibomian gland-related articles, ranked by journal  $h_{MG}$ -index.

\*Journals with  $\leq$ 18 papers and h<sub>MG</sub> < 18: Optometry and Vision Science (12), Contact Lens and Anterior Eye (8).

- a. Includes Archives of Ophthalmology
- b. Includes CLAO Journal



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1. Given Name (First Name) Philip	2. Surname (Last Name) Morgan	3. Date 12-January-2021
4. Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name Jason Nichols
5. Manuscript Title Bibliometric analysis of the meibomia	n gland literature	
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Section 1. Identifying Information		
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4. Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name Jason J Nichols
5. Manuscript Title Bibliometric analysis of the meibomia	n gland literature	
6. Manuscript Identifying Number (if you	know it)	
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any aspect of the submitted work (includin		rom a third party (government, commercial, private foundation, etc.) fo s, data monitoring board, study design, manuscript preparation,
statistical analysis, etc.)? Are there any relevant conflicts of inte	erest? Yes 🖌 N	ю
Section 3. Relevant financia	I activities outside t	ne submitted work.
of compensation) with entities as desc	cribed in the instruction	whether you have financial relationships (regardless of amount s. Use one line for each entity; add as many lines as you need by were <b>present during the 36 months prior to publication</b> .
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Section 1. Identifying Infor	mation					
1. Given Name (First Name) Lyndon	2. Surna Jones	me (Last Name)			3. Date 12-January-2021	
4. Are you the corresponding author?	Yes	✓ No	Correspon Jason Nic	ding Author's I hols	Name	
5. Manuscript Title Bibliometric analysis of the meibomia	n gland lite	rature				
6. Manuscript Identifying Number (if you	know it)					
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Did you or your institution <b>at any time</b> rec any aspect of the submitted work (includir statistical analysis, etc.)?						c.) for
Are there any relevant conflicts of inte	rest?	Yes 🖌 No				
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IMedPharma	$\checkmark$					
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Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
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Nature's Way	$\checkmark$				
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Ophtecs	$\checkmark$	$\checkmark$			
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PS Therapy	$\checkmark$				
Shire	1				
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Dr. Jones reports grants and personal fees from Alcon, grants from Allergan, grants from Contamac, grants and personal fees from CooperVision, grants from GL Chemtech, grants from IMedPharma, grants and personal fees from J&J Vision, grants from Lubris, grants and personal fees from Menicon, grants from Nature's Way, grants from Novartis, grants and personal fees from Ophtecs, grants from Ote, grants from PS Therapy, grants from Shire, grants from Sightglass, personal fees from Santen, outside the submitted work; .

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### 1 RESEARCH CORRESPONDENCE

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- 31
- 32 Short title
- 33 Bibliometric analysis of the meibomian gland literature

There is a rich history of interest in the sebaceous glands located posterior to the tarsal plates in the eyelids, to which we refer today as the meibomian glands (MGs). Although there is acknowledgement of the MGs preceding the work of Johann Heinrich Meibom in the 1600's, he is credited with advancing our knowledge and study of these glands.[1]

39 The MGs produce a distinct lipid secretion ('meibum') made up of a variety of lipid classes. 40 mostly composed of nonpolar wax and cholesterol esters, although other nonpolar and 41 polar lipids are certainly known to exist in the meibum.[2] The normal function of meibum 42 is to make its way to the tear film lipid layer, ultimately forming a resistive barrier to evaporation of the aqueous component of the tear film. In disease, the MGs lose their 43 44 ability to secrete a normal meibum composition and/or are impeded due to factors such 45 as atrophy of the MGs, keratinization of the orifice of the gland from which the meibum is secreted onto the eyelid margin, or bacterial colonization of the eyelid, altering the 46 47 secretion itself once expressed.[3, 4] These conditions today are known as blepharitis. 48 including anterior and posterior blepharitis (which includes meibomian gland 49 dysfunction).[5]

50

51 Given the extensive study of MGs, a bibliometric analysis is warranted to acknowledge 52 and celebrate those contributing to this important part of ophthalmic research.

53

A bibliometric search was undertaken on January 5, 2021 of the titles of papers on the Scopus database. The goals of the search were to identify the most relevant meibomian gland-related documents published in peer-reviewed journals that are primarily meibomian gland driven, rather than to include secondary MG themes in this search; thus, only 'title' identifiers were used to capture this field of research with the highest sensitivity
 and specificity. To identify MG-related articles, the following search terms was used:

TITLE(meibum) OR TITLE(meibomian) OR TITLE(blepharitis) OR
 TITLE(meibomitis) OR TITLE(blepharon-conjunctivitis) OR TITLE(meibography\*)
 AND (LIMIT-TO(SRCTYPE, "j")) AND (LIMIT-TO(LANGUAGE, "English"))

64

The 25 most highly cited papers were determined from the total list of 1,462 papers found. The search term above was also limited to the last 10 years to determine the top contemporary articles in the field of meibomian gland research. A subject-specific meibomian gland-related h-index (h<sub>MG</sub>-index) was derived for authors, institutions, countries and journals to serve as a measure of impact in the field.[6] The top constituents of each category were ranked by h<sub>MG</sub>-index and tabulated for consideration.

71

The  $h_{MG}$ -index of the field was determined to be 85. The 1,462 papers have been cited a total of 32,657 times, and 18.2% of these papers have never been cited. The number of papers in the field published each year between 1849 and 2020 is shown in Figure 1, with a rapid increase evident from 2008.

76

The 25 most highly cited papers are listed in Table 1 of the Supplementary Data. Seven of the top 25 papers are affiliated with the International Workshop on Meibomian Gland Dysfunction conducted under the auspices of the Tear Film and Ocular Surface Society (TFOS), including the paper ranked #1 by first author Erik Knop ("anatomy, physiology, and pathophysiology of the meibomian glands").[7] Outside of this, six cover MG 82 physiology or pathophysiology, six relate to clinically oriented research (meibography,

83 evaporation, clinical outcomes), and five cover grading and classification schemes.

84

There is undoubtedly keen interest in defining and classifying MGD, as noted by the 85 86 number of Top 25 articles devoted to this topic and diagnostic criteria associated with the 87 condition. Further to this, another key theme of the Top 25 articles is that of the study of 88 MG physiology and pathophysiology, particularly as these relate to MG function and 89 meibum secretion. Several papers report on various basic science concepts, while others 90 describe clinical techniques (such as meibography) that are used to assess either MG 91 health and/or the lipid layer of the tear film. Others describe less common but important 92 related assessments such as evaporimetry. Further to this, several of these papers 93 address the apparent overlap between dry eye (aqueous deficiency) and evaporative 94 diseases, such as MGD and blepharitis. It is clear that the TFOS International Workshop 95 on Meibomian Gland Dysfunction has had a substantial impact, in that 7 of the Top 25 96 articles are among the Top 25.

97

Table 2 shows the top 10 contemporary articles related to the study of the meibomian glands. It is clear that the top cited contemporary literature relates to the treatment of meibomian gland dysfunction (5 of 10 articles) and assessment of the meibomian glands and/or lipid layer (4 of 10 articles); the remaining (and top cited) article is focused on the pathophysiology of meibomian gland dysfunction.

103

While citation analyses can be helpful in identifying trends in research, they do have limitations. For instance, older research is more likely to have higher citation counts than more recent research simply due to time, which itself allows for the accumulation of 107 citations. Along these lines, it is clear from the most current research in MGD that, 108 particularly over the very most recent years, therapeutic and diagnostic approaches are 109 key areas of research in MGD. For instance, there is no doubt that innovations in imaging 110 approaches (e.g., optical coherence tomography, meibography, confocal microscopy) are 111 of vital importance to the field of MGD research, particularly through their utility in 112 diagnosis and follow-up, once treatment is initiated. Likewise, new diagnostic imaging 113 approaches that are able to detect MGD absent of symptoms are of significant interest. 114 as recent studies and reviews have suggested that asymptomatic MGD is much more 115 frequent than is traditionally thought.[8-10] Further to this, newer understandings of the 116 biochemical composition of the meibum and tear film lipids as key biomarkers or 117 therapeutic targets are of substantial importance to the field going forward. In particular, 118 the O-acyl-ω-hydroxy fatty acids (OAHFAs) have shown themselves recently to play major 119 functional roles in allowing the tear film to structure itself properly as highly effective 120 surfactants.[9, 11] While lipid emulsions are available for tear supplementation, most 121 contain large, hydrophobic lipids such as mineral or caster oils, not present in human 122 meibum otherwise. The OAHFAs could serve as potential therapeutic supplements along 123 these lines, as they naturally occur in the meibum and tear film. There is much to be 124 considered along these lines for the future of research associated with MGD.

125

Tables 3, 4, 5, and 6 of the Supplementary Data lists the 10 most impactful authors, institutions, countries, and journals publishing meibomian gland-related articles, respectively. This is also summarized in Figure 1.

129

This bibliometric analysis has summarized the most important papers and themes in thefield of the study of the meibomian glands. It is clear that the TFOS International Workshop

132 on Meibomian Gland Dysfunction has had a substantial impact on the field of meibomian 133 gland research. Based on a prior bibliometric analysis of the entire dry eye field, it is clear 134 from the current bibliometric analysis of the MG-related literature that while there is some 135 overlap in content and top-ranked authors, the MG field is distinct in contributions and 136 growing perhaps at an equivalent rate to that of the entire dry eye literature.[12] 137 Notwithstanding the rich history of the study of MGs, current research activities appear to 138 be growing exponentially, so a re-analysis of this area of research in the years to come is 139 certainly warranted.

140

### 141 FINANCIAL DISCLOSURES

142 Jason Nichols: In 2019 and 2020, Dr. Jason J. Nichols has received honoraria from 143 Paragon Vision Sciences and CooperVision. He has also received research funding from 144 Alcon, Bruder, Johnson and Johnson Vision, and Mallinckrodt over the last 3 years. Also, 145 Dr. Kelly Nichols is the spouse of Dr. Jason Nichols, extending her declarations to him. In 146 the past 12 months, Dr. Kelly Nichols has consulted for and received honorarium from: 147 Bruder, Dompe, Kala, Novartis/Shire (Medical Exchange International), Osmotica, Oyster 148 Point, Sight Sciences, Tear Film Innovations/Alcon/Acquiom, Thea, Tarsus, and TopiVert. 149 She has received research funding from: Allergan, Kala, and Tear Science.

150

151 Phillip Morgan: Nothing to declare.

152

Lyndon Jones: Over the past 3 years Dr Jones' research group (CORE) or he personally has received research support or lectureship honoraria from: Alcon, Allergan, CooperVision, GL Chemtec, iMed Pharma, J&J Vision, Lubris, Menicon, Nature's Way, Novartis, Ote, PS Therapy, Safilens, Santen, Shire, SightGlass and Visioneering. Dr Jones is also a consultant and/or serves on an advisory board for Alcon, CooperVision, J&J Vision, Novartis and Ophtecs.

159

160 Nathan Efron: Nothing to declare.

161

### 162 **REFERENCES**

163 [1] Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on 164 meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and

- pathophysiology of the meibomian gland. Invest Ophthalmol Vis Sci. 2011;52:1938-78.
- 166 [2] Chen J, Nichols KK, Wilson L, Barnes S, Nichols JJ. Untargeted lipidomic analysis of
- 167 human tears: A new approach for quantification of O-acyl-omega hydroxy fatty acids. Ocul
- 168 Surf. 2019;17:347-55.
- 169 [3] Jester JV, Parfitt GJ, Brown DJ. Meibomian gland dysfunction: hyperkeratinization or
- atrophy? BMC Ophthalmol. 2015;15 Suppl 1:156.

- 171 [4] Suzuki T, Sutani T, Nakai H, Shirahige K, Kinoshita S. The Microbiome of the Meibum
- and Ocular Surface in Healthy Subjects. Invest Ophthalmol Vis Sci. 2020;61:18.
- 173 [5] Daniel Nelson J, Shimazaki J, Benitez-del-Castillo JM, Craig J, McCulley JP, Den S,
- 174 et al. The international workshop on meibomian gland dysfunction: Report of the definition
- and classification subcommittee. Invest Ophthalmol Vis Sci. 2011;52:1930-7.
- 176 [6] Hirsch JE. An index to quantify an individual's scientific research output. Proc Natl
- 177 Acad Sci U S A. 2005;102:16569-72.
- 178 [7] Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on
- 179 meibomian gland dysfunction: Report of the subcommittee on anatomy, physiology, and
- pathophysiology of the meibomian gland. Invest Ophthalmol Vis Sci. 2011;52:1938-78.
- 181 [8] Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. TFOS DEWS
- 182 II Epidemiology Report. Ocul Surf. 2017;15:334-65.
- 183 [9] Bland HC, Moilanen JA, Ekholm FS, Paananen RO. Investigating the Role of Specific
- 184 Tear Film Lipids Connected to Dry Eye Syndrome: A Study on O-Acyl-ω-hydroxy Fatty
- 185 Acids and Diesters. Langmuir. 2019;35:3545-52.
- 186 [10] Miyamoto M, Sassa T, Sawai M, Kihara A, Radhakrishnan A. Lipid polarity gradient
- 187 formed by  $\omega$  hydroxy lipids in tear film prevents dry eye disease. eLife. 2020;9.
- 188 [11] Schuett BS, Millar TJ. An investigation of the likely role of (O-acyl) ω-hydroxy fatty
- acids in meibomian lipid films using (O-oleyl)  $\omega$ -hydroxy palmitic acid as a model.
- 190 Experimental Eye Research. 2013;115:57-64.
- 191 [12] Nichols JJ. Citation analysis of the dry eye literature. Ocul Surf. 2013;11:35-46.

192

## 193 Figure Caption

194	Figure 1.	Number of publications and summary information in the field of meibomian
195		gland research published each year between 1849 and 2020. For brevity,
196		the Figure is truncated to works occurring on or after 1900.