

Alzheimer's Disease Research: Scientific Productivity and Impact of the Top 100 Investigators in the Field

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Abstract. The online availability of scientific-literature databases and natural-language-processing (NLP) algorithms has enabled large-scale bibliometric studies within the field of scientometrics. Using NLP techniques and Thomson ISI reports, an initial analysis of the role of Alzheimer's disease (AD) within the neurosciences as well as a summary of the various research foci within the AD scientific community are presented. Citation analyses and productivity filters are applied to post-1984, AD-specific subsets of the PubMed and Thomson ISI Web-of-Science literature bases to algorithmically identify a pool of the top AD researchers. From the initial pool of AD investigators, top-100 rankings are compiled to assess productivity and impact. One of the impact and productivity metrics employed is an AD-specific H-index. Within the AD-specific H-index ranking, there are many cases of multiple AD investigators with similar or identical H-indices. In order to facilitate differentiation among investigators with equal or near-equal H indices, two derivatives of the H-index are proposed: the Second-Tier H-index and the Scientific Following H-index. Winners of two prestigious AD-research awards are highlighted, membership to the Institute of Medicine of the US National Academy of Sciences is acknowledged, and an analysis of highly-productive, high-impact, AD-research collaborations is presented.

Keywords: Alzheimer's disease, amyloid- β , amyloid- β protein precursor, citation, citation analysis, H-index, highly-cited, history of science, neurodegenerative diseases, oxidative stress, Scientific following H, scientometrics, Second-tier H-index, tau

INTRODUCTION

The field of Alzheimer's disease (AD) research, which in 2006 marked its centennial, has progressed at a rapid rate since the late 1970s [1]. Considering the broader field of neuroscience [2], of the estimated 135,000 actively publishing scientists worldwide, roughly 18% (or 25,000), have published one or more papers on AD. This ratio of AD scientists to all neuroscientists remains constant at 19% when assessing the 100 most-cited neuroscientists during the period 1997–2007 [3]. In spite of the increasing share of neuroscience activity focusing on AD, there has not been

a comprehensive, objective analysis of AD research through scientometrics [4].

METHODS

The following three dimensions were selected as a basis to measure the work in AD by individual investigators: total citations, total publications, and H-index [5,6]. The underlying data used in the tabulation of each dimension originate from MEDLINE and Thomson ISI Web of Science.

Two selection filters were used in determining which papers would contribute to an individual scientist's metrics. The first filter was a requirement that all papers to be included in the analysis mention AD at least once in the Title, Abstract, or Key-Words sections. The second filter is temporal: only papers published between 1

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January 1985 and 21 April 2008 were considered. It is important to recognize the effects of the temporal filter as researchers who made fundamental contributions to the field prior to 1985 but have since slowed in the areas of impact and productivity will be underrepresented in this study due to the 1985 limitation. George Glenner, with his 1984 amyloid-beta-protein discovery, is a case in point. Also of importance is the AD-specific filter, as some prominent AD scientists have strong interests in other areas. Their impact and productivity in non-AD fields will not be recognized in this analysis. Mark Mattson of the National Institute on Aging (with a dual appointment at Johns Hopkins University) is a prime example of this phenomenon.

While the underlying paper-level data were provided by MEDLINE and ISI, the Author-specific tabulations of number of papers, total citations, and H-index were achieved by querying the Collexis-Thomson Alzheimer Dashboard [7]. This tool facilitates author-level bibliometric analysis within a given scientific area [8]. Full names for the AD researchers in this study were derived from the publically-available BiomedExperts repository, which allows the accurate extraction of full names (i.e., last name, first name, middle initial) through author-disambiguation algorithms [9]. While powerful, it was clear during the analysis that the automated, author-disambiguation routines used in assigning papers to the individual scientists are not perfect. The metrics, therefore, represent a good approximation of impact and productivity rather than an exact measurement. The productivity and impact of some scientists, due to variations in the spelling of their last names, are unavoidably underrepresented.

BiomedExperts.com was also utilized in determining each scientist's main line of investigation. The top five MeSH terms from each scientist's research profile in BiomedExperts were considered. The highest-ranked MeSH term within the top five for a given scientist that could be considered an AD line-of-investigation was chosen as the main line of investigation for the researcher in question. It is important to note that the papers used to generate the top five MeSH terms for each scientist were not restricted to those papers mentioning AD, but were taken from a collection of PubMed papers representative of an investigator's entire corpus of published work. It follows, then, that the line of investigations chosen for each researcher is not necessarily the line of investigation most frequently found within that scientist's AD papers. The MeSH term chosen is, however, one that the scientist has applied to their AD research and, more importantly, is the line of

investigation most representative of the entire research portfolio of the scientist in question. This approach to line-of-investigation identification has as its goal the assignment of a single MeSH term that describes what a given scientist "brings to bear" within the world of AD research without attempting to compare competing MeSH-term frequencies within an investigator's AD-specific paper corpus.

As part of the H-index analysis, two new metrics are proposed. The Scientific Following H (sfH) is exactly the same as the traditional H index except for the fact that the numbers generated are at the author, as opposed to the paper, level. In other words, a scientist has an sfH of 7 if there are at least 7 investigators who have cited that scientist's work at least seven times (considering all papers of the scientist for whom the SFH is being calculated as well as all papers of the all investigators who have ever cited any paper of the scientist in question). The sheer number of papers needed to calculate the sfH means that it cannot be tallied by hand, but requires a powerful author-disambiguation algorithm working on a comprehensive citation database. The high-level numbers used to calculate the sfH were generated by a Collexis author-disambiguation algorithm running on top of the raw, ISI Web-of-Science citation data from 1 January 1985 to 1 May 2008. The Second-Tier H-index (SeTH) is defined as the recalculation of an author's H-index after removing the papers belonging to the author's H-Core [10]. SeTH can be viewed as the author's H-Core pipeline and may be used to predict the rate of increase of an author's H-Index rank within the AD community in the near term.

As a measure of the acceptance of a given researcher within the AD scientific community, the winners of the MetLife Alzheimer Award for Medical Research [11] and the Potamkin Prize for Research in Pick's, Alzheimer's, and Related Diseases [12] are acknowledged. Membership to the Institute of Medicine of the US National Academy of Sciences is also noted.

Finally, a co-author analysis of the collaboration patterns of the 25 top-ranked scientists (in terms of H-index) was conducted on the MDLogix Visualizer [13] platform using co-author relationships extracted from Thomson WoS and biomedexperts.com

RESULTS

A brief analysis of the field of AD research was conducted with the underlying goal of understanding its importance first within the field of neurodegenerative diseases and subsequently within the greater realm of neuroscience research.

The role of AD within the fields of neurodegenerative diseases and neuroscience

In order to get a rough idea of the place that AD research holds within neurodegenerative investigation, the Collexis clustering algorithms that are part of the Mediator knowledge discovery platform [14] were utilized to create a semantic grouping of all disease-and-pathologic-process-related MeSH terms that have appeared within PubMed papers on neurodegenerative diseases from 1996 to the present. In order to keep the cluster to a reasonable size, an arbitrary threshold of the top 30 terms was set. The ranking of the terms within the neurodegenerative cluster was based on number of PubMed papers containing the term in question. The top five terms in the cluster are, in descending order of number of PubMed papers, Cerebrovascular Accident, Alzheimer Disease, Dementia, Parkinson Disease, and Atrophy.

A similar process was undertaken to identify the top MeSH concepts within the AD literature. The semantic analysis of the AD-specific literature was conducted using the Thomson-Collexis AD Dashboard. Table 1 contains the top 30 MeSH terms (along with paper counts) for the AD literature base (within PubMed/WoS since 1985). Some of these, such as “mice” and “pathology,” are throw-away terms that do not reveal much about the directions of mainstream AD research. Other terms, such as “Amyloid β -Protein Precursor,” “Risk Factors,” and “Phosphorylation,” give some indication of the prevalence of various lines of investigation within the AD research community.

AD is the second most mentioned MeSH term within the neurodegenerative literature. Of note is the fact that the MeSH categories are not mutually exclusive. Many papers on neurodegeneration will contain a number of the above concepts. For instance it is not uncommon for a paper on AD to mention atrophy and dementia.

Moving beyond the neurodegenerative diseases to neuroscience as a whole, the Thomson ISI Neuroscience Journal Citation Report was used to define which journals (and subsequently which papers and, by extension, which authors) should be included in a bibliometric overview of the field. The list of neuroscience journals is updated by Thomson ISI every year. The most recent version (2007) lists 211 journals as falling squarely within the realm of neuroscience.

Thomson ISI Web of Science (WoS) was queried for the number papers published by all 211 journals for the year 2007. The query returned 40,801 papers. A technical clarification is that a Thomson query restricts the

Table 1
Shows, in descending order, the top 30 terms (and paper counts) for MESH terms in the AD literature

Dementia	17,836
Amyloid	12,188
Rats	7,715
Mice	7,694
Genes	7,307
Risk	5,675
Amyloid β -Protein Precursor	5,550
Aging	5,483
Pathology	5,340
Parkinson Disease	4,464
Genetics	4,231
Apolipoproteins E	4,020
Mutation	3,831
Risk Factors	3,416
Antibodies	3,190
Alleles	3,128
Oxidative Stress	2,921
Death	2,900
Cell Death	2,675
Apoptosis	2,388
Screening	2,369
Phosphorylation	2,338
Mice, Transgenic	2,274
Dementia, Vascular	2,239
tau Proteins	2,211
Cerebrovascular Accident	2,148
Atrophy	2,145
Amyloid β -Protein	2,116
Protein Isoforms	2,093
Syndrome	2,033

end user to a maximum of 50 Boolean terms per query resulting in a total of five queries (i.e., 50 journals per query) needed to calculate the total output of the neuroscience journals for 2007. Using Thomson’s advanced analysis feature, for each resulting query, an estimate of the number of unique authors who collaborated on the papers in question was generated. The Thomson estimate for the total number of authors collaborating on the 40,801 papers appearing in the 211 journals in 2007 was 135,649. This number will be inflated by the double-counting of authors as the 50-boolean-term restriction limits the effectiveness of the Thomson author-disambiguation algorithms in tabulating author counts. The inflation in the author count is likely offset by the fact that the list of 211 journals cannot be considered comprehensive. The list does not, for instance, include journals such as The Lancet or The New England Journal of Medicine, which, while not considered to be neuroscience journals *per se*, surely publish many articles each year by neuroscientists. Another factor that offsets the inflation inherent in the Thomson-based estimate is the fact that in any given year, there may be active neuroscientists who did not publish a single pa-

Table 2

Most Prolific AD Investigators from 1 January 1985 through 21 April 2008 using a combined (minus duplicate papers) PubMed and WoS AD paper count (institutional affiliation and ALZForum ID indicated)

Rank	Author	Institutional affiliation	ALZForum profile ID (to view profile, append ID to following base URL: http://www.alzforum.org/com/res/detail.asp?id=	PubMed + Thomson WoS papers on AD (1985–2008)
1	Winblad, Bengt	Karolinska Institute	{E43DF156-ED34-4D58-BF6C-0877090A0298}	575
2	Perry, George	University of Texas at San Antonio	{AF7F6C7C-A7F3-4E6D-96BB-6BF5FA53F1AE}	516
3	Smith, Mark A	Case Western Reserve University	{EB2B9380-C464-4652-A816-1511461825B9}	405
4	Morris, John C	Washington University	{99215FD7-EE99-46AA-BA1E-E268A3519A30}	384
5	Masters, Colin L	University of Melbourne		381
6	Cummings, Jeffrey L	University of California, Los Angeles	{8C11591E-4E55-4AE5-94FC-1B971473592F}	366
7	Hyman, Bradley T	Harvard University	{84BB57D7-3CF3-4171-ABD5-52EDDC50D0F5}	365
8	Beyreuther, Konrad	University of Heidelberg		355
9	Hardy, John	Institute of Neurology, University College London	{609139A5-33DA-47C0-80A8-39008CC32589}	351
10	Lee, Virginia M-Y	University of Pennsylvania	{40D45C85-D2AB-4CE4-9B0A-43987940E6F8}	337
10	Trojanowski, John Q	University of Pennsylvania	{A64BEA2F-3B60-44E8-8234-1D04B74A86B8}	337
12	Masliah, Eliezer	University of California, San Diego		324
13	Blennow, Kaj	University of Göteborg	{0CF2EA98-1EAB-49B3-9EC7-3F3C06A761DB}	322
14	Soininen, Hilikka	University of Kuopio	{B4939E15-F8FD-4F2B-AB64-DD997AD4D1A0}	312
15	Selkoe, Dennis J	Harvard University	{6380DD6F-FE33-486A-849D-7A0C29F9D11F}	310
15	Stern, Yaakov	Columbia University		310
17	Thal, Leon J	University of California, San Diego	{4E295BE2-A736-4C92-B3F1-C2EDD637C81D}	307
18	Dickson, Dennis	Mayo Clinic – Florida		296
18	Mayeux, Richard	Columbia University	{95988961-9E7A-4FAA-9175-67FF33CAD981}	296
20	Scheltens, Philip	Vrije Universiteit Amsterdam		295
21	DeKosky, Steven T	University of Virginia	{E5C66A9A-A258-415C-8BC5-0296A5C8519C}	291
22	Mattson, Mark P	National Institutes on Aging/John Hopkins University	{26C09C83-AE3A-44CB-B141-499C7B06C7F9}	287
23	Iqbal, Khalid	New York State Institute of Basic Research	{7A550DCA-F8C5-4F69-BB7D-F4D8A2FDE1C8}	273
23	Markesbery, William R	University of Kentucky		273
25	Petersen, Ronald C	Mayo Clinic – Minnesota	{5B456F01-5380-4FA7-80D4-1CFF6DEBE61B}	269
26	Miller, Bruce L	University of California, San Francisco		259
27	Cotman, Carl W	University of California, Irvine	{961C9734-8A09-42EB-B6E8-D53B8E57F0D4}	256
28	Bennett, David A	Rush University Medical Center	{C7893C4E-7F1E-466D-AFD2-468F845193CE}	253
29	Rossor, Martin N	Institute of Neurology, London		252
30	Roses, Allen D	Duke University		248
30	Tanzi, Rudolph E	Harvard University	{BE74EFC0-7CCD-4285-ADA0-98744E847CB1}	248

Table 2, continued

Rank	Author	Institutional affiliation	ALZForum profile ID (to view profile, append ID to following base URL: http://www.alzforum.org/com/res/detail.asp?id=	PubMed + Thomson WoS papers on AD (1985–2008)
32	Perry, Robert H	University of Newcastle		244
32	St George-Hyslop, Peter	University of Toronto		244
34	Cairns, Nigel J	Washington University	{197D5DED-35D9-43C2-8F10-F1833C6729B0}	239
35	Jellinger, Kurt A	University of Vienna	{ECAC7439-DC8C-436D-AB6D-28142DEAB970}	237
36	Gauthier, Serge	McGill University		234
37	Mann, David M A	University of Manchester	{4E8997D2-7CD4-423F-8BE5-561501ACC706}	233
38	Arai, Heii	Juntendo University		231
39	Butterfield, D Allan	University of Kentucky	{26A78291-1528-4C14-B010-BF1C13AFD864}	230
40	McGeer, Patrick L	University of British Columbia	{72AE9E7E-AAD5-4D44-9F32-C853AB0376F6}	227
41	Wisniewski, Henryk M	NY State Institute of Basic Research	{1991F36B-97A4-48B2-B894-3518017523F0}	226
42	Hodges, John R	University of Cambridge		221
43	McKeith, Ian G	Newcastle University		218
43	Rapoport, Stanley I	National Institute on Aging		218
45	Frangione, Blas	New York University	{8ED69192-D1E1-4E51-92CA-E95BF09A5B0B}	215
46	Riekkinen, PJ	University of Kuopio		213
46	Weiner, Michael W	University of California, San Francisco	{74BDBD98-E4D8-42AF-9F21-5B3E36BC7672}	213
48	Hampel, Harald	University of Dublin	{A3072FDB-0B98-4AAA-8B52-BD4CC7D24487}	210
48	Zhu, Xiongwei	Case Western Reserve University	{509699B4-2A3F-494D-8920-D4CBB55D8781}	210
50	Kurz, Alexander	University of Munich		209
51	Lannfelt, Lars	Uppsala University	{5C19D4CD-FA3F-4CCA-AF88-2F3700E848C0}	208
52	Delacourte, André	Inserm	{DC4117FC-DD3E-49DF-9A82-AC19E1C0A75D}	207
52	Nordberg, Agneta	Karolinska Institute	{180B457E-96CF-4F7E-A764-E46EFE91A5BA}	207
54	Albert, Marilyn S	John Hopkins University	{670FF754-CEB5-4B65-910F-10F3987AE0F2}	203
55	Farlow, Martin R	Indiana University		202
56	Pericak-Vance, Margaret A	University of Miami		201
57	Hofman, Albert	Erasmus MC, Rotterdam		200
57	Wilson, Robert S	Rush Medical Center		200
59	Iwatsubo, Takeshi	University of Tokyo	{FB389991-D859-4E72-8CBA-111EEDEE7152}	199
60	Swaab, Dick F	University of Amsterdam		194
61	Salmon, David P	University of California, San Diego		193
62	Price, Donald L	John Hopkins University	{EA5E79C9-2531-481F-A2B9-C390BFBEE188}	190
63	Ballard, Clive	King's College London		187
63	Haass, Christian	Ludwig-Maximilians-University München	{32B49F40-2A4B-4D08-8097-E48A52277D68}	187
63	Perry, Elaine K	Newcastle University		187
63	Small, Gary W	University of California, Los Angeles		187
67	Larson, Eric B	University of Washington		186

Table 2, continued

Rank	Author	Institutional affiliation	ALZForum profile ID (to view profile, append ID to following base URL: http://www.alzforum.org/com/res/detail.asp?id=	PubMed + Thomson WoS papers on AD (1985–2008)
67	Saunders, Ann M	GlaxoSmithKline		186
69	Whitehouse, Peter J	Case Western Reserve University		185
69	Wilcock, Gordon K	University of Bristol	{FDEA1208-6FAB-4F04-B5C0-EC23770AB48E}	185
71	Growdon, John H	Harvard University		183
71	O'Brien, John T	Newcastle University		183
71	Sorbi, Sandro	University of Florence	{F5712128-4E65-4730-B87A-455670822025}	183
74	Ikeda, Kenji	Tokyo Institute of Psychiatry		182
74	Riederer, Peter	Universität Würzburg		182
76	Davies, Peter	Albert Einstein College of Medicine	{DCB4F0CB-E49B-4CA8-AA8D-52B7ABECAFA6A}	180
76	Vellas, Bruno	Inserm, Toulouse		180
78	Knopman, David S	Mayo Clinic – Minnesota		178
78	Sunderland, Trey	National Institute on Aging		178
80	Davis, Kenneth L	Mt. Sinai		172
80	Hansen, Lawrence A	University of California, San Diego		172
82	Goate, Alison M	Washington University	{12EDC4D8-4B4B-4070-BCFD-682C40E46C8E}	171
82	Younkin, Steven G	Mayo Clinic – Florida		171
84	Galasko, Douglas	University of California, San Diego	{7BE13DDE-7F10-4209-977C-F3DDB26D24E4}	170
84	Goedert, Michel	University of Cambridge		170
86	Lovestone, Simon	King's College London		169
87	Avila, Jesús	Universidad Autónoma de Madrid	{22E78B64-C398-4396-8FFE-7FD1D13C59B2}	167
87	Haines, Jonathan L	Vanderbilt University		167
89	Braak, Heiko	Johann Wolfgang Goethe-Universität		166
89	Schellenberg, Gerard D	University of Washington	{ADFAA4F6-4CFE-4B0E-B226-254B305438FD}	166
91	Fox, Nick C	Imperial College London	{BB6AD238-6411-4932-B7E9-B8B32B8867F2}	164
91	Hutton, Michael	Mayo Clinic – Florida		164
93	Mohs, Richard C	Eli Lilly	{6CF5D84E-78BA-46E8-BA98-B2F4FEC7A81B}	163
94	Jagust, William J	University of California, Berkeley		162
95	Hof, Patrick R	Mt. Sinai		161
95	Mufson, Elliott J	Rush University	{7F9B1AF5-9253-4214-94A7-ABA2BF687B67}	161
95	Schneider, Lon S	University of Southern California	{E6787F54-6A48-4124-8151-93EE69EF470F}	161
98	Grossman, Murray	University of Pennsylvania		160
99	Nitsch, Roger M	University of Zurich	{8E530CE7-874F-4166-97E6-464130F3831D}	158
99	Wallin, Anders	University Göteborg		158

per. An example of this phenomenon would be neuroscientists working within a pharmaceutical or biotech company that has placed a publication embargo on their current research. Considering the possible inflation due the double counting of authors but the counteracting nature of the underestimation of total papers and the inability to account for non-publishing neuroscientists in any given year, an estimate of 135,000 active neu-

roscentists worldwide is likely a fair estimate of the true number. Knowing the approximate total number of neuroscience papers and authors provides an opportunity to calculate the contribution that AD makes to the field. Considering that the number of WoS papers published in 2007 that mentioned AD is 7,002 (note: the fact that, when put together, the year and quantity of AD papers combine to form a numeric palindrome

Table 3

Most-Cited authors from 1 January 1985 through 21 April 2008 based on citation rates for AD papers appearing in Thomson ISI WoS (the main line of investigation from BiomedExperts for each scientist is also indicated)

Rank	Author	Main line of investigation	Times cited in Alzheimer's work since 1985
1	Selkoe, Dennis J	Amyloid β -Protein	40,100
2	Beyreuther, Konrad	Amyloid β -Protein Precursor	25,231
3	Roses, Allen D	Apolipoproteins E	24,500
4	Mattson, Mark P	Calcium	23,704
5	Hardy, John	tau Proteins	23,046
6	Masters, Colin L	Amyloid β -Protein Precursor	22,768
7	Pericak-Vance, Margaret A	Pedigree (genealogy)	21,638
8	Lee, Virginia M-Y	tau Proteins	21,341
9	Tanzi, Rudolph E	Amyloid β -Protein	21,144
10	Trojanowski, John Q	tau Proteins	20,190
11	Morris, John C	Neuropsychological Tests	19,938
12	Hyman, Bradley T	Amyloid β -Protein	18,864
13	Masliah, Eliezer	Nerve Tissue Proteins	18,636
14	Saunders, Ann M	Apolipoproteins E	17,098
15	Cummings, Jeffrey L	Neuropsychological Tests	16,498
16	Perry, George	Oxidative Stress	16,293
17	Cotman, Carl W	Amyloid β -Protein	16,198
18	Dickson, Dennis	tau Proteins	15,995
19	Goedert, Michel	tau Proteins	15,974
20	Lieberburg, I	Amyloid β -Protein	15,863
21	Winblad, Bengt	Neuropsychological Tests	15,157
22	Younkin, Steven G	Amyloid β -Protein	15,028
23	McGeer, Patrick L	Choline O-Acetyltransferase	14,108
24	Smith, Mark A	Oxidative Stress	13,772
25	Price, Donald L	Amyloid β -Protein Precursor	13,735
26	Petersen, Ronald C	Neuropsychological Tests	13,588
87	St George-Hyslop, Peter	Presenilin-1	13,271
28	Strittmatter, Warren J	Apolipoproteins E	13,180
29	Thal, Leon J	Choline O-Acetyltransferase	13,159
30	Mayeux, Richard	Apolipoproteins E	13,081
31	Schmechel, Donald E	Apolipoproteins E	12,900
32	Rogers, Jack T	Amyloid β -Protein Precursor	12,805
33	Multhaup, Gerd	Amyloid β -Protein Precursor	12,761
34	Haass, Christian	Amyloid Precursor Protein Secretases	12,758
35	Markesbery, William R	Neurofibrillary Tangles	12,687
36	Schenk, Dale	Amyloid β -Protein	12,429
37	Frangione, Blas	Amyloid	12,299
38	Hofman, Albert	Risk Factors	12,279
39	Haines, Jonathan L	Chromosome Mapping	12,202
40	Sisodia, Sangram S	Amyloid β -Protein Precursor	12,037
41	Hansen, Lawrence A	Lewy Bodies	11,900
42	Perry, Robert H	Lewy Bodies	11,753
43	Fraser, Paul E	Presenilin-1	11,731
44	Myers, Richard H	Risk Factors	11,257
45	Miller, Bruce L	Neuropsychological Tests	11,172
46	Stern, Yaakov	Neuropsychological Tests	11,161
47	Rossor, Martin N	Magnetic Resonance Imaging	10,978
48	Goate, Alison M	Presenilin-1	10,974
49	Growdon, John H	Choline	10,962
50	Beal, M Flint	Disease Models, Animal	10,616
51	Seubert, Peter	Amyloid β -Protein	10,524
52	Wilson, Robert S	Neuropsychological Tests	10,452
53	Mohs, Richard C	Neuropsychological Tests	10,131
54	Mann, David M A	Neurofibrils	10,126
55	Albert, Marilyn S	Neuropsychological Tests	10,081
56	Lansbury, Peter T	Amyloid	10,040
57	Minoshima, Satoshi	Tomography, Emission-Computed	9,983

Table 3, continued

Rank	Author	Main line of investigation	Times cited in Alzheimer's work since 1985
58	Salmon, David P	Neuropsychological Tests	9,966
59	Koo, Edward H	Amyloid β -Protein Precursor	9,744
60	Hutton, Michael	tau Proteins	9,686
61	Iqbal Khalid	tau Proteins	9,530
62	Schellenberg, Gerard D	Apolipoproteins E	9,496
63	Davies, Peter	Tau Proteins	9,493
64	Hodges, John R	Neuropsychological Tests	9,380
65	Bird, Thomas D	Pedigree (genealogy)	9,377
66	Butterfield, D Allan	Oxidative Stress	9,319
67	Braak, Heiko	Neurofibrillary Tangles	9,277
68	McKeith, Ian G	Lewy Bodies	9,208
69	Eckman, Christopher B	Amyloid β -Protein	9,116
70	Perry, Elaine K	Receptors, Nicotinic	9,032
71	Iwatsubo, Takeshi	Amyloid β -Protein	8,901
72	Farlow, Martin R	Cholinesterase Inhibitors	8,841
73	DeKosky, Steven T	Neuropsychological Tests	8,776
74	Ihara, Yasuo	tau Proteins	8,768
75	Kokmen, Emre	Risk Factors	8,761
76	Bennett, David A	Neuropsychological Tests	8,734
77	Citron, Martin	Amyloid Precursor Protein Secretases	8,702
78	Jellinger, Kurt A	Autopsy	8,674
79	Small, Gary W	Apolipoproteins E	8,663
80	Wisniewski, Henryk M	Neurofibrils	8,605
81	Breteler, Monique M B	Risk Factors	8,559
82	Lannfelt, Lars	Amyloid β -Protein Precursor	8,518
83	McGeer, Edith G	Choline O-Acetyltransferase	8,497
84	Teplow, David B	Amyloid β -Protein	8,284
85	Galasko, Douglas	Neuropsychological Tests	8,259
86	Bush, Ashley I	Amyloid β -Protein	8,244
87	Gusella, James F	Chromosome Mapping	8,133
88	Mandelkow, Eckhard	tau Proteins	8,106
88	Mandelkow, Eva-Maria	tau Proteins	8,106
90	Mirra, Suzanne S	Apolipoproteins E	8,015
91	Soininen, Hilkka	Apolipoproteins E	8,004
92	Gilbert, John R	Polymorphism, Single Nucleotide	7,916
93	Braak, Eva	Neurofibrillary Tangles	7,905
94	Kramer, Joel H	Neuropsychological Tests	7,882
95	Mullan, Michael	Amyloid β -Protein	7,835
96	Gandy, Samuel E	Amyloid β -Protein Precursor	7,767
97	Golde, Todd E	Amyloid β -Protein	7,729
98	Katzman, Robert	Apolipoproteins E	7,567
99	Davis, Kenneth L	Physostigmine	7,545
100	Gauthier, Serge	Cholinesterase Inhibitors	7,526

does not represent a typographical error) and that the Thomson estimate for actively-publishing AD authors is 24,768, we can conclude that overall, AD papers represent approximately 17% of the neuroscience literature and 18% of neuroscientists.

One way to check the validity of this estimate is to test whether or not the percentages remain true when checked against Thomson's list of the 100 most highly cited neuroscientists for the period 1997–2007 [3]. Each name on the most-highly-cited neuroscientist list was checked against each of the three AD top-100 lists compiled for this study (i.e., most prolific, most-cited, and highest H-index). If an author on the neuroscience

list also appeared on any of the three AD lists, they were given an AD designation. This exercise resulted in the categorization of 19 of the 100 most-cited neuroscientists as being AD researchers. This number confirms the previous approximation that AD investigators make up approximately 18% of the neuroscience research community.

Productivity and impact among AD investigators – the three metrics

Having established the role AD plays within the area of neurodegenerative and nervous-system diseases, the

focus of the analysis was turned to understanding the field of AD research from a scientometric viewpoint with the ultimate objective being that of determining which AD investigators have contributed the most to the field since 1985. A pool of the top 150 AD researchers was generated by consulting biomedexperts.com (a PubMed-based data source) and the Collexis-Thomson WoS Dashboard on AD. Included in the master list of 150 were the most prolific AD authors (based on PubMed and WoS AD paper counts) as well as the most highly-cited authors using WoS AD citation counts. H-indices, total paper counts, and total citations were calculated for all authors. For each category, a top-100 list was generated.

Tables 2, 3, and 5 are the top-100 lists for each category.

Lines of investigation at the summit of the AD scientific community

Below are the numbers of investigators (of the 150 evaluated) who focus on the various lines of investigation (as listed in Table 3). Although it is clear that certain interrelated lines of investigation might be best combined to form single line of investigation (e.g., Amyloid- β Protein, Amyloid β -Protein Precursor, and Amyloid Protein Precursor Secretases), it was determined that the defining of such composite, line-of-investigation categories was beyond the scope of the current study and could lead to bias.

Further refining impact measures – scientific-following H

While the H-index tracks impact by analyzing the body of published work of given investigator, it does not give a clear indication of the thought-leadership position that a given scientist holds within the core community of investigators comprising the research community for a focused field. In other words, the H-index provides an understanding for the overall impact of an investigator but not how concentrated or dispersed that impact is among that investigator's closest scientific peers. In order to assess the scientific following of a given investigator, the scientific-following H-index (sfH) is proposed. The sfH is calculated in the same way as person's standard H-index, the only difference being that instead of counting the number of papers that have been cited a given number of times, one counts the number of scientists who, in all of their work, have cited a particular investigator in all of that investiga-

Table 4
AD lines of investigation among pool of top 150 researchers

Neuropsychological tests	22
Tau Proteins	20
Amyloid β -Protein	16
Apolipoproteins E	12
Amyloid β -Protein Precursor	9
Magnetic Resonance Imaging	8
Risk Factors	6
Neurofibrillary Tangles	5
Choline O-Acetyltransferase	4
Oxidative Stress	4
Cholinesterase Inhibitors	3
Lewy Bodies	3
Pedigree (genealogy)	3
Presenilin-1	3
Amyloid	2
Amyloid Precursor Protein Secretases	2
Chromosome Mapping	2
Nerve Tissue Proteins	2
Neurofibrils	2
Receptors, Nicotinic	2
Age of Onset	1
Autopsy	1
Calcium	1
Choline	1
Disease Models, Animal	1
Electroencephalography	1
Estradiol	1
Immunohistochemistry	1
Longitudinal Studies	1
Monoamine Oxidase	1
Nootropic Agents	1
Nutrition Assessment	1
Phosphoproteins	1
Physostigmine	1
Polymorphism, Single Nucleotide	1
Positron-Emission Tomography	1
Scopolamine	1
Tacrine	1
Tomography, Emission-Computed	1
Vasopressins	1

tor's work. In other words, one must simply substitute people, as represented by all of their work, for papers in the H-index calculation. Considering the case of a scientist with an sfH of 5, one would know that there are five investigators (other than scientist under analysis) who have cited (considering all of their papers) that scientist's work (considering all of the scientist's papers) at least five times. Just as the H-index provides lower bounds on the quantity and quality of the entire body of a given scientist's highest impact work, so the sfH provides lower bounds on the quantity and quality of the scientific following, within an investigator's immediate research community, that a given investigator has achieved. For two or more scientists with similar impact measures (i.e., H-index, total citations, or average citation per paper), the sfH will facilitate an un-

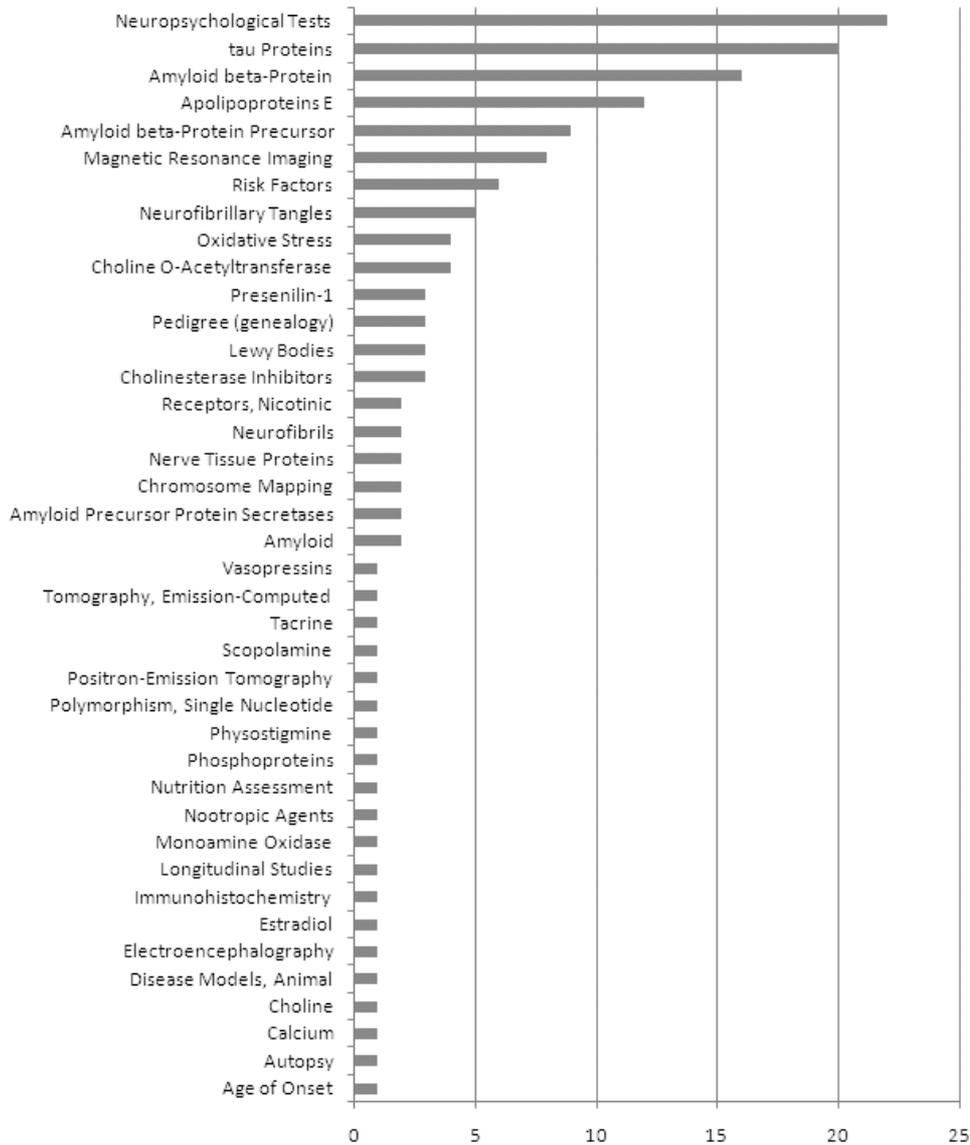


Fig. 1. Distribution of line-of-investigation (based on top MeSH terms in biomedexperts.com) among the top-150 AD researchers.

understanding of which of them has had the biggest role in school-of-thought leadership. Holding total impact constant, a scientist with a low sfH will have that level of impact spread out across a relatively large number of investigators who may or may not have the same research focus. Again holding total impact constant, a scientist with a high sfH, however, has their impact concentrated in a relatively small number of investigators who typically work in the same area of investigation. In this way, school-of-thought leadership can be inferred through analysis of sfH levels among in-

vestigators contributing to the same research area (see Table 5 for sfH scores for the top-100 H-indices).

Thinking about the future – the second-tier H-index

Hirsch has presented compelling arguments that the H-index is an excellent predictor of future impact and productivity [6]. The H-index is of little help, however, in predicting future movement of individuals up and down a ranking in which many of the scientists have identical or nearly-identical Alzheimer H-indices. An

Table 5
 Authors with Highest H-indices calculated from same document base as used for the total-citation tabulations in Tables 2 and 3

Rank	Author * = Winner of MetLife Award ^ = Winner of Potomkin Prize + = Institute of Medicine member	H-index	Second-tier H-index	H rank – SeTH rank	Scientific following H-index
1	Selkoe, Dennis J * ^ +	102	53	0	29
2	Mattson, Mark P	86	48	0	23
3	Lee, Virginia M-Y * ^ +	82	47	0	24
4	Trojanowski, John Q * ^ +	74	45	0	27
5	Beyreuther, Konrad * ^	72	44	0	24
5	Hyman, Bradley T ^	72	42	-2	25
7	Masliah, Eliezer	71	40	-2	20
8	Morris, John C ^	70	40	-1	27
9	Goedert, Michel * ^	67	29	-23	17
10	Perry, George	66	42	3	24
10	Tanzi, Rudolph E * ^	66	35	-6	23
12	Masters, Colin L ^	65	43	6	24
12	Hardy, John * ^	65	37	-2	37
12	Dickson, Dennis *	65	32	-8	24
12	Mayeux, Richard ^ +	65	31	-15	23
16	Winblad, Bengt	64	40	7	21
16	Cummings, Jeffrey L	64	34	-2	13
18	Cotman, Carl W *	63	38	6	13
19	McGeer, Patrick L	62	35	3	12
20	Price, Donald L * ^ +	61	30	-10	22
21	Frangione, Blas * ^	60	37	7	15
22	Smith, Mark A	59	34	4	26
23	Haass, Christian ^	58	32	3	22
23	Stern, Yaakov	58	32	3	22
23	Markesbery, William R	58	31	-4	22
26	Roses, Allen D * ^ +	57	32	6	17
27	Petersen, Ronald C ^	56	29	-5	28
27	Thal, Leon J ^	56	28	-8	19
27	Sisodia, Sangram S * ^	56	27	-15	21
27	Hansen, Lawrence A	56	26	-21	9
31	Hofman, Albert	55	28	-4	30
32	Mann, David M A	54	28	-3	13
33	Perry, Robert H	53	32	13	14
33	St George-Hyslop, Peter * ^ +	53	25	-23	21
33	Younkin, Steven G ^	53	24	-31	15
36	Hodges, John R	52	32	16	20
37	Davies, Peter	51	26	-11	21
38	Butterfield, D Allan	50	32	18	20
38	Albert, Marilyn S	50	28	3	17
38	Growdon, John H	50	28	3	11
38	Fraser, Paul E	50	25	-18	20
38	Beal, M Flint +	50	24	-26	21
43	DeKosky, Steven T	49	28	8	23
43	Miller, Bruce L	49	27	1	23
43	Iwatsubo, Takeshi	49	25	-13	22
43	Bush, Ashley I ^	49	22	-30	18
47	McGeer, Edith G	48	38	35	11
47	Soininen, Hilka	48	31	20	17
47	Rapoport, Stanley I	48	30	17	14
47	Iqbal, Khalid ^	48	27	5	14
47	Hof, Patrick R	48	26	-1	13
47	Saunders, Ann M	48	25	-9	17
47	Larson, Eric B	48	22	-26	13
47	Multhaup, Gerd	48	21	-32	18
55	McKeith, Ian G	47	29	23	13
55	Rossor, Martin N	47	26	7	19

Table 5, continued

Rank	Author	H-index	Second-tier H-index	H rank – SeTH rank	Scientific following H-index
	*= Winner of MetLife Award				
	^ = Winner of Potomkin Prize				
	+ = Institute of Medicine member				
55	Mohs, Richard C	47	24	–9	9
55	Ihara, Yasuo * ^	47	24	–9	2
55	Schellenberg, Gerard D * ^	47	23	–14	18
55	Koo, Edward H	47	20	–30	14
55	Mandelkow, Eckhard	47	17	–39	12
55	Mandelkow, Eva-Maria	47	17	–39	12
63	Perry, Elaine K	46	27	21	10
63	Breteler, Monique M B	46	25	7	24
63	Davis, Kenneth L	46	25	7	12
63	Greengard, Paul * +	46	19	–26	20
63	Pericak-Vance, Margaret A +	46	18	–30	24
68	Blennow, Kaj	45	27	26	20
68	Delacourte, André	45	26	20	14
68	Wisniewski, Henryk M	45	26	20	9
68	Salmon, David P	45	22	–5	9
72	Gandy, Samuel E	44	23	3	10
72	Galasko, Douglas	44	21	–7	9
72	Goate, Alison M * ^	44	20	–13	29
72	Kokmen, Emre	44	19	–17	21
76	Hutton, Michael ^	43	24	12	27
76	Braak, Heiko	43	23	7	16
76	Lansbury, Peter T	43	11	–27	20
76	Lieberburg, I	43	6	–28	21
80	Riekkinen, PJ	42	27	38	12
80	Bennett, David A	42	26	32	17
80	Mufson, Elliott J	42	26	32	13
80	Jellinger, Kurt A	42	25	24	13
80	Sano, Mary	42	20	–5	17
80	Bird, Thomas D *	42	19	–9	19
85	Swaab, Dick F	41	28	51	12
85	Nordberg, Agneta	41	23	17	13
85	Farlow, Martin R	41	21	7	10
85	Breitner, John C S	41	19	–3	12
85	Grundke-Iqbal, Inge	41	16	–12	8
85	Teplov, David B	41	15	–15	20
92	Jagust, William J	40	22	19	12
93	Cairns, Nigel J	39	25	37	12
93	Smith, Glenn E	39	22	20	20
93	Nitsch, Roger M ^	39	21	14	12
93	Wilcock, Gordon K	39	20	8	8
93	Braak, Eva	39	17	–1	13
93	Rogers, Jack T	39	17	–1	6
93	Haines, Jonathan L	39	16	–5	24
93	Schenk, Dale ^	39	16	–5	22
93	Spillantini, Maria Grazia ^	39	12	–9	17

example of this is the fact that Dickson, Masters, and Hardy all have an AD H-index of 65. Using only the H-index, we are unable to discriminate between them in terms of how they might fare in the same ranking if conducted at a future date. In order to address this issue, a new metric called the Second-Tier H, or SeTH is proposed. The SeTH is calculated first by removing from consideration all papers that make up an individual's H-core. The H-core represents all papers that have enough citations to contribute to a given individual's

H-index calculation [10]. Once the H-core has been removed, a scientist's H-index is recalculated. The new H-index is the researcher's Second-Tier H. SeTH can be helpful to discriminate between the future potential of authors with equivalent (or nearly equivalent) H-indices for the simple reason that an individual's SeTH is a quantification of the highly-cited work of a given scientist that is not currently being considered when calculating that person's H-index.

A sports analogy exists in professional baseball in

the U.S. or professional soccer in many other countries. The major league teams often have one or more affiliated minor league teams with players who do not yet have the skills to play on the top team. Over time, the best players from the minor-league or “farm” teams will make their way to the roster of the major league team. So it is with the papers in SeTH. These papers represent a given author’s “minor-league” papers, which, as they gather more citations over time, will likely contribute the growth of a given scientist’s H-index. Holding the H-index constant, the higher the SeTH, the greater potential for H-index growth in the near-term. Differences between an individual’s H-index rank and the same person’s SeTH rank (referred to below as “H-Rank-minus-SeTH-Rank”) might be analyzed in a future study to give some indication of a given scientist’s likely future movement within the H-index ranking. Assuming that SeTH is a good estimation for future H-index growth, the size of a given investigator’s H-Rank-minus-SeTH-Rank disparity as well as its “polarity” (i.e., whether the number is negative or positive) should predict future movement up or down in the H-index ranking. An investigator with a highly positive H-Rank-minus-SeTH-Rank disparity will be expected to move up in the H-index ranking over time since that investigator’s “minor-league” papers are more highly-cited as a group than those of the people immediately above them in the current H-index ranking. On the other hand, individuals with a significantly negative H-Rank-minus-SeTH-Rank should expect downward movement in the AD H-index ranking as their minor-league papers are not as competitive as those of the people directly beneath them in today’s H-index ranking. Finally, those with an H-Rank-minus-SeTH-Rank of zero can expect to stay at their current spot in the rankings for the foreseeable future assuming that there are not upwardly-mobile scientists directly below them who are poised to displace them (see Table 5 for H-minus-SeTH scores for the top-100 H-indices).

Using SeTH and sfH to discriminate between similar (or identical) H-indices

Using the Dickson-Masters-Hardy H-index tie (all have an AD H-index of 65) as a test case, SeTH and sfH can be used to understand differences among investigators with the same H-index.

If one wanted to predict which of the three investigators was most likely to break the H-index tie through upward mobility in the next ranking, one approach would be to calculate the SeTH of each investigator (32,

43, and 37 respectively). Based on these numbers, it would appear that Masters is poised for much stronger H-index growth than the other two and will likely move ahead of them in future H-index rankings.

If, on the other hand, there was interest in determining school-of-thought leadership in a given line of investigation, then the sfH can be applied as a distinguishing factor in this area. Using the same investigators, we can apply the sfH to Dickson and Hardy, both of whom have “tau Proteins” as their main line of investigation. By comparing their sfH scores (24 and 37 respectively), it is clear that while both investigators have achieved similar overall scientific impact (i.e., the same H-index) working in similar research areas, Hardy’s impact is much more centered around a group of scientists who closely follow his work and who cite it repeatedly in their own work over an extended period time. The scientific impact of Dickson, on the other hand, while equally as great (as measured only by the H-index), is spread out among a wider number of scientists, many of whom only cite his work sporadically in theirs. In other words, based on the comparison of their Scientific-Following H-indices, one could easily argue for Hardy (over Dickson) to be awarded a hypothetical school-of-thought-leadership prize within AD research.

AD awards

When assessing the impact of AD researchers on their field, another parameter to be considered is the bestowing of research awards upon AD scientists. The two principal awards in this field are the MetLife Alzheimer Award for Medical Research and the Potamkin Prize for Research in Pick’s, Alzheimer’s, and Related Diseases. Table 5 indicates which scientists have won these awards. It also indicates membership in the Institute of Medicine of the US National Academy of Sciences.

Due to its subjective or “soft” nature, it is unclear how, exactly, to utilize the award-related data to further refine a bibliometric analysis of the impact of the top AD scientists. The information is presented here for completeness rather than as an integral part of the analysis. One observation, however, is that while a fair percentage of the top AD researchers have been honored with one or more award/membership, there are multiple cases of top-ranked investigators who have never been honored. Similarly, there are various instances of award-winners who do not fair exceptionally well under bibliometric analysis. One explanation for this

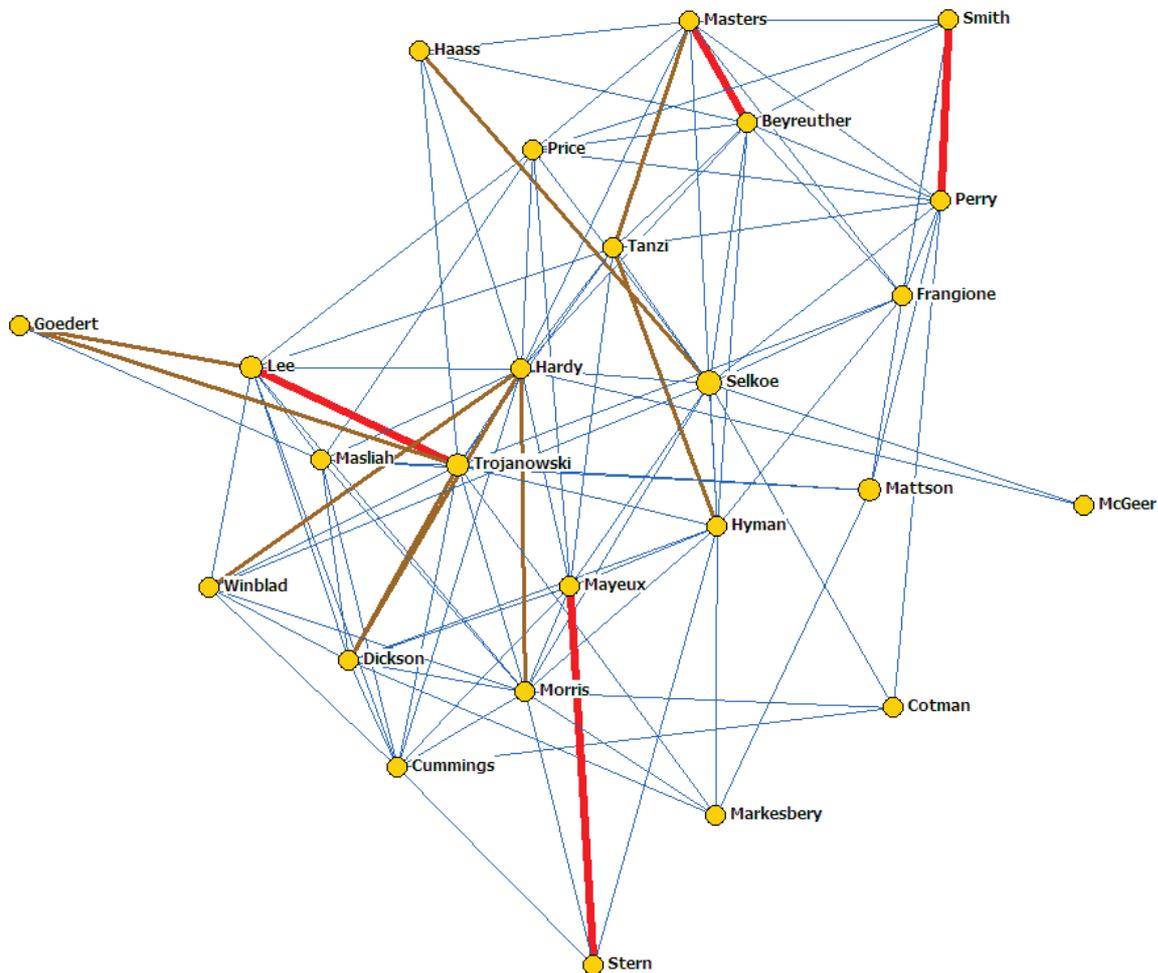


Fig. 2. Co-authorship network for top 25 AD investigators (based on H-index). Blue = 1–10 papers written together (1 pixel wide); Brown = 11–40 papers written together (3 pixels wide); Red = 41–370 papers written together (5 pixels wide). (Colours are visible in the electronic version of the article at www.iospress.nl.)

might be the existence of social factors in addition to scientometric criteria being used as inputs to the award-granting process. Another possible explanation of the variation between the award-granting process and a bibliometric analysis of the top scientists is the fact that a bibliometric analysis measures an individual's total contributions over an extended period of time, while a prize might be awarded to a given scientist for a single discovery that has proven to be important or promises to be important to the field.

Collaboration among Top 25

The final phase of the scientometric analysis of the top AD scientist was a co-author analysis of the top 25

AD investigators based on data extracted from Thomson WoS and biomedexperts.com. Figure 2 is a simple network view showing strength of collaboration among the top twenty-five AD investigators. The total area of each investigator's circle corresponds to that scientist's H-index.

One point of interest is that the four, two-person co-author teams connected by the red lines represent partnerships that are highly productive: the average number of papers per team (papers where both investigators are co-authors) is 255.5 for a total of 1022 team-written papers for the eight scientists. These co-author "duos" (i.e., Masters & Beyreuther, Smith & Perry, Lee & Trojanowski, and Mayeux & Stern) also generate significant impact with each team's shared papers averaging 14,610 total citations for a total of 58,441

team-generated citations for the group of eight scientists. The phenomenon of high-impact co-authorship teams observed in the AD research community corresponds to the findings of scientometric studies of other fields [15].

CONCLUSIONS

The spirit of Lotka's law [16], which suggests that in any given scientific field the majority of the work is done by a small percentage of the total investigators, seems to hold true in AD not only in terms of the quantity of research but also in terms of the quality of the science. There are two interesting directions for future research that naturally follow the work presented in this paper. The first involves conducting a similar, but more granular, analysis of scientific leadership within the AD research community in which the identification of excellence within the principal AD lines of investigation is emphasized. The second future direction is that of exploring further the Second-Tier H-index and the Scientific-Following H-index to better understand the temporal dynamics of AD research activity. This would allow one to make predications as to which established investigators are peaking in terms of their productivity and impact and which Young Turks are poised to revolutionize the scientific approaches of the mainstream AD research community.

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