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Ninety-one *Citation Classics* from the *Journal of Experimental Medicine*

Number 28 July 13, 1987

Since its inception as the Rockefeller Institute for Medical Research in 1901, The Rockefeller University has played an important role in the advancement of medical research in the US and throughout the world. I am proud to be associated with this institution not only as a member of The Rockefeller University Council but also because of my respect and admiration for its president, Joshua Lederberg.[1] I also think that the university represents the best in private medical research in the service of humanity.

From the 1850s to the turn of the century, the US was growing in wealth, the desire for education, and the need for scientists to communicate and develop ideas.[2] (p. 1-3),[3] Private research laboratories existed throughout the US, but they suffered from lack of financial support and public confidence,[4] and as a result many US scientists worked in small, inadequately equipped laboratories, relying heavily on European institutions and publications for current information.[5] With the successes of Louis Pasteur, Robert Koch, and other European pioneers in bacteriology during the late 1800s,[4] the scientific community and the public began to realize the important relationship between research and the treatment of disease. The Rockefeller Institute was the first major foundation dedicated to supporting medical research efforts in the US.

John Davison Rockefeller, the magnate of the Standard Oil Company, having decided to donate some of his vast wealth to worthy causes, agreed to finance the development of medical research. The Rockefeller Institute began with an initial gift of $200,000 to be distributed over 10 years. Guided by a Board of Scientific Directors that included some of the most distinguished US research physicians of the time, the institute initially awarded grants and scholarships to US scientists working in medical research laboratories at home and abroad. But as the need to centralize medical research and devote full-time efforts to laboratory work became apparent, Rockefeller provided additional funds to build the medical research center. In 1905 the institute began publishing the *Journal of Experimental Medicine (JEM)* and in 1906 opened its first laboratory building.[6] Opened in 1910, the Rockefeller Institute Hospital was the first clinical research hospital in the US.[7]

From this base the institute, hospital, and journal grew to produce some of the most enduring worldwide efforts to improve life, including the first isolation and successful tests of antibiotics, the development of preserving whole blood, and the first proof that viruses can cause animal cancer.[7] Today, The Rockefeller University consists of 50 laboratories specializing in both basic and clinical research in the biomedical and related behavioral and physical sciences. In addition to publishing *JEM*, The Rockefeller University Press publishes four other medical research journals: the *Journal of Clinical Investigation*, which was the subject of a recent citation study,[8] the *Journal of General Physiology*, the *Journal of Cell Biology*,

and *Biophysical Journal*. Probably the best-known journal of The Rockefeller University Press, however, is *JEM*, the subject of this study.

JEM began in 1896 with a $1,000 annual contribution from Johns Hopkins University.[9] (p. 243) The first editor was William H. Welch (1850-1934), a renowned US pathologist who revolutionized medical school education by combining course work, clinical duties, and laboratory work in the Johns Hopkins University curriculum.[10] The Johns Hopkins medical library is named in his honor. (In a previous essay, I discussed how my work on the Welch Medical Library Indexing Project laid the foundation for my interest in citation indexing and for the subsequent development of ISI®.[11])

Welch edited the journal for over five years with great success; however, as the volume of research manuscripts submitted increased and his involvement as chairman of the Rockefeller Institute's Board of Scientific Directors began to consume most of his time, the journal stopped being published. In 1905 Welch appointed fellow board member Simon Flexner as his successor to the position of chief editor and Eugene L. Opie as assistant editor.[9] (p. 249) Since then, the journal has continued to attract accomplished scientists to serve on the editorial board. Previous editors have included Vincent P. Dole, Jr., René Dubos, Herbert S. Gasser, James Hirsch, Richard Krause, Henry Kunkel, and Peyton Rous.

Its current editors, Anthony Cerami, Zanvil A. Cohn, and Maclyn McCarty, are also distinguished for their contributions to science. Together with Oswald T. Avery and Colin M. MacLeod at The Rockefeller University, McCarty coauthored one of the most important papers in the history of science—one that provided the first evidence that DNA was responsible for transmitting hereditary information.[12] McCarty has received several awards for this research contribution and has written a book entitled *The Transforming Principle: Discovering That Genes Are Made of DNA*.[13] He has also written a *Citation Classic*® commentary about his work.[14] Nineteen other articles in the Bibliography are also the subjects of *Classics* commentaries, as indicated by asterisks.

With such a distinguished group of editors over the years, it is not surprising that *JEM* has continued to be one of the world's most respected medical research journals. According to data from the 1985 *Journal Citation Reports*® section of the *Science Citation Index*® (*SCI*®), *JEM* has an impact factor of 11.2, placing it among the top 5 medical and immunology journals and 17th among the 4,072 journals ranked by impact factor.

Classics from High-Impact Journals

In the past few years we've published a series of essays in which we identify lists of classic papers from such high-impact journals as the *New England Journal of Medicine* (*NEJM*),[15] the *Lancet*,[16] the *British Medical Journal*,[17] and the *Journal of the American Medical Association*.[18] In these studies the citation threshold, the least number of cites received by items in each Bibliography, is between 158 and 270. However, as will be seen, the number of articles in *JEM* at these thresholds is quite high; therefore, we limited the analysis as described below. It is not surprising that many of the papers listed in the Bibliography have also appeared in previous citation studies.[19-21]

To develop this Bibliography, we used the 1955-1985 *SCI* to identify the most-cited articles regardless of the year that they were published in *JEM*. The 91 articles identified are those cited over 420 times during the 31-year period. The articles are listed alphabetically by first author. The average number of citations for the articles in the Bibliography is 764. For the 50 papers that have *not* appeared in any of ISI's previous cita-

Table 1: The *SCI*® research fronts that include 10 or more 1985 citing documents published in the *Journal of Experimental Medicine* (*J. Exp. Med.*). A = number of citing documents from *J. Exp. Med.* for each research front. Following in parentheses is the percent these documents represent of the total number of citing documents. B = total number of citing documents. C = total number of core documents. The research fronts are listed in descending order by the percent of citing documents that are from *J. Exp. Med.*

Number	Name	A	B	C
85-3391	Characterization of T-cell populations and their selected activities in mice	11 (17.2)	64	2
85-4831	Effects of monoclonal antibodies, anti-L3T4, and IA antigens on T-cell activation and accessory cell population; and clonal analysis of expression and recognition of T-cell receptor	13 (10.0)	130	3
85-7939	Major histocompatibility complex-linked control of the murine immune response to myelin basic protein; role of Ia antigen and T-cell clones specific to myelin basic protein immunotherapy	13 (9.0)	145	2
85-2050	Characterization of complement receptors for C3B, LFA-1, and related antigens in the activation and function of cytotoxic T-cells and macrophages	20 (6.3)	320	17
85-5994	Characterization, structural analysis, and expression of class I and class II genes from major histocompatibility complexes in mice, humans, and other mammals	21 (6.2)	337	13
85-0178	Monoclonal antibody activation of T-cells and antigen receptor gene expression	43 (5.8)	740	39
85-1272	Antigen processing and presentation by macrophages, dendritic cells, and B-cells; accessory cell heterogeneity and mechanisms of T-cell activation in the immune response	25 (4.3)	578	23
85-3532	Characterization of anti-idiotypic antibodies and idiotypic regulation in mice and humans	12 (4.3)	281	12
85-3696	Effects of interleukin-2 and studies of its receptors on human T-cell lymphocytes	27 (3.7)	721	20
85-1729	Effects of interferons on the expression of class I and class II cell surface antigens in mononuclear cells	13 (3.5)	374	13
85-1728	T-cell subsets and actions in allograft rejection, antitumor activity, and allergic neuritis	10 (2.9)	346	16
85-0081	Antigen expression, activity, and other aspects of natural killer cell cytotoxicity in human lymphocytes	16 (2.8)	569	25
85-0134	Hematopoietic studies using human and murine bone-marrow cell cultures	11 (2.5)	436	25
85-0129	Antigens, differentiation, role of interferons, and other aspects of B-cells and T-cells in leukemia patients and other humans	25 (2.2)	1,144	58
85-1379	Biochemical characterization, biological activities, and cellular production of interleukin-1	13 (2.1)	614	31
85-2912	Isolation, purification, and characterization of proteins and antigens from various species using monoclonal antibodies and other methods	48 (0.6)	7,571	4
85-1406	Isolation, characterization, expression, and cloning of DNA and RNA nucleotide sequences	32 (0.5)	6,184	26

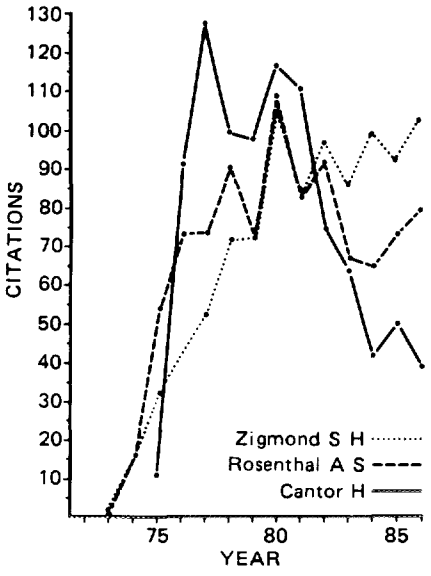
tion studies, the average number is 553. Full bibliographic references for these articles are given. For the remaining 41 a brief citation is provided as well as references to the previous studies. (For those readers who would like full citations for all papers in the Bibliography, you can contact me at ISI.)

By looking more closely at this list of most-cited papers, it is obvious that immunology articles predominate. Approximately 37 of the 50 "new" articles in the Bibliography are related to this specialty—a fact noted in a previous citation study that compared *JEM* with the *Journal of Immunology*.[22] "The analyses reveal an important point about this journal [*JEM*]. It is probably badly named. No other journal seems to play as important a role today in the transfer of information on immunology."[22] Apparently its name has not impeded its continued impact.

Research Fronts

Research-front analysis of *JEM* confirms its strong emphasis in the field of immunol-

Figure 1: Year-by-year distribution of citations received by three highly cited articles. **Solid Line** = Cantor H. 141:1390-9, 1975 (878 cites). **Broken line** = Rosenthal A S. 138:1194-212, 1973 (862 cites). **Dotted line** = Zigmond S H. 137:387-410, 1973 (845 cites).



ogy. We identified about 8,500 research fronts in 1985. Of these, 236 fronts involved articles published in *JEM*. Seventeen of these topics contain 10 or more papers published in *JEM* (see Table 1).

The research-front topics are arranged by percentage of articles published in *JEM*. Consequently, the first front listed, "Characterization of T-cell populations and their selected activities in mice" (#85-3391), is not the largest. Of the 64 articles published on this topic, however, over 17 percent (11) were published in *JEM*. Two recent papers, published in 1980 and 1981, constitute the "core" of this research front. In contrast, the 14th research front listed in Table 1, entitled "Antigens, differentiation, role of interferons, and other aspects of B-cells and T-cells in leukemia patients and other humans" (#85-0129), involved over 1,100 published articles. Just over 2 percent, or 25, of the articles in this front were published by *JEM*. Fifty-eight core papers were identified, 11 of which are *JEM* articles.

All the papers in the Bibliography are by definition *Citation Classics*, but 32 of them are also core documents in current research fronts. The 1975 paper (878 citations) by Harvey Cantor, Harvard Medical School, Boston, and Edward A. Boyse, Memorial Sloan-Kettering Cancer Center, New York, is the second of a two-part article describing the "Cooperation between subclasses of Ly^+ cells in the generation of killer activity." Part 1 turned up in our citation study of most-cited articles from 1961 to 1982. Both parts are core to "Characterization of T-cell differentiation, activities, and antigens in mice" (#85-3695). About 125 papers were published on this topic in 1985.

Another two-part study by Alan S. Rosenthal and Ethan M. Shevach, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, discusses the "Requirement for histocompatible macrophages and lymphocytes" (Part 1) and the role of the macrophage in controlling the immune response genetically (Part 2). The former part is 1 of 23 core papers that helped identify the research front on antigen processing and related mechanisms (#85-1272).

Another paper in the Bibliography was authored by two Rockefeller University researchers, Sally H. Zigmond and former editor James G. Hirsch. We lament his recent death on May 25, 1987. Their 1973 paper, "Leukocyte locomotion and chemotaxis," was cited 845 times and is 1 of 11 core papers on "Studies on neutrophil function and polymorphonuclear leukocyte chemotactic activity" (#85-3073).

Figure 1 shows the year-by-year citations to each of the three papers noted above. As the graph shows, the Cantor paper received its highest number of citations within the first two years after its publication in 1975. In contrast, the Rosenthal and Zigmond papers experienced a more gradual increase in citations.

Table 2: Frequency distribution of publication dates for the 91 items in the Bibliography, 1955-1985 *SCI®*.

Publication Date	Distribution of All Articles
1930-1939	2
1940-1949	2
1950-1954	5
1955-1959	6
1960-1964	17
1965-1969	21
1970-1974	18
1975-1979	17
1980-1985	3

Author and Institutional Information

The number of Nobel laureates who have published in *JEM* is significant. Five of them appear in the Bibliography alone. Most have associations with The Rockefeller University. Baruj Benacerraf, current chairman of the Pathology Department, Harvard Medical School, and former associate editor of *JEM*, shared the award in 1980 with Jean Dausset, University of Paris, and George D. Snell, Jackson Laboratory, Bar Harbor, Maine, for work on the genetic control of immunological reactions.

Renato Dulbecco, Salk Institute for Biological Studies, La Jolla, California, and former visiting professor at The Rockefeller University, was honored in 1975 with David Baltimore, Massachusetts Institute of Technology and Rockefeller University alumnus, and Howard Martin Temin, University of Wisconsin, Madison, for work on tumor viruses and cell genetics. In 1974 George Emil Palade, now a senior research scientist, Yale University School of Medicine, and former professor at The Rockefeller University, was awarded the Nobel for work on cell structure and function. He shared the award with Albert Claude, Catholic University of Louvain, Belgium, and Christian De Duve, also of Rockefeller. Two other Nobelists, Gerald Maurice Edelman and Charles Huggins, appear in the Bibliography. Edelman, a 1960 graduate of The Rockefeller University who is also distinguished as a Vincent

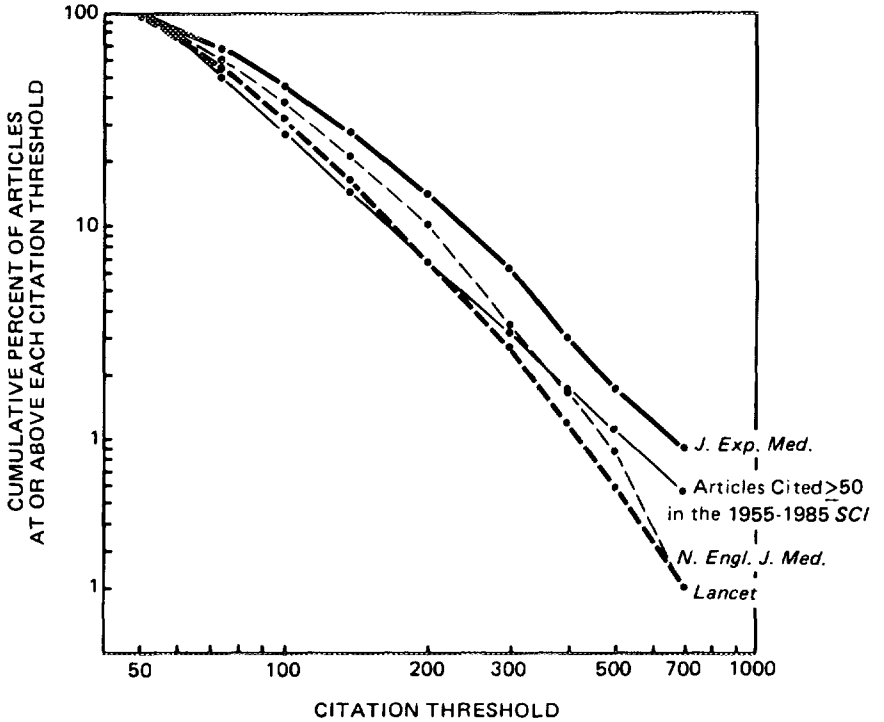
Table 3: Geographic areas represented by the institutional affiliations for all 91 entries in the Bibliography, listed in descending order according to the number of papers produced.

Geographic Location of Institutions		Distribution of All Articles
United States		71
New York	32	
Massachusetts	11	
California	10	
Maryland	7	
Colorado	4	
Connecticut	4	
Alabama	2	
Minnesota	2	
New Jersey	2	
Pennsylvania	2	
Florida	1	
Illinois	1	
Missouri	1	
New Mexico	1	
Ohio	1	
Texas	1	
Vermont	1	
Washington	1	
Washington, DC	1	
United Kingdom		5
Australia		7
Sweden		4
Switzerland		1
Canada		2
Italy		2
Japan		1

Astor Professor, received the prize in 1972 with Rodney R. Porter, University of Oxford, UK, for research on antibody structure. Huggins, University of Chicago, was honored in 1966 for his work on prostatic cancer treatments.

The institutional affiliations of other authors in the Bibliography show that *JEM*, which originally began as an outlet for the Rockefeller Institute papers, "has always welcomed articles from outside and applied the same criteria for judging their acceptability as for those from inside the Institute."[2] (p. 63) Fifty-nine institutions are represented in the Bibliography, with 39 appearing only once. The Rockefeller University appears most frequently (17 times), followed by Harvard University (10), Scripps Clinic and Research Foundation (7), and both the Memorial Sloan-Kettering Cancer Center and the National Institutes of Health (6).

Figure 2: Graph of the cumulative citation-frequency distribution, 1955-1985 *SCI*®, for articles with 50 or more citations and for those articles cited 50 or more times from the *Journal of Experimental Medicine* and two other comparable medical journals.



Citation Threshold	Cumulated Number of Articles for the Journals, with the Cumulated Percent of Total in Parentheses							
	J. Exp. Med.		*Lancet*		*N. Engl. J. Med.*		1955-1985 *SCI*	
700	29	(0.9)	10	(0.2)	9	(0.2)	1,964	(0.5)
500	60	(1.8)	25	(0.6)	33	(0.9)	4,034	(1.1)
400	103	(3.1)	54	(1.2)	66	(1.7)	6,470	(1.8)
300	208	(6.3)	119	(2.7)	125	(3.3)	11,851	(3.2)
250	326	(9.8)	193	(4.3)	220	(5.8)	17,380	(4.7)
200	487	(14.7)	319	(7.2)	389	(10.2)	27,572	(7.5)
150	830	(25.0)	624	(14.0)	719	(18.8)	49,523	(13.4)
100	1,569	(47.3)	1,472	(33.1)	1,492	(39.0)	109,218	(29.5)
75	2,248	(67.8)	2,481	(55.8)	2,334	(61.0)	185,708	(50.2)
50	3,316	(100.0)	4,445	(100.0)	3,824	(100.0)	369,916	(100.0)

Age of Papers and Geographic Affiliations

Table 2 compares the number of articles published according to their publication dates from 1930 to 1985. Eighty percent of the articles in the Bibliography were published between 1960 and 1980. Rebecca C. Lancefield, Hospital of the Rockefeller Institute for Medical Research, authored the oldest paper in the Bibliography, a 1933 methodology paper entitled "A serological differentiation of human and other groups of hemolytic streptococci." In contrast, Tuomo Timonen and colleagues, National Cancer Institute, Bethesda, wrote the most recent paper, a 1981 discussion of the "Characteristics of human large granular

Table 4: Comparison of total items published with total items cited 50 or more times for three medical journals, 1955-1985 *SCI*®.

Journal	Number of Items Published, 1955-1985	Number of Items Cited ≥ 50, 1955-1985 *SCI*	Percent of Total Cited ≥ 50, 1955-1985 *SCI*
J. Exp. Med.	6,563	2,914	44.4
Lancet	88,158	4,198	4.8
N. Engl. J. Med.	41,594	3,694	8.9

lymphocytes and relationship to natural killer and K cells."

The geographic distribution of authors appearing in the Bibliography according to their institutional affiliations is listed in Table 3. Eight countries are represented: Australia, Canada, Italy, Japan, Sweden, Switzerland, the UK, and the US. Two papers are multinational collaborations. Ellis L. Reinherz, J.M. Breard, and S.F. Schlossman, all of the Sidney Farber Cancer Institute and Harvard Medical School, coauthored a paper about human T lymphocyte subpopulations with L. Moretta, University of Genoa, Italy, and M. Roper and M.D. Cooper, University of Alabama, Birmingham. The other collaborative article is by Tomio Tada and Masaru Taniguchi, Chiba University, Japan, and Chella S. David, Washington University School of Medicine, St. Louis.

Citation-Frequency Distribution

Another way to examine the output of a journal is to look at its citation-frequency distribution, that is, the percentage of articles at or above a particular citation level. We compiled citation-frequency distribution data using the 1955-1985 *SCI* for three important medical journals: *JEM*, the *Lancet*, and *NEJM*. The percentage and distribution of articles from these journals cited at least 50 times in the *SCI* are shown in Table 4 and Figure 2.

Prestigious medical journals, like the three we have selected for graphic representation, consistently publish papers that are cited above the average. For the 1955-1985 *SCI*, the total number of articles, regardless of journal, cited *at least* 50 times is about 370,000. *JEM*, the *Lancet*, and *NEJM* alone produced a significant proportion of these items—over 3 percent, or 11,585.

For these journals Table 4 includes data on articles published from 1955 to 1985 as well as articles cited over 50 times. *JEM* has a remarkable 30-year impact. Out of 6,500 articles published, over 2,900, or 44 percent, were cited over 50 times. *JEM* has published far fewer articles than the other journals; nevertheless, as the data demonstrate, it has been exceptionally influential.

By comparison, while the *Lancet* and *NEJM* have published over 88,000 and 41,000 items, respectively, the percentage cited over 50 times was 4.8 and 8.9.

Figure 2 compares the citation-frequency distribution of articles cited over 50 times for the three journals and a baseline average for the 1955-1985 *SCI* articles cited 50 times or more. We used the tabular data listed below the graph to plot each curve. Naturally, as the citation-frequency threshold increases, the percentage of articles decreases for all journals shown. Yet, as the graph demonstrates, *JEM* clearly has a larger percentage of articles at the higher levels. For example, 0.9 percent of *JEM* articles were cited over 700 times, while the comparable figure for the entire file cited over 50 times is 0.5. Believe it or not, the curve for the entire file presents a nearly perfect hyperbolic distribution.

JEM's many contributions to medical research over the years have clearly ranked it as a valuable source of information. These illustrations are one more indication that *JEM* is a journal *extraordinaire*.

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My thanks to Carole Gan, Karen Maguire, and Pat Taylor for their help in the preparation of this essay.

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