Essays of an Information Scientist, Vol:9, p.389, 1986
Current Contents, #49, p.3-17, December 8, 1986

Current Comments®

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The Most-Cited 1984 Life-Sciences Articles Highlight AIDS Research

Number 49 December 8, 1986

In 1979 we began using two years of citation data for our annual series identifying the articles most cited in the *Science Citation Index®* (*SCI®*). Our first two-year study discussed the 1976 articles most cited in 1976 and 1977.[1] Previously we counted only the number of cites a paper received in the year it was published. Initially, we categorized articles into life- or physical-sciences studies. Later we added other categories such as chemistry.

Our intent in this series is twofold. Annual citation-frequency analyses identify the papers that attract immediate and widespread attention in the science community. These papers indicate new, active, or controversial research areas. In addition to pinpointing the "hot" areas of research, this series of essays can be used in trend analysis for science policy and research administration. The year-to-year progress or decline in prominent research areas can be used as a type of general science indicator. The series also shows how the research interests of high-impact authors advance. It should be noted, however, that there are many incipient fields where one may have to wait many years before observing significant publication rates.

AIDS Research

In our series of most-cited life-sciences papers, acquired immunodeficiency syndrome (AIDS) research is an excellent illustration of the trend analysis feature. When this series first began, AIDS research was nonexistent. In fact, our study of 1976 life-sciences articles showed that the most popular *new* area of research concerned endorphins and enkephalins, the opiates found primarily in the brain and pituitary glands. Twenty percent of the 100 articles were concerned with this topic.[1] I stressed new because there were many other older fields that were more active but did not necessarily produce papers of high immediacy.

AIDS research did not appear in our annual lists until we studied the 1982 papers. In that study six papers dealt with this new disease[2]—quite a jump from the previous year. These papers were all of a descriptive nature, discussing the immunological abnormalities of homosexual men suffering from AIDS. Kaposi's sarcoma and *Pneumocystis carinii* pneumonia were two of the principal opportunistic infections of AIDS patients. In contrast, that same year only six of the papers concerned opiate receptors. However, by then we had identified dozens of research fronts for this now relatively "stable" field. Indeed, some of the papers we had identified in earlier years continued to be well cited.

Reviewing this study's Bibliography of the 102 most-cited life-sciences papers, it is clear that by 1984 AIDS had developed into one of the most active areas of research. Most of the 23 AIDS-related papers have advanced far beyond descriptions of the physical manifestations of this disease. By 1984 scientists had established that AIDS is caused by a virus that suppresses the immune system, leaving the victim open to attack by a range of opportunistic infections.

The virus works by depleting T-lymphocytes, the agents mediating the cellular immune response. In addition, we now realize that AIDS is not restricted to certain populations, such as homosexual men and intravenous drug abusers, but can be transmitted, at least occasionally, between women to men via heterosexual activity.

Monitoring future studies of the most-cited life-sciences articles will highlight the high-impact breakthroughs in AIDS research. You might ask why this is necessary considering the attention AIDS receives from the general press. The point is that our citation analyses of the scientific literature seem to mirror, with a few significant exceptions, what has been reported in the general press and in the science news section of general science journals such as *Nature* and *Science*. If this is true for such a visible subject, then we hope and expect it is equally true for less visible areas.

While AIDS research dominates our list of 1984 articles, studies concerning oncogenes, antigen presentation, and signal-transduction research are also well represented. Overall, the 102 articles in the Bibliography garnered an average of 117 citations, 22 in 1984 and 95 in 1985.

We used research fronts to categorize these papers into broad subject areas. Research fronts develop as authors cite certain papers to indicate the connection to their own research. Papers that are frequently cited together, or co-cited, identify the shared features of current papers. In this way the citing authors themselves categorize papers into subject-related clusters of research. These co-citation groups help identify research fronts. Of the 102 papers in this study, 90 are already core documents for ISI® research fronts.

Table 1 lists the 19 fronts that include at least two papers from the Bibliography as core documents. The size of a front is determined by the number of published papers that cite into it. For instance, the largest front in this study is the "Role of phorbol ester receptor in activation of calcium mobilization, phosphorylation of inositol, and protein kinase C activity" (#85-0289), with over 1,600 citing papers and 58 core (cited) papers, 9 of which are included in the Bibliography. By comparison, the front on the "Role of African-type retrovirus in epidemiology of AIDS and Kaposi's sarcoma" (#84-3901) is the smallest front, with 61 papers. This research front was identified by a group of four core documents, two of which are included in the Bibliography. The other two were well cited but did not meet the criterion for this study of having been published in 1984.[3,4]

This latter research front is one of five from Table 1 that deal with AIDS, compared with three from last year's study.[5] The second and third most-cited papers in the study, both published in the same issue of *Science*, deal with AIDS. Mikulas Popovic, Laboratory of Tumor Cell Biology, National Cancer Institute (NCI), Bethesda; M.G. Sarngadharan, Department of Cell Biology, Litton Bionetics, Inc., Kensington, Maryland; and Elizabeth Read and Robert C. Gallo, also of NCI, developed a cell culture system from a human T-cell line that can maintain growth even after being infected by the AIDS virus. Previously, they could not get the AIDS virus to grow in culture because it killed the cells that it infected. The new cell system allows the AIDS virus to be produced in large quantities, making it easier to analyze and elucidate the precise mechanism of activity of the AIDS virus.[6] The paper describing this method is the third most-cited paper in the Bibliography.

In the second most-cited paper, Gallo and colleagues described how they used this cell system to grow large quantities of HTLV-III, the virus that was detected in and isolated from patients who have AIDS or who show pre-AIDS symptoms. They concluded that the HTLV-III virus is the causative agent of AIDS.[7] Both of these papers are core to the fronts concerning "Association of human T-cell leukemia virus and other retroviruses with leukemia-lymphoma, AIDS, and related immune disorders"

Table 1: The 1984 and 1985 *SCI®/SSCI®* research fronts that include at least two of the 1984 most-cited life-sciences papers as core documents. A = research-front number. B = research-front name. C = number of 1984 most-cited life-sciences papers included in the core of each research front. D = total number of core papers and 1984 or 1985 citing papers for the year designated by the prefix in column A.

A	B	C	D
84-0171	Clinical aspects and characterization of human T-cell subsets	4	47/1,206
84-0319	Phosphorylation and calcium binding of phorbol and inositol; stimulation of protein-kinase release	4	58/1,119
84-1914	Association of human T-cell leukemia virus and other retroviruses with leukemia-lymphoma, AIDS, and related immune disorders	8	41/608
84-3901	Role of African-type retrovirus in epidemiology of AIDS and Kaposi's sarcoma	2	4/61
84-4992	Isolation and characterization of ANF	2	12/108
84-6753	Intracellular distribution and structure of the estrogen-receptor and other steroid-hormone receptors	2	5/86
85-0178	Monoclonal antibody activation of T-cells and antigen-receptor gene expression	11	39/740
85-0208	Expression of c-*myc* gene and other oncogenes causing human and mouse cell cancers	4	51/1,085
85-0289	Role of phorbol ester receptor in activation of calcium mobilization, phosphorylation of inositol, and protein kinase C activity	9	58/1,632
85-0647	Antibodies and antigens in response to disease, characterization of nuclear RNAs, and nucleotide sequences for messenger RNA splicing in human genes	2	34/777
85-0745	Immunology, epidemiology, and virology of AIDS and HTLV-III virus infections	2	9/268
85-0822	Characterization of rat and human nuclear estrogen receptors	2	17/300
85-1307	Biological activity, receptor distribution, and the systemic and renal hemodynamic effects of ANF	8	45/319
85-1677	Regulation, characterization, and expression of transcription-promoter genes in viruses and human and non-human cells	2	32/829
85-1825	Effects of leukemia virus and other retroviruses on human T-cells in patients with leukemia and AIDS	13	56/118
85-2553	HTLV-III antibody prevalence in epidemiology studies of AIDS in Africa	2	7/147
85-2623	Oncogenes and growth-factor receptors and their roles in gene expression and transformation in normal and cancer cells	2	7/607
85-3538	Characterization of MPTP neurotoxicity in dopamine neurons in parkinsonism	4	16/158
85-6203	Effects of platelet-derived growth factor, epidermal growth factors, phorbol ester, and various viruses on the metabolism of inositol phospholipids and differentiation of various cells	2	3/129

(#84-1914) and "Effects of leukemia virus and other retroviruses on human T-cells in patients with leukemia and AIDS" (#85-1825).

French and American Contributions

Last year we briefly discussed the controversy between AIDS researchers in the US and France.[5] Gallo and colleagues isolated the virus HTLV-III and were credited by the general media as the discoverers of the cause of AIDS. It has since been shown that this virus is the same as the virus LAV, discovered earlier by Luc Montagnier, Pasteur Institute, Paris, and colleagues.[8] This priority controversy escalated when the French team applied for a US patent in December 1983 for a test that detects antibodies to the AIDS virus. Four months later, in April 1984, the US team applied for a patent for their own antibody test. The US team's application was approved in May 1985, while the French patent application is still pending. A complex legal process has been set in motion to sort out the competing claims of both sides and decide who is the true inventor of the blood test. Despite this controversy, the 1986 Lasker Award has recognized the achievements of six scientists, including both Montagnier and Gallo, as well as Myron Essex, Department of Cancer Biology, Harvard School of Public Health, for their work in identifying the virus that causes AIDS.[9]

While US research seems to be attracting the most attention from the general media in the US, AIDS research in France is very highly regarded by the international community of scientists. Of the five papers in the Bibliography that are coauthored by scientists with French affiliations, four deal with AIDS research. Montagnier and F.

Table 2: National locations of the institutional affiliations listed by authors in the Bibliography, according to total appearances (column A). B = number of papers coauthored with researchers affiliated with institutions in other countries. C = national locations of institutions listed by coauthors.

Country	A	B	C
US	79	17	Australia, Belgium, Canada, FRG, France, Israel, Japan, Kenya, Switzerland, UK, Zaire
UK	13	6	Israel, Kenya, Switzerland, US
Canada	6	4	US
France	5	2	US
Switzerland	5	2	UK, US
Australia	4	2	FRG, US
Japan	4	1	US
Belgium	3	2	US, Zaire
Israel	2	2	UK, US
FRG	1	1	Australia, US
Kenya	1	1	UK, US
Sweden	1	0	
Zaire	1	1	Belgium, US

Barré-Sinoussi, also of the Pasteur Institute, are coauthors of these four papers. They also coauthored one of the papers on AIDS from last year. A *Citation Classic*® commentary by Barré-Sinoussi is currently in preparation.

Author Affiliations

The 469 authors in this study are affiliated with institutions in 13 countries. Table 2 provides the number of papers produced by authors affiliated with institutions in each nation. US-affiliated authors appeared in 79 papers, 17 of which were coauthored with scientists affiliated with institutions of other nations, including Australia, Belgium, France, and the UK.

There are two articles in this study by authors affiliated with the Weizmann Institute of Science, Rehovot, Israel, as well as one article by authors affiliated with two institutions in Zaire. These two countries were not represented in last year's studies of most-cited papers. Keep in mind, however, that the cut-off point for papers included in these essays is arbitrary. Only a few citations separate those selected from those omitted.

Table 3 lists the 108 institutions represented in the Bibliography. Sixty-one of the in-

Table 3: Institutional affiliations listed in papers in the Bibliography in descending order of number of appearances.

NIH, Bethesda, MD		22
NCI	14	
Bethesda, MD	11	
Frederick, MD	3	
NIAID	3	
Clin. Ctr.	2	
NIADDKD	2	
NIMH	1	
Harvard Univ., MA		13
Boston	8	
Cambridge	5	
Univ. California, CA		10
Los Angeles	4	
San Francisco	4	
Berkeley	1	
La Jolla	1	
Litton Bionet., Inc., Kensington, MD		7
Stanford Univ., CA		6
AFRC, Cambridge, UK		5
Inst. Anim. Physiol.	2	
Unit Insect Neurophysiol. Pharmacol.	2	
Unit Invertebrate Chem. Physiol.	1	
Caltech, Pasadena, CA		5
Dana-Farber Cancer Inst., Boston, MA		5
Univ. Cambridge, UK		5
MIT, Cambridge, MA		4
Pasteur Inst., Paris, France		4
Univ. Toronto, Canada		4
CDC, Atlanta, GA		3
Claude Bernard Hosp., Paris, France		3
Cornell Univ. Med. Coll., New York, NY		3
Genentech, Inc., San Francisco, CA		3
Mem. Sloan-Kettering Cancer Ctr., New York, NY		3
Ontario Cancer Inst., Toronto, Canada		3
Univ. Texas, TX		3
Dallas	2	
Houston	1	
Walter Reed Army Inst. Res., Washington, DC		3
Washington, DC	2	
Walter Reed Project, Nairobi, Kenya	1	
Australian Natl. Univ., Canberra, Australia		2
Basel Univ., Switzerland		2
California Biotech, Inc., Mountain View, CA		2
Clin. Res. Inst. Montreal, Canada		2
Hosp. Infant Dis., Paris, France		2
Imperial Cancer Res. Fund Labs., London, UK		2
Kobe Univ., Japan		2
MRC, UK		2
Immunochem. Unit, Oxford	1	
Secretory Cntrl. Res. Grp., Liverpool	1	

NY Hosp., NY	2
Natl. Inst. Basic Biol., Okazaki, Japan	2
New Engl. Deaconess Hosp., Boston, MA	2
Prince Leopold Inst. Trop. Med., Antwerp, Belgium	2
Salk Inst. Biol. Stud., San Diego, CA	2
Univ. Chicago, IL	2
Univ. London, UK	2
Univ. Med. Dent. New Jersey, Newark, NJ	2
Univ. Pennsylvania, Philadelphia, PA	2
Vanderbilt Univ., Nashville, TN	2
Washington Univ., St. Louis, MO	2
Weizmann Inst. Sci., Rehovot, Israel	2
Addenbrooke's Hosp., Cambridge, UK	1
American Cancer Soc., New York, NY	1
Anderlecht Hosp., Brussels, Belgium	1
Basel Inst. Immunol., Switzerland	1
Beth Israel Med. Ctr., New York, NY	1
Biogen Inc., Cambridge, MA	1
Biotech Res. Labs., Inc., Rockville, MD	1
Boston Univ., MA	1
Brugmann Hosp., Brussels, Belgium	1
California Dept. Hlth. Serv., Berkeley, CA	1
Cedars-Sinai Med. Ctr., Los Angeles, CA	1
Cetus Corp., Emeryville, CA	1
Columbia Univ., New York, NY	1
Dartmouth Coll., Hanover, NH	1
Dept. Publ. Hlth. Trop. Med., Paris, France	1
Hokkaido Univ., Sapporo, Japan	1
Indiana Univ., Bloomington, IN	1
Inst. Cancer Res.: Royal Cancer Hosp., London, UK	1
Intl. Agcy. Res. Cancer, Lyon, France	1
Jefferson Cnty. Dept. Publ. Hlth., Birmingham, AL	1
Liverpool Sch. Trop. Med., UK	1
Ludwig Inst. Cancer Res., Sydney, Australia	1
Mama Yemo Hosp., Kinshasa, Zaire	1
Med. Coll. Virginia, Richmond, VA	1
Merck Sharp & Dohme Res. Labs., West Point, PA	1
Michael Reese Hosp., Chicago, IL	1
Miyazaki Med. Coll., Japan	1
Monsanto Co., St. Louis, MO	1
N. London Blood Transfusion Ctr., Edgware, UK	1
NY City Dept. Hlth., NY	1
NYU, NY	1
Natl. Inst. Biol. Stand., London, UK	1
Natl. Jewish Hosp. Res. Ctr., Denver, CO	1
North Shore Univ. Hosp., Manhasset, NY	1
Northwestern Univ., Evanston, IL	1
Oklahoma Med. Res. Fdn., Oklahoma City, OK	1
Oxford Univ., UK	1
Paris Univ., France	1
Philipps Univ., Marburg, FRG	1
Pitie-Salpetriere Hosp., Paris, France	1
Rice Univ., Houston, TX	1
Royal Melbourne Hosp., Parkville, Australia	1
Saint Pierre Hosp., Brussels, Belgium	1
Saint-Luc Hosp., Brussels, Belgium	1
Santa Clara Valley Med. Ctr., San Jose, CA	1
SRI Intl., Menlo Park, CA	1
SUNY, Stony Brook, NY	1
Tennessee Dept. Publ. Hlth., Nashville, TN	1
Tufts Univ., Boston, MA	1
Univ. Antwerp, Belgium	1
Univ. Cincinnati, OH	1
Univ. Geneva, Switzerland	1
Univ. Hlth. Sci., Bethesda, MD	1
Univ. Kinshasa, Zaire	1
Univ. Louvain, Belgium	1
Univ. Liverpool, UK	1
Univ. Melbourne, Parkville, Australia	1
Univ. Miami, FL	1
Univ. North Carolina, Chapel Hill, NC	1
Univ. Pittsburgh, PA	1
Univ. Rochester, NY	1
Univ. Southern California, Los Angeles, CA	1
Univ. Virginia, Charlottesville, VA	1
Univ. Wisconsin, Madison, WI	1
Univ. Zurich, Switzerland	1
Uppsala Univ., Sweden	1
VA Med. Ctr., Palo Alto, CA	1
Withington Hosp., Manchester, UK	1

stitutions (56 percent) are located in the US, 13 in the UK, 7 each in Belgium and France, 4 each in Japan, Australia, and Switzerland, and 3 in Canada. As mentioned earlier, two institutions are from Zaire, while Israel, the Federal Republic of Germany, Kenya, and Sweden each have one institution represented in the Bibliography.

The number of multi-institutional studies is growing significantly. It is necessary to interpret these figures carefully. It also makes the job of cataloging these studies more complex. Thus, while seven Belgian institutions are represented, there are only three papers involved.

Multiauthored Works

All but nine of the papers in the Bibliography have more than one author. Table 4 shows the number of authors per paper. Fifteen papers have two authors, 6 papers have three authors, and 14 papers have four. One paper has 20 authors.

Eighty-five authors have more than one paper listed in the Bibliography. Since AIDS research was so active in 1984, it is not surprising that the most prolific authors in our study are AIDS researchers. Gallo coauthored eight of the papers in the Bibliography, Sarngadharan has six papers, while Popovic has five papers in the study. M.M.

Table 4: The number of authors per paper for the 1984 life-sciences articles most cited in the *SCI®*, 1984-1985.

Number of Authors	Number of Papers	Number of Authors	Number of Papers
20	1	9	3
19	1	8	2
17	1	7	8
15	2	6	12
14	3	5	16
13	1	4	14
12	1	3	6
11	4	2	15
10	3	1	9

Davis also coauthored five papers. In addition to Montagnier and Barré-Sinoussi, mentioned earlier, five other authors wrote four papers each: M.J. Berridge, J.C. Chermann, L.E. Hood, R.F. Irvine, and T.W. Mak.

The 102 papers in the Bibliography were published in the 21 journals listed in Table 5. As is usual in these studies, almost 60 percent of the papers were published in *Nature* (31 papers), *Science* (16 papers), or *Cell* (11 papers). Table 5 also includes 1984 impact factors, calculated by dividing the 1984 citations to 1982 and 1983 articles published in a journal by the number of articles published by that journal in those two years. For a more extensive discussion of high-impact journals, see my recent paper in *Annals of Internal Medicine*.[10]

Signal-Transduction Studies

Two of the top five most-cited articles were published in *Nature*. Both deal with signal transduction, a field that is growing rapidly. Cell behavior is governed by signaling systems that transduce external signals from hormones, growth factors, or neurotransmitters into certain types of internal signals, known as second messengers. These second messengers control cellular processes, such as metabolism, secretion, contraction, and cell growth. One signal-transduction system uses inositol phospholipids as part of the transduction mechanism. The inositol phospholipid called phosphatidylinositol 4,5-bisphosphate is hydrolyzed to diacylglycerol and inositol trisphosphate.[11]

Table 5: The 21 journals represented in the list of 1984 life-sciences papers most cited in the *SCI®*, 1984-1985. The numbers in parentheses are the 1984 impact factors for the journals. (The 1984 impact factor equals the number of 1984 citations received by the 1982-1983 articles in a journal divided by the number of articles published by the journal during that same period.) Data were taken from the *JCR®*. The figures at the right indicate the number of papers from each journal that appear in the list.

Journal	Number of Papers
Nature (10.3)	31
Science (8.2)	16
Cell (16.2)	11
N. Engl. J. Med. (16.0)	8
Proc. Nat. Acad. Sci. USA (9.0)	7
Lancet (9.4)	6
J. Biol. Chem. (6.1)	5
Biochem. Biophys. Res. Commun. (3.0)	3
Biochem. J. (3.4)	2
Nucl. Acid Res. (6.0)	2
Acta Biochim. Biophys. (2.5)	1
Ann. Intern. Med. (8.2)	1
Ann. Trop. Med. Parasitol. (1.1)	1
Annu. Rev. Immunol. (17.1)	1
Brain Res. (2.8)	1
Ca-A Cancer J. Clin. (3.3)	1
FEBS Lett. (3.0)	1
J. Clin. Invest. (6.1)	1
J. Immunol. (6.3)	1
Microbiol. Rev. (18.8)	1
Rev. Infec. Dis. (2.5)	1

Yasutomi Nishizuka, Department of Biochemistry, School of Medicine, Kobe University, Japan, reviewed the studies establishing diacylglycerol as a second messenger that activates protein kinase C, an enzyme that regulates a wide variety of cell functions and proliferation. Nishizuka proposed that protein kinase C is a prime target for the actions of tumor-promoting phorbol esters.[11] This field is attracting a great deal of attention because an imbalance of protein kinase C activity may be responsible for normal cells becoming cancerous. Nishizuka's review article was cited over 500 times, making it the most-cited 1984 life-sciences article.

In another highly cited signal-transduction study, Michael J. Berridge, Department of Zoology, University of Cambridge, proposes that inositol trisphosphate is released into the cytoplasm to function as a second messenger for mobilizing intracellular cal-

cium.[12] Cited over 350 times, Berridge's review paper is the fifth most-cited paper in this study. Berridge is writing a survey of this research area for the *ISI Atlas of Science®: Pharmacology*, which will be published in 1987. Berridge, along with Montagnier, mentioned earlier, and Desiré Collen, Center for Thrombosis and Vascular Research, University of Louvain, Belgium, are the recipients of the annual award of the Louis Jeantet Foundation for Medicine. This award, established in 1983, supports the ongoing research efforts of scientists in Western Europe.[13]

Both of these papers are core to "Phosphorylation and calcium binding of phorbol and inositol; stimulation of protein-kinase release" (#84-0319) and research front #85-0289, mentioned earlier as the largest front in our study.

Oncogene Studies

Certain areas of research have been prominent in these citation-frequency studies over the past few years. One such area is the study of oncogenes, normally unexpressed genes that, when activated, can produce tumors in cell culture. Walter Bodmer, Imperial Cancer Research Fund, London, UK, believes that oncogenes are simply altered normal genes that now have this additional tumor-producing capability.[14]

Ten papers in the Bibliography involve oncogene investigations. The fourth most-cited paper, by J. Downward, Protein Chemistry Laboratory, Imperial Cancer Research Fund, and colleagues, found that each of six peptides derived from the human epidermal growth factor (EGF) receptor is similar to a part of the sequence of the oncogene v-*erb-B* transforming protein. These studies are important because the mechanism by which the oncogene transforms cells may involve a protein with functions similar to those of EGF during cell growth. Abnormal expression of an EGF-like protein may lead to uncontrolled growth by tumor cells.[14] This paper was cited 115 times in 1984 and 249 times in 1985, and it is core to the research front on "Oncogenes and growth-factor receptors and their roles in gene expression and transformation in normal and cancer cells" (#85-2623).

Another active area of research here and in past studies concerns antigen presentation. Eleven of the 39 core papers in "Monoclonal antibody activation of T-cells and antigen-receptor gene expression" (#85-0178) are in this study. These papers investigate T-cell receptors and their role in the cellular immune response. Scientists are trying to establish a structural model of the T-cell receptor that explains how it functions in antigen recognition. For example, scientists are studying how T-cell receptors distinguish between an antigen normally present in the body ("self" antigen) and a foreign antigen that may pose a danger to the body ("non-self" antigen).

Yueh-hsiu Chien and colleagues, Department of Medical Microbiology, School of Medicine, Stanford University, California, studied a T-cell receptor gene and found that part of its sequence closely resembles part of the genetic sequence of immunoglobulins, those proteins involved in the humoral immune response. Chien and colleagues propose that it is this section of the T-cell receptor gene that is involved in antigen recognition.[15] Published in *Nature*, this paper was cited about 100 times in 1984 and 1985.

A new area of research not previously represented in these annual studies concerns the atrial natriuretic factor (ANF), a hormone released by the atrium of the heart. ANF inhibits reabsorption of sodium by the renal tubules of the kidney, thereby promoting both diuresis, an increased excretion of urine, and natriuresis, the excessive loss of cations such as sodium in the urine.

ANF is a small polypeptide hormone derived from a 126-amino acid precursor. Kenji Kangawa and Hisayuki Matsuo, Department of Biochemistry, Miyazaki Medical College, Japan, extracted a 28-amino acid peptide that they labeled α-human atrial natriuretic polypeptide (α-hANP). This peptide elicits diuretic and natriuretic activities

and is thought to represent the principal active molecule of ANF.[16] One of eight papers in this study investigating ANF, this paper was cited about 130 times in 1984 and 1985.

All eight papers on this topic are core to the front on "Biological activity, receptor distribution, and the systemic and renal hemodynamic effects of ANF" (#85-1307), which attracted over 300 published papers in 1985. Monitoring the release of ANF could play a role in understanding disorders related to salt and water imbalance. However, since this hormone has only recently been identified, more information about ANF must be accumulated before the therapeutic potential of this peptide hormone can be ascertained. The subject of ANF will also be covered in the 1987 *ISI Atlas of Science: Pharmacology*. It will be discussed by John H. Laragh, Hypertension Center, Cornell University Medical College, New York, a coauthor of the first paper in the Bibliography.[17]

Conclusion

While this list of 102 papers represents only a fraction of the important research occurring in 1984, it does give excellent examples of those newer areas of research that were the most active. These annual citation-frequency studies help us monitor the progress made from year to year. The scientific community is engaged in a continuing quest to understand phenomena such as AIDS, oncogenes, antigen presentation, and ANF. Each new discovery opens up new areas of knowledge. New information technologies help us exploit this knowledge so rapidly that we often lose track of the short history involved. In the past, we would not have considered five years much time to wait for a progress report on a new field. Today, changes are produced in five years that might have required an entire generation in the past. Many different teams working in parallel produce solutions to problems by a catalytic process that social scientists need to study more carefully.

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

REFERENCES

1. **Garfield E.** The 1976 articles most cited in 1976 and 1977. Part 1. Life sciences. *Essays of an information scientist.* Philadelphia: ISI Press, 1981. Vol. 4. p. 81-99.
2. ----------. The 1982 articles most cited in 1982 and 1983. 1. Life sciences. *Ibid.*, 1985. Vol. 7. p. 353-65.
3. **Pape J W, Liautaud B, Thomas F, Mathurin J-R, St. Amand M-M A, Boncy M, Pean V, Pamphile M, Laroche A C & Johnson W D.** Characteristics of the acquired immunodeficiency syndrome (AIDS) in Haiti. *N. Engl. J. Med.* 309:945-50, 1983.
4. **Bygbjerg I C.** Letter to editor. (AIDS in a Danish surgeon. Zaire, 1976.) *Lancet* 1:925, 1983.
5. **Garfield E.** The 1983 articles most cited in 1983 and 1984. 1. Life sciences. *Current Contents* (47):3-18, 25 November 1985. (Reprinted in: *Essays of an information scientist: ghostwriting and other essays.* Philadelphia: ISI Press, 1985. Vol. 8. p. 444-59.)
6. **Popovic M, Sarngadharan M G, Read E & Gallo R C.** Detection, isolation, and continuous production of cytopathic retroviruses (HTLV-III) from patients with AIDS and pre-AIDS. *Science* 224:497-500, 1984.
7. **Gallo R C, Salahuddin S Z, Popovic M, Shearer G M, Kaplan M, Haynes B F, Palker T J, Redfield R, Oleske J, Safai B, White G, Foster P & Markham P D.** Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS. *Science* 224:500-3, 1984.
8. **Barré-Sinoussi F, Chermann J C, Rey F, Nugeyre M T, Chamaret S, Gruest J, Dauguet C, Axler-Blin C, Vézinet-Brun F, Rouzioux C, Rozenbaum W & Montagnier L.** Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). *Science* 220:868-71, 1983.
9. **Schmeck H M.** AIDS research rivals share a major award. *New York Times* 23 September 1986. p. C1; C3.

10. **Garfield E.** Which medical journals have the greatest impact? *Ann. Intern. Med.* 105(2):313-20, 1986.
11. **Nishizuka Y.** The role of protein kinase C in cell surface signal transduction and tumour promotion. *Nature* 308:693-8, 1984.
12. **Berridge M J.** Inositol trisphosphate and diacylglycerol as second messengers. *Biochem. J.* 220:345-60, 1984.
13. **Louis Jeantet Foundation for Medicine.** Press release. 24 January 1986. 1 p.
14. **Downward J, Yarden Y, Mayes E, Scrace G, Totty N, Stockwell P, Ullrich A, Schlessinger J & Waterfield M D.** Close similarity of epidermal growth factor receptor and v-*erb-B* oncogene protein sequences. *Nature* 307:521-7, 1984.
15. **Chien Y-h, Gascoigne N R J, Kavaler J, Lee N E & Davis M M.** Somatic recombination in a murine T-cell receptor gene. *Nature* 309:322-6, 1984.
16. **Kangawa K & Matsuo H.** Purification and complete amino acid sequence of α-human atrial natriuretic polypeptide (α-hANP). *Biochem. Biophys. Res. Commun.* 118:131-9, 1984.
17. **Atlas S A, Kleinert H D, Camargo M J, Januszewicz A, Sealey J E, Laragh J H, Schilling J W, Lewicki J A, Johnson L K & Maack T.** Purification, sequencing and synthesis of natriuretic and vasoactive rat atrial peptide. *Nature* 309:717-9, 1984.

Bibliography: The 1984 life-sciences articles most cited in the *SCI®*, 1984-1985. Articles are listed in alphabetic order by first author. The authors' affiliations follow each citation. Code numbers indicate the 1984 and 1985 *SCI/SSCI®* research-front specialties for which these are core papers. A=1984 citations. B=1985 citations. C=total. D=bibliographic data.

A	B	C	D
15	94	109	**Atlas S A, Kleinert H D, Camargo M J, Januszewicz A, Sealey J E, Laragh J H, Schilling J W, Lewicki J A, Johnson L K & Maack T.** Purification, sequencing and synthesis of natriuretic and vasoactive rat atrial peptide. *Nature* 309:717-9, 1984. Cornell Univ. Med. Coll., Hypertension Ctr. and Dept. Physiol., New York, NY; California Biotech. Inc., Mountain View, CA. 85-1307
8	54	62	**Benjamin D C, Berzofsky J A, East I J, Gurd F R N, Hannum C, Leach S J, Margoliash E, Michael J G, Miller A, Prager E M, Reichlin M, Sercarz E E, Smith-Gill S J, Todd P E & Wilson A C.** The antigenic structure of proteins: a reappraisal. *Annu. Rev. Immunol.* 2:67-101, 1984. Univ. Virginia, Dept. Microbiol., Charlottesville, VA; NIH, NCI and NIADDKD, Bethesda, MD; Indiana Univ., Dept. Chem., Bloomington, IN; Natl. Jewish Hosp. Res. Ctr., Denver, CO; Univ. Melbourne, Russell Grimwade Sch. Biochem., Parkville, Australia; Northwestern Univ., Dept. Biochem., Molec. Biol., Cell Biol., Evanston, IL; Univ. Cincinnati, Dept. Microbiol. Immunol., OH; Univ. California, Dept. Microbiol., Los Angeles and Dept. Biochem., Berkeley, CA; Oklahoma Med. Res. Fdn., Arthritis Immunol. Lab., Oklahoma City, OK. 85-1308
9	56	65	**Berget S M.** Are U4 small nuclear ribonucleoproteins involved in polyadenylation? *Nature* 309:179-82, 1984. Rice Univ., Dept. Biochem., Houston, TX. 85-2329
33	320	353	**Berridge M J.** Inositol trisphosphate and diacylglycerol as second messengers. *Biochem. J.* 220:345-60, 1984. Univ. Cambridge, Dept. Zool.; AFRC, Unit Insect Neurophysiol. Pharmacol., UK. 84-0319, 85-0289
0	220	220	**Berridge M J & Irvine R F.** Inositol trisphosphate, a novel second messenger in cellular signal transduction. *Nature* 312:315-21, 1984. Univ. Cambridge, Dept. Zool.; AFRC, Unit Insect Neurophysiol. Pharmacol. and Inst. Anim. Physiol., UK. 85-0289
11	66	77	**Bokoch G M, Katada T, Northup J K, Ui M & Gilman A G.** Purification and properties of the inhibitory guanine nucleotide-binding regulatory component of adenylate cyclase. *J. Biol. Chem.* 259:3560-7, 1984. Univ. Texas, Hlth. Sci. Ctr., Dallas, TX; Hokkaido Univ., Fac. Pharm. Sci., Sapporo, Japan. 85-2866
0	70	70	**Broder S & Gallo R C.** A pathogenic retrovirus (HTLV-III) linked to AIDS. *N. Engl. J. Med.* 311:1292-7, 1984. NIH, NCI, Bethesda, MD. 85-3258
22	86	108	**Brun-Vezinet F, Barre-Sinoussi F, Saimot A G, Christol D, Montagnier L, Rouzioux C, Klatzmann D, Rozenbaum W, Gluckmann J C & Chermann J C.** Detection of IgG antibodies to lymphadenopathy-associated virus in patients with AIDS or lymphadenopathy syndrome. *Lancet* 1:1253-6, 1984. Claude Bernard Hosp., Microbiol.-Virol. Lab. and Inst. Med. Trop. Epidemiol.; Pasteur Inst., Dept. Virol.; Dept. Publ. Hlth. Trop. Med., Immunol.-Nephrol. Lab.; Pitie-Salpetriere Hosp., Paris, France. 84-1914, 85-1825
33	100	133	**Burgess G M, Godfrey P P, McKinney J S, Berridge M J, Irvine R F & Putney J W.** The second messenger linking receptor activation to internal Ca release in liver. *Nature* 309:63-6, 1984. Med. Coll. Virginia, Dept. Pharmacol., Richmond, VA; Univ. Cambridge, Dept. Zool.; AFRC, Unit Invertebrate Chem. Physiol. and Inst. Anim. Physiol., UK. 84-0319, 85-0289

A	B	C	D
34	97	131	**Campisi J, Gray H E, Pardee A B, Dean M & Sonenshein G E.** Cell-cycle control of c-*myc* but not c-*ras* expression is lost following chemical transformation. *Cell* 36:241-7, 1984. Harvard Univ., Med. Sch.; Dana-Farber Cancer Inst., Div. Cell Growth Regulat.; Boston Univ., Med. Sch., Boston, MA. 85-0208
16	48	64	**Carroll M C, Campbell R D, Bentley D R & Porter R R.** A molecular map of the human major histocompatibility complex class III region linking complement genes C4, C2 and factor B. *Nature* 307:237-41, 1984. MRC, Immunochem. Unit; Oxford Univ., Dept. Biochem., UK. 85-0638
10	71	81	**Cheingsong-Popov R, Weiss R A, Dalgleish A, Tedder R S, Shanson D C, Jeffries D J, Ferns R B, Briggs E M, Weller I V D, Mitton S, Adler M W, Farthing C, Lawrence A G, Gazzard B G, Weber J, Harris J R W, Pinching A J, Craske J & Barbara J A J.** Prevalence of antibody to human T-lymphotropic virus type III in AIDS and AIDS-risk patients in Britain. *Lancet* 2:477-80, 1984. Inst. Cancer Res.: Royal Cancer Hosp., Chester Beatty Res. Inst.; Univ. London, Middlesex Hosp. Med. Sch., St. Stephen's Hosp. Med. Sch., and St. Mary's Hosp. Med. Sch., London; Withington Hosp., Labs. Regional Virus and Publ. Hlth., Manchester; N. London Blood Transfusion Ctr., Edgware, UK.
6	61	67	**Chiba K, Trevor A & Castagnoli N.** Metabolism of the neurotoxic tertiary amine, MPTP, by brain monoamine oxidase. *Biochem. Biophys. Res. Commun.* 120:574-8, 1984. Univ. California, Depts. Pharmacol. and Pharm. Chem., San Francisco, CA. 85-3538
23	76	99	**Chien Y-h, Gascoigne N R J, Kavaler J, Lee N E & Davis M M.** Somatic recombination in a murine T-cell receptor gene. *Nature* 309:322-6, 1984. Stanford Univ., Sch. Med., CA. 85-0178
4	85	89	**Chien Y-h, Becker D M, Lindsten T, Okamura M, Cohen D I & Davis M M.** A third type of murine T-cell receptor gene. *Nature* 312:31-5, 1984. Stanford Univ., Sch. Med., CA. 85-0178
10	62	72	**Church G M & Gilbert W.** Genomic sequencing. *Proc. Nat. Acad. Sci. USA* 81:1991-5, 1984. Harvard Univ., Biol. Labs.; Biogen Inc., Cambridge, MA.
26	62	88	**Clumeck N, Sonnet J, Taelman H, Mascart-Lemone F, De Bruyere M, Vandeperre P, Dasnoy J, Marcelis L, Lamy M, Jonas C, Eyckmans L, Noel H, Vanhaeverbeek M & Butzler J-P.** Acquired immunodeficiency syndrome in African patients. *N. Engl. J. Med.* 310:492-7, 1984. Saint Pierre Hosp., Div. Infect. Dis.; Saint-Luc Hosp., Depts. Med., Hematol., Virol., and Pathol.; Brugmann Hosp., Dept. Med.; Anderlecht Hosp., Dept. Med., Brussels; Inst. Trop. Dis., Dept. Med., Antwerp, Belgium. 84-3901, 85-2553
26	96	122	**Cochet C, Gill G N, Meisenhelder J, Cooper J A & Hunter T.** C-kinase phosphorylates the epidermal growth factor receptor and reduces its epidermal growth factor-stimulated tyrosine protein kinase activity. *J. Biol. Chem.* 259:2553-8, 1984. Univ. California, San Diego, Sch. Med., La Jolla; Salk Inst. Biol. Stud., Labs. Molec. Biol. and Virol., San Diego, CA. 85-0289
8	54	62	**Corcoran L M, Adams J M, Dunn A R & Cory S.** Murine T-lymphomas in which the cellular *myc* oncogene has been activated by retroviral insertion. *Cell* 37:113-22, 1984. Royal Melbourne Hosp., Walter and Eliza Hall Inst. Med. Res. and Melbourne Tumor Biol. Unit, Parkville; Ludwig Inst. Cancer Res., Sydney, Australia. 85-0208
64	111	175	**Curran J W, Lawrence D N, Jaffe H, Kaplan J E, Zyla L D, Chamberland M, Weinstein R, Lui K-J, Schonberger L B, Spira T J, Alexander W J, Swinger G, Ammann A, Solomon S, Auerbach D, Mildvan D, Stoneburner R, Jason J M, Haverkos H W & Evatt B L.** Acquired immunodeficiency syndrome (AIDS) associated with transfusions. *N. Engl. J. Med.* 310:69-75, 1984. CDC, AIDS Prog., Atlanta, GA; Michael Reese Hosp., Dept. Intern. Med., Chicago, IL; NY City Dept. Hlth.; Beth Israel Med. Ctr., NY; Tennessee Dept. Publ. Hlth., Nashville, TN; Jefferson Cnty. Dept. Publ. Hlth., Birmingham, AL; Univ. California, Med. Ctr., San Francisco, CA. 84-1914, 85-0745
49	111	160	**Currie M G, Geller D M, Cole B R, Siegel N R, Fok K F, Adams S P, Eubanks S R, Galluppi G R & Needleman P.** Purification and sequence analysis of bioactive atrial peptides (atriopeptins). *Science* 223:67-9, 1984. Washington Univ., Sch. Med.; Monsanto Co., Molec. Biol. Dept., St. Louis, MO. 84-4992, 85-1307
16	136	152	**Dinarello C A.** Interleukin-1. *Rev. Infec. Dis.* 6:51-95, 1984. Tufts Univ., Sch. Med., Boston, MA. 85-1379
115	249	364	**Downward J, Yarden Y, Mayes E, Scrace G, Totty N, Stockwell P, Ullrich A, Schlessinger J & Waterfield M D.** Close similarity of epidermal growth factor receptor and v-*erb-B* oncogene protein sequences. *Nature* 307:521-7, 1984. Imperial Cancer Res. Fund, Protein Chem. Lab., London, UK; Weizmann Inst. Sci., Dept. Chem. Immunol., Rehovot, Israel; Genentech Inc., San Francisco, CA. 84-1033, 85-2623
19	55	74	**Emerson B M & Felsenfeld G.** Specific factor conferring nuclease hypersensitivity at the 5 end of the chicken adult β-globin gene. *Proc. Nat. Acad. Sci. USA* 81:95-9, 1984. NIH, NIADDKD, Bethesda, MD. 85-0540

A	B	C	D
49	125	174	**Fauci A S, Macher A M, Longo D L, Lane H C, Rook A H, Masur H & Gelmann E P.** Acquired immunodeficiency syndrome: epidemiologic, clinical, immunologic, and therapeutic considerations. *Ann. Intern. Med.* 100:92-106, 1984. NIH, Clin. Ctr., Bethesda, MD. 85-5383
12	57	69	**Feorino P M, Kalyanaraman V S, Haverkos H W, Cabradilla C D, Warfield D T, Jaffe H W, Harrison A K, Gottlieb M S, Goldfinger D, Chermann J-C, Barre-Sinoussi F, Spira T T, McDougal J S, Curran J W, Montagnier L, Murphy F A & Francis D P.** Lymphadenopathy associated virus infection of a blood donor-recipient pair with acquired immunodeficiency syndrome. *Science* 225:69-72, 1984. CDC, Ctr. Infect. Dis., Atlanta, GA; Univ. California, Sch. Med.; Cedars-Sinai Med. Ctr., Los Angeles, CA; Pasteur Inst., Dept. Virol., Paris, France. 85-1825
21	49	70	**Finer-Moore J & Stroud R M.** Amphipathic analysis and possible formation of the ion channel in an acetylcholine receptor. *Proc. Nat. Acad. Sci. USA* 81:155-9, 1984. Univ. California, Sch. Med., San Francisco, CA. 85-1426
19	76	95	**Fung M C, Hapel A J, Ymer S, Cohen D R, Johnson R M, Campbell H D & Young I G.** Molecular cloning of cDNA for murine interleukin-3. *Nature* 307:233-7, 1984. Australian Natl. Univ., John Curtin Sch. Med. Res., Canberra, Australia. 85-3101
115	404	519	**Gallo R C, Salahuddin S Z, Popovic M, Shearer G M, Kaplan M, Haynes B F, Palker T J, Redfield R, Oleske J, Safai B, White G, Foster P & Markham P D.** Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS. *Science* 224:500-3, 1984. NIH, NCI, Bethesda; Litton Bionet., Inc., Dept. Cell Biol., Kensington, MD; North Shore Univ. Hosp., Div. Infect. Dis., Manhasset; Mem. Sloan-Kettering Cancer Ctr., Dermatol. Serv., New York, NY; Duke Univ., Sch. Med., Durham; Univ. North Carolina, Dept. Med., Chapel Hill, NC; Walter Reed Army Inst. Res., Dept. Virus Dis., Washington, DC; Univ. Med. Dent. New Jersey, Div. Allergy, Immunol. Infect. Dis., Newark, NJ. 84-1914, 85-1825
9	60	69	**Gascoigne N R J, Chien Y-h, Becker D M, Kavaler J & Davis M M.** Genomic organization and sequence of T-cell receptor β-chain constant- and joining-region genes. *Nature* 310:387-91, 1984. Stanford Univ., Sch. Med., CA. 85-0178
17	136	153	**Gilman A G.** G-proteins and dual control of adenylate cyclase. *Cell* 36:577-9, 1984. Univ. Texas, Hlth. Sci. Ctr. and Southwestern Grad. Sch., Dallas, TX.
4	73	77	**Goedert J J, Biggar R J, Winn D M, Greene M H, Mann D L, Gallo R C, Sarngadharan M G, Weiss S H, Grossman R J, Bodner A J, Strong D M & Blattner W A.** Determinants of retrovirus (HTLV-III) antibody and immunodeficiency conditions in homosexual men. *Lancet* 2:711-6, 1984. NIH, NCI; Univ. Hlth. Sci., Uniformed Serv., Bethesda; Litton Bionet., Inc., Dept. Cell Biol., Kensington; Biotech Res. Labs., Inc., Rockville, MD. 85-1825
3	74	77	**Greenberg M E & Ziff E B.** Stimulation of 3T3 cells induces transcription of the c-*fos* proto-oncogene. *Nature* 311:433-8, 1984. NYU, Med. Ctr., NY. 85-0208
1	66	67	**Groopman J E, Salahuddin S Z, Sarngadharan M G, Markham P D, Gonda M, Sliski A & Gallo R C.** HTLV-III in saliva of people with AIDS-related complex and healthy homosexual men at risk for AIDS. *Science* 226:447-9, 1984. New Engl. Deaconess Hosp., Dept. Med., Boston, MA; NIH, NCI, Bethesda and Frederick; Litton Bionet., Inc., Dept. Cell Biol., Kensington, MD. 85-6135
4	77	81	**Halliwell B & Gutteridge J M C.** Oxygen toxicity, oxygen radicals, transition metals and disease. *Biochem. J.* 219:1-14, 1984. Univ. London, King's Coll.; Natl. Inst. Biol. Stand., London, UK. 85-2053
12	58	70	**Haseltine W A, Sodroski J, Patarca R, Briggs D, Perkins D & Wong-Staal F.** Structure of 3′ terminal region of type II human T lymphotropic virus: evidence for new coding region. *Science* 225:419-21, 1984. Harvard Univ., Med. Sch. and Sch. Publ. Hlth.; Dana-Farber Cancer Inst., Boston, MA; NIH, NCI, Bethesda, MD. 85-1825
10	59	69	**Hay R, Bohni P & Gasser S.** How mitochondria import proteins. *Acta Biochim. Biophys.* 779:65-87, 1984. Basel Univ., Biocenter, Switzerland. 85-6398
67	133	200	**Hedrick S M, Nielsen E A, Kavaler J, Cohen D I & Davis M M.** Sequence relationships between putative T-cell receptor polypeptides and immunoglobulins. *Nature* 308:153-8, 1984. NIH, NIAID, Bethesda, MD; Stanford Univ., Sch. Med., CA. 84-0171, 85-0178
58	133	191	**Hedrick S M, Cohen D I, Nielsen E A & Davis M M.** Isolation of cDNA clones encoding T cell-specific membrane-associated proteins. *Nature* 308:149-53, 1984. NIH, NIAID, Bethesda, MD; Stanford Univ., Sch. Med., CA. 84-0171, 85-0178
5	73	78	**Heikkila R E, Manzino L, Cabbat F S & Duvoisin R C.** Protection against the dopaminergic neurotoxicity of 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine by monoamine oxidase inhibitors. *Nature* 311:467-9, 1984. Univ. Med. Dent. New Jersey, Dept. Neurol., Newark; Rutgers Univ., Med. Sch., Piscataway, NJ. 85-3538
8	92	100	**Heldin C-H & Westermark B.** Growth factors: mechanism of action and relation to oncogenes. *Cell* 37:9-20, 1984. Uppsala Univ., Depts. Med. Physiol. Chem. and Pathol., Sweden.

A	B	C	D
19	67	86	**Iwashita S & Fox C F.** Epidermal growth factor and potent phorbol tumor promoters induce epidermal growth factor receptor phosphorylation in a similar but distinctively different manner in human epidermoid carcinoma A431 cells. *J. Biol. Chem.* 259:2559-67, 1984. Univ. California, Dept. Microbiol. and Molec. Biol. Inst., Los Angeles, CA. 85-0289
51	140	191	**Joseph S K, Thomas A P, Williams R J, Irvine R F & Williamson J R.** *myo*-Inositol 1,4,5-trisphosphate: a second messenger for the hormonal mobilization of intracellular Ca^{2+} in liver. *J. Biol. Chem.* 259:3077-81, 1984. Univ. Pennsylvania, Sch. Med., Philadelphia, PA; AFRC, Inst. Anim. Physiol., Cambridge, UK. 84-0319, 85-0289
34	95	129	**Kangawa K & Matsuo H.** Purification and complete amino acid sequence of α-human atrial natriuretic polypeptide (α-hANP). *Biochem. Biophys. Res. Commun.* 118:131-9, 1984. Miyazaki Med. Coll., Dept. Biochem., Japan. 84-4992, 85-1307
19	65	84	**Karin M, Haslinger A, Holtgreve H, Richards R I, Krauter P, Westphal H M & Beato M.** Characterization of DNA sequences through which cadmium and glucocorticoid hormones induce human metallothionein-II_A gene. *Nature* 308:513-9, 1984. Univ. Southern California, Sch. Med., Los Angeles, CA; Australian Natl. Univ., Res. Sch. Biolog. Sci., Canberra, Australia; Philipps Univ., Physiol. Chem. Inst., Marburg, FRG. 85-1677
20	81	101	**Kaufman J F, Auffray C, Korman A J, Shackelford D A & Strominger J.** The class II molecules of the human and murine major histocompatibility complex. *Cell* 36:1-13, 1984. Basel Inst. Immunol., Switzerland; Harvard Univ., Dept. Biochem. Molec. Biol., Cambridge, MA. 85-7037
31	122	153	**King W J & Greene G L.** Monoclonal antibodies localize oestrogen receptor in the nuclei of target cells. *Nature* 307:745-7, 1984. Univ. Chicago, Ben May Lab. Cancer Res., IL. 84-6753, 85-0822
15	79	94	**Klatzmann D, Barre-Sinoussi F, Nugeyre M T, Dauguet C, Vilmer E, Griscelli C, Brun-Vezinet F, Rouzioux C, Gluckman J C, Chermann J-C & Montagnier L.** Selective tropism of lymphadenopathy associated virus (LAV) for helper-inducer T lymphocytes. *Science* 225:59-63, 1984. Paris Univ., UER Pitie-Salpetriere; Pasteur Inst., Dept. Virol.; Hosp. Infant Dis., Dept. Pediat.; Claude Bernard Hosp., Virol. Lab., Paris, France. 85-1825
28	108	136	**Kozak M.** Compilation and analysis of sequences upstream from the translational start site in eukaryotic mRNAs. *Nucl. Acid Res.* 12:857-72, 1984. Univ. Pittsburgh, Dept. Biol. Sci., PA.
13	62	75	**Langston J W, Forno L S, Rebert C S & Irwin I.** Selective nigral toxicity after systemic administration of 1-methyl-4-phenyl-1,2,5,6-tetrahydropyrine (MPTP) in the squirrel monkey. *Brain Res.* 292:390-4, 1984. Santa Clara Valley Med. Ctr., Dept. Neurol., San Jose; Stanford Univ., Sch. Med.; Vet. Admin. Med. Ctr., Dept. Pathol., Palo Alto; SRI Intl., Menlo Park, CA. 84-3825, 85-3538
11	105	116	**Levy J A, Hoffman A D, Kramer S M, Landis J A, Shimabukuro J M & Oshiro L S.** Isolation of lymphocytopathic retroviruses from San Francisco patients with AIDS. *Science* 225:840-2, 1984. Univ. California, Sch. Med., San Francisco; California Dept. Hlth. Serv., Viral Rickettsial Dis. Lab., Berkeley, CA. 85-1825
7	59	66	**Lewis R A & Austen K F.** The biologically active leukotrienes: biosynthesis, metabolism, receptors, functions, and pharmacology. *J. Clin. Invest.* 73:889-97, 1984. Harvard Univ., Med. Sch. and Brigham and Women's Hosp., Boston, MA. 85-1368
15	67	82	**Macara I G, Marinetti G V & Balduzzi P C.** Transforming protein of avian sarcoma virus UR2 is associated with phosphatidylinositol kinase activity: possible role in tumorigenesis. *Proc. Nat. Acad. Sci. USA* 81:2728-32, 1984. Univ. Rochester, Sch. Med. Dent., NY. 85-6203
13	56	69	**Maki M, Takayanagi R, Misono K S, Pandey K N, Tibbetts C & Inagami T.** Structure of rat atrial natriuretic factor precursor deduced from cDNA sequence. *Nature* 309:722-4, 1984. Vanderbilt Univ., Sch. Med., Nashville, TN. 85-1307
10	59	69	**Malissen M, Minard K, Mjolsness S, Kronenberg M, Goverman J, Hunkapiller T, Prystowsky M B, Yoshikai Y, Fitch F, Mak T W & Hood L.** Mouse T cell antigen receptor: structure and organization of constant and joining gene segments encoding the β polypeptide. *Cell* 37:1101-10, 1984. Caltech, Div. Biol., Pasadena, CA; Univ. Chicago, Dept. Pathol., IL; Univ. Toronto, Ontario Cancer Inst., Canada. 85-0178
4	67	71	**Markey S P, Johannessen J N, Chiueh C C, Burns R S & Herkenham M A.** Intraneuronal generation of a pyridinium metabolite may cause drug-induced parkinsonism. *Nature* 311:464-7, 1984. NIH, NIMH, Bethesda, MD. 85-3538
14	55	69	**Marquardt H, Hunkapiller M W, Hood L E & Todaro G J.** Rat transforming growth factor type 1: structure and relation to epidermal growth factor. *Science* 223:1079-82, 1984. NIH, NCI, Frederick, MD; Caltech, Div. Biol., Pasadena, CA. 85-1294
19	46	65	**McGinnis W, Levine M S, Hafen E, Kuroiwa A & Gehring W J.** A conserved DNA sequence in homoeotic genes of the *Drosophila* Antennapedia and bithorax complexes. *Nature* 308:428-33, 1984. Basel Univ., Biocenter, Switzerland. 84-2344, 85-0374

A	B	C	D
7	69	76	**McGrath J P, Capon D J, Goeddel D V & Levinson A D.** Comparative biochemical properties of normal and activated human *ras* p21 protein. *Nature* 310:644-9, 1984. Genentech, Inc., Dept. Molec. Biol., San Francisco, CA. 85-0208
0	107	107	**Melton D A, Krieg P A, Rebagliati M R, Maniatis T, Zinn K & Green M R.** Efficient *in vitro* synthesis of biologically active RNA and RNA hybridization probes from plasmids containing a bacteriophage SP6 promoter. *Nucl. Acid Res.* 12:7035-56, 1984. Harvard Univ., Dept. Biochem. Molec. Biol., Cambridge, MA. 85-7714
15	65	80	**Merion R M, White D J G, Thiru S, Evans D B & Calne R Y.** Cyclosporine: five years experience in cadaveric renal transplantation. *N. Engl. J. Med.* 310:148-54, 1984. Univ. Cambridge, Depts. Surg. and Pathol.; Addenbrooke's Hosp., UK. 85-2493
2	62	64	**Meuer S C, Hussey R E, Fabbi M, Fox D, Acuto O, Fitzgerald K A, Hodgdon J C, Protentis J P, Schlossman S F & Reinherz E L.** An alternative pathway of T-cell activation: a functional role for the 50 kd T11 sheep erythrocyte receptor protein. *Cell* 36:897-906, 1984. Dana-Farber Cancer Inst., Div. Tumor Immunol.; Harvard Univ., Med. Sch., Boston, MA.
10	60	70	**Meuer S C, Hussey R E, Cantrell D A, Hodgdon J C, Schlossman S F, Smith K A & Reinherz E L.** Triggering of the T3-Ti antigen-receptor complex results in clonal T-cell proliferation through an interleukin 2-dependent autocrine pathway. *Proc. Nat. Acad. Sci. USA* 81:1509-13, 1984. Dana-Farber Cancer Inst., Div. Tumor Immunol.; Harvard Univ., Med. Sch., Boston, MA; Dartmouth Coll., Med. Sch., Hanover, NH. 85-3696
14	62	76	**Misono K S, Fukumi H, Grammer R T & Inagami T.** Rat atrial natriuretic factor: complete amino acid sequence and disulfide linkage essential for biological activity. *Biochem. Biophys. Res. Commun.* 119:524-9, 1984. Vanderbilt Univ., Sch. Med., Nashville, TN. 85-1307
13	53	66	**Murray H W, Rubin B Y, Masur H & Roberts R B.** Impaired production of lymphokines and immune (gamma) interferon in the acquired immunodeficiency syndrome. *N. Engl. J. Med.* 310:883-9, 1984. Cornell Univ. Med. Coll., Dept. Med.; NY Hosp.; Sloan-Kettering Inst. Cancer Res., New York, NY; NIH, Clin. Ctr., Bethesda, MD. 84-2324
58	465	523	**Nishizuka Y.** The role of protein kinase C in cell surface signal transduction and tumour promotion. *Nature* 308:693-8, 1984. Kobe Univ., Sch. Med.; Natl. Inst. Basic Biol., Dept. Cell Biol., Okazaki, Japan. 84-0319, 85-0289
2	98	100	**Nishizuka Y.** Turnover of inositol phospholids and signal transduction. *Science* 225:1365-70, 1984. Kobe Univ., Sch. Med.; Natl. Inst. Basic Biol., Okazaki, Japan.
3	60	63	**Padgett R A, Konarska M M, Grabowski P J, Hardy S F & Sharp P A.** Lariat RNA's as intermediates and products in the splicing of messenger RNA precursors. *Science* 225:898-903, 1984. MIT, Ctr. Cancer Res. and Dept. Biol., Cambridge, MA; SUNY, Stony Brook, NY. 85-0647
10	62	72	**Parker C S & Topol J.** A Drosophila RNA polymerase II transcription factor binds to the regulatory site of an hsp 70 gene. *Cell* 37:273-83, 1984. Caltech, Div. Chem., Pasadena, CA. 85-1677
18	61	79	**Petersen O H & Maruyama Y.** Calcium-activated potassium channels and their role in secretion. *Nature* 307:693-6, 1984. Univ. Liverpool, Physiol. Lab.; MRC, Secretory Cntrl. Res. Grp., Liverpool, UK. 84-8516, 85-0215
27	53	80	**Picard D & Schaffner W.** A lymphocyte-specific enhancer in the mouse immunoglobulin κ gene. *Nature* 307:80-2, 1984. Univ. Zurich, Molec. Biol. Inst. II, Switzerland.
13	57	70	**Piot P, Taelman H, Minlangu K B, Mbendi N, Ndangi K, Kalambayi K, Bridts C, Quinn T C, Feinsod F M, Wobin O, Mazebo P, Stevens W, Mitchell S & McCormick J B.** Acquired immunodeficiency syndrome in a heterosexual population in Zaire. *Lancet* 2:65-9, 1984. Inst. Trop. Med.; Univ. Antwerp, Belgium; Mama Yemo Hosp.; Univ. Kinshasa, Univ. Hosp., Zaire; NIH, NIAID, Bethesda, MD; CDC, Ctr. Infect. Dis., Atlanta, GA. 84-3901, 85-2553
89	326	415	**Popovic M, Sarngadharan M G, Read E & Gallo R C.** Detection, isolation, and continuous production of cytopathic retroviruses (HTLV-III) from patients with AIDS and pre-AIDS. *Science* 224:497-500, 1984. NIH, NCI, Bethesda; Litton Bionet., Inc., Dept. Cell Biol., Kensington, MD. 84-1914, 85-1825
19	68	87	**Prentki M, Biden T J, Janjic D, Irvine R F, Berridge M J & Wollheim C B.** Rapid mobilization of Ca^{2+} from rat insulinoma microsomes by inositol-1,4,5-trisphosphate. *Nature* 309:562-4, 1984. Univ. Geneva, Med. Biochem. Inst., Switzerland; AFRC, Inst. Anim. Physiol. and Unit Insect Neurophysiol. Pharmacol.; Univ. Cambridge, Dept. Zool., UK. 85-0289
11	62	73	**Quesada J R, Reuben J, Manning J T, Hersh E M & Gutterman J U.** Alpha interferon for induction of remission in hairy-cell leukemia. *N. Engl. J. Med.* 310:15-8, 1984. Univ. Texas, M.D. Anderson Hosp. Tumor Inst., Houston, TX. 85-0129
10	69	79	**Rosenberg S A, Grimm E A, McGrogan M, Doyle M, Kawasaki E, Koths K & Mark D F.** Biological activity of recombinant human interleukin-2 produced in *Escherichia coli*. *Science* 223:1412-5, 1984. NIH, NCI, Bethesda, MD; Cetus Corp., Emeryville, CA. 85-6121

A	B	C	D
4	78	82	**Ruskin B, Krainer A R, Maniatis T & Green M R.** Excision of an intact intron as a novel lariat structure during pre-mRNA splicing in vitro. *Cell* 38:317-31, 1984. Harvard Univ., Dept. Biochem. Molec. Biol., Cambridge, MA. 85-0647
20	96	116	**Safai B, Groopman J E, Popovic M, Schupbach J, Sarngadharan M G, Arnett K, Sliski A & Gallo R C.** Seroepidemiological studies of human T-lymphotropic retrovirus type III in acquired immunodeficiency syndrome. *Lancet* 1:1438-40, 1984. Mem. Sloan-Kettering Cancer Ctr., New York, NY; Litton Bionet., Inc., Dept. Cell Biol., Kensington; NIH, NCI, Bethesda, MD; New Engl.-Deaconess Hosp., Dept. Med., Boston, MA. 84-1914, 85-1825
20	71	91	**Saito H, Kranz D M, Takagaki Y, Hayday A C, Eisen H N & Tonegawa S.** Complete primary structure of a heterodimeric T-cell receptor deduced from cDNA sequences. *Nature* 309:757-62, 1984. MIT, Ctr. Cancer Res. and Dept. Biol., Cambridge, MA. 84-0171, 85-0178
4	81	85	**Saito H, Kranz D M, Takagaki Y, Hayday A C, Eisen H N & Tonegawa S.** A third rearranged and expressed gene in a clone of cytotoxic T lymphocytes. *Nature* 312:36-40, 1984. MIT, Ctr. Cancer Res. and Dept. Biol., Cambridge, MA. 85-0178
79	250	329	**Sarngadharan M G, Popovic M, Bruch L, Schupbach J & Gallo R C.** Antibodies reactive with human T-lymphotropic retroviruses (HTLV-III) in the serum of patients with AIDS. *Science* 224:506-8, 1984. Litton Bionet., Inc., Dept. Cell Biol., Kensington; NIH, NCI, Bethesda, MD. 84-1914, 85-1825
58	158	216	**Schupbach J, Popovic M, Gilden R V, Gonda M A, Sarngadharan M G & Gallo R C.** Serological analysis of a subgroup of human T-lymphotropic retroviruses (HTLV-III) associated with AIDS. *Science* 224:503-5, 1984. NIH, NCI, Bethesda and Frederick; Litton Bionet., Inc., Dept. Cell Biol., Kensington, MD. 84-1914, 85-1825
20	46	66	**Scott G B, Buck B E, Leterman J G, Bloom F L & Parks W P.** Acquired immunodeficiency syndrome in infants. *N. Engl. J. Med.* 310:76-81, 1984. Univ. Miami, Sch. Med., FL. 84-0752, 85-0745
17	83	100	**Seidah N G, Lazure C, Chretien M, Thibault G, Garcia R, Cantin M, Genest J, Nutt R F, Brady S F, Lyle T A, Paleveda W J, Colton C D, Ciccarone T M & Veber D F.** Amino acid sequence of homologous rat atrial peptides: natriuretic activity of native and synthetic forms. *Proc. Nat. Acad. Sci. USA* 81:2640-4, 1984. Clin. Res. Inst. Montreal, Protein Pituitary Hormone Lab. and MRC Grp. Hypertension, Canada; Merck Sharp & Dohme Res. Labs., West Point, PA. 85-1307
10	54	64	**Silverberg E.** Cancer statistics, 1984. *Ca-A Cancer J. Clin.* 34:7-23, 1984. American Cancer Soc., Dept. Epidemiol. Statist., New York, NY.
17	63	80	**Siu G, Clark S P, Yoshikai Y, Malissen M, Yanagi Y, Strauss E, Mak T W & Hood L.** The human T cell antigen receptor is encoded by variable, diversity, and joining gene segments that rearrange to generate a complete V-gene. *Cell* 37:393-401, 1984. Caltech, Div. Biol., Pasadena, CA; Univ. Toronto, Dept. Med. Biophys.; Ontario Cancer Inst., Canada. 85-0178
8	56	64	**Siu G, Kronenberg M, Strauss E, Haars R, Mak T W & Hood L.** The structure, rearrangement and expression of *D* gene segments of the murine T cell antigen receptor. *Nature* 311:344-50, 1984. Caltech, Div. Biol., Pasadena, CA; Columbia Univ., Coll. Physns. Surgs., New York, NY; Univ. Toronto, Dept. Med. Biophys.; Ontario Cancer Inst., Canada. 85-0178
28	84	112	**Slamon D J, deKernion J B, Verma I M & Cline M J.** Expression of cellular oncogenes in human malignancies. *Science* 224:256-62, 1984. Univ. California, Ctr. Hlth. Sci., Los Angeles; Salk Inst. Biol. Stud., San Diego, CA. 85-7317
15	56	71	**Smith D H, Wellde B T, Sabwa C L, Reardon M J & Hockmeyer W T.** A complement fixation test for visceral leishmaniasis using homologous parasite antigen II. *Ann. Trop. Med. Parasitol.* 78:495-500, 1984. Liverpool Sch. Trop. Med., Dept. Trop. Med., UK; Walter Reed Project, Nairobi, Kenya; Walter Reed Army Inst. Res., Washington, DC.
7	87	94	**Sodroski J G, Rosen C A & Haseltine W A.** *Trans*-acting transcriptional activation of the long terminal repeat of human T lymphotropic viruses in infected cells. *Science* 225:381-5, 1984. Dana-Farber Cancer Inst.; Harvard Univ., Med. Sch. and Sch. Publ. Hlth., Boston, MA. 85-1825
30	95	125	**Sugimoto Y, Whitman M, Cantley L C & Erikson R L.** Evidence that the Rous sarcoma virus transforming gene product phosphorylates phosphatidylinositol and diacylglycerol. *Proc. Nat. Acad. Sci. USA* 81:2117-21, 1984. Harvard Univ., Depts. Cell. Dev. Biol. and Biochem. Molec. Biol., Cambridge, MA. 85-6203
22	43	65	**Taub R, Moulding C, Battey J, Murphy W, Vasicek T, Lenoir G M & Leder P.** Activation and somatic mutation of the translocated c-*myc* gene in Burkitt lymphoma cells. *Cell* 36:339-48, 1984. Harvard Univ., Med. Sch., Boston, MA; Intl. Agcy. Res. Cancer, Lyon, France.
23	46	69	**Thibault G, Garcia R, Cantin M, Genest J, Lazure C, Seidah N G & Chretien M.** Primary structure of a high M_r form of rat atrial natriuretic factor. *FEBS Lett.*

A	B	C	D
			167:352-6, 1984. Clin. Res. Inst. Montreal, MRC Grp. Hypertension and Labs. Biochem. Molec. Neuroendocrinol., Canada. 85-1307
10	54	64	**Thomas A P, Alexander J & Williamson J R.** Relationship between inositol polyphosphate production and the increase of cytosolic free Ca^{2+} induced by vasopressin in isolated hepatocytes. *J. Biol. Chem.* 259:5574-84, 1984. Univ. Pennsylvania, Sch. Med., Philadelphia, PA. 85-0289
17	145	162	**Ullrich A, Coussens L, Hayflick J S, Dull T J, Gray A, Tam A W, Lee J, Yarden Y, Libermann T A, Schlessinger J, Downward J, Mayes E L V, Whittle N, Waterfield M D & Seeburg P H.** Human epidermal growth factor receptor cDNA sequence and aberrant expression of the amplified gene in A431 epidermoid carcinoma cells. *Nature* 309:418-25, 1984. Genentech, Inc., Dept. Molec. Biol., San Francisco, CA; Weizmann Inst. Sci., Dept. Chem. Immunol., Rehovot, Israel; Imperial Cancer Res. Fund, Protein Chem. Lab., London, UK. 85-2623
20	78	98	**Unanue E R, Beller D I, Lu C Y & Allen P M.** Antigen presentation: comments on its regulation and mechanism. *J. Immunol.* 132:1-5, 1984. Harvard Univ., Med. Sch., Boston, MA.
18	63	81	**Van de Werf F, Ludbrook P A, Bergmann S R, Tiefenbrunn A J, Fox K A A, de Geest H, Verstraete M, Collen D & Sobel B E.** Coronary thrombolysis with tissue-type plasminogen activator in patients with evolving myocardial infarction. *N. Engl. J. Med.* 310:609-13, 1984. Washington Univ., Sch. Med., St. Louis, MO; Univ. Louvain, Belgium. 85-0829
55	96	151	**Vilmer E, Rouzioux C, Brun F V, Fischer A, Chermann J C, Barre-Sinoussi F, Gazengel C, Dauguet C, Manigne P, Griscelli C & Montagnier L.** Isolation of new lymphotropic retrovirus from two siblings with haemophilia B, one with AIDS. *Lancet* 1:753-7, 1984. Hosp. Child. Dis., Pediat. Immunol. Hematol. Unit; Pasteur Inst., Dept. Virol.; Claude Bernard Hosp., Cent. Virol. Lab., Paris, France. 84-1914, 85-1825
11	129	140	**Walker G C.** Mutagenesis and inducible responses to deoxyribonucleic acid damage in *Escherichia coli*. *Microbiol. Rev.* 48:60-93, 1984. MIT, Dept. Biol., Cambridge, MA. 85-0730
27	105	132	**Welshons W V, Lieberman M E & Gorski J.** Nuclear localization of unoccupied oestrogen receptors. *Nature* 307:747-9, 1984. Univ. Wisconsin, Depts. Biochem., Human Oncol., and Anim. Sci., Madison, WI. 84-6753, 85-0822
11	57	68	**Yamanaka M, Greenberg B, Johnson L, Seilhamer J, Brewer M, Friedemann T, Miller J, Atlas S, Laragh J, Lewicki J & Fiddes J.** Cloning and sequence analysis of the cDNA for the rat atrial natriuretic factor precursor. *Nature* 309:719-22, 1984. California Biotechnol. Inc., Mountain View, CA; Cornell Univ. Med. Coll., Hypertension Ctr.; NY Hosp., New York, NY. 85-1307
70	176	246	**Yanagi Y, Yoshikai Y, Leggett K, Clark S P, Aleksander I & Mak T W.** A human T-cell-specific cDNA clone encodes a protein having extensive homology to immunoglobulin chains. *Nature* 308:145-9, 1984. Ontario Cancer Inst.; Univ. Toronto, Dept. Med. Biophys., Canada. 84-0171, 85-0178