Current Comments®

EUGENE GARFIELD
INSTITUTE FOR SCIENTIFIC INFORMATION®
3501 MARKET ST., PHILADELPHIA, PA 19104

The Most-Cited 1985 Life-Sciences Articles Highlight Signal Transduction, Atrial Natriuretic Factor, and AIDS Research

Number 41 October 12, 1987

This is the ninth consecutive year that we have published our annual hit parade of putative *Citation Classics*®. For those who have followed this series regularly it will come as no surprise that citation frequency is not an absolute indicator of the most important papers in a particular year. Furthermore, the most-cited articles for that year do not necessarily include all those that will later turn into classics. It is impossible to predict the papers not included in this list that will suddenly or gradually become important in the future. As in popular music, the hot tunes of today may be forgotten in a few years, and oldies may have a revival. But these qualifications have never diminished our interest in the lists of current best-sellers.

The 100 most-cited 1985 life-sciences articles appear in the Bibliography at the end of this essay. They are listed alphabetically by first author. These papers attracted immediate and widespread attention in the science community because they represent "hot," growing, new, or controversial research areas. Papers on signal transduction, atrial natriuretic factor (ANF), and acquired immunodeficiency syndrome (AIDS) have turned up in the two most recent studies in our series.[1,2] That pattern demonstrates not only widespread research activity but also indicates there is no sign of lessening in the near future. This illustrates how these studies document the progress or decline of hot research areas and can be combined with other indicators to mold science policy and research administration.

Research Fronts

To categorize these papers into broad subject areas, we used ISI®'s database of research fronts. Table 1 lists 15 fronts that include at least two papers from the Bibliography as core documents. The size of these fronts is determined by the number of published, or citing, documents. The largest front identified involves "Protein kinase-C activity, calcium mobilization, and inositol phosphorylation stimulated by phorbol ester receptors" (#86-1983). Over 2,000 papers were published on this topic. The front itself was identified by the same basic co-citation clustering methods we have discussed before. Of the 45 papers in the "core" cluster, 3 are listed in the Bibliography.

The most cited of these is by William L. Farrar, Laboratory of Molecular Immunoregulation, National Cancer Institute (NCI)-Frederick Cancer Research Facility, Frederick, Maryland, and Wayne B. Anderson, Laboratory of Tumor Immunology and Biology, NCI, Bethesda, Maryland. They found that the regulatory peptide interleukin-2 combines with its specific receptor to cause protein kinase-C to be transported to the plasma membrane. This interaction plays a crucial role in signal transduction, the body's signaling system for controlling cellular processes such as metabolism, secretion, contraction, and cell growth. This paper was cited by over 90 papers in 1985 and 1986, and it has been cited over 55 times in the first four months of 1987.

Atrial Natriuretic Factor Studies

Our study of 1985 papers also shows that ANF has developed into one of the most active areas of research, with 10 percent of the papers in the Bibliography dealing with this topic. ANF studies first appeared in our analysis of 1984 papers.[2]

Early hormone research concentrated on the hormones secreted by the endocrine system, such as the pituitary and thyroid glands. In recent years, there has been increased interest in hormones produced by organs outside of the endocrine system. One such hormone is ANF, which is secreted by the atrium of the heart. It plays a key role in the regulation of blood pressure, sodium, and volume homeostasis. The most-cited 1985 ANF paper was published by R.E. Lang and colleagues, German Institute for High Blood Pressure Research and the Department of Pharmacology, University of Heidelberg, Federal Republic of Germany. This study demonstrates that an increase in body-fluid volumes causes an increase in the concentration of ANF in the blood. Cited 200 times, this paper is 1 of 8 core papers related to "Specific binding sites and systemic and renal hemodynamic effects of rat and human ANF" (#86-1290); 625 papers were published on this topic in 1986 alone. Note that this paper was already a core paper in 1985, and in 1987 it continues to be cited quite heavily.

In a research survey featured in the first edition of the *ISI Atlas of Science®: Pharmacology*, John H. Laragh, Cardiovascular Center, New York Hospital-Cornell University Medical Center, New York, notes that "although a vast amount of information has accumulated over the past five years, a more complete understanding of the role of [ANF] in normal physiology and in disease is needed before it is possible to determine the therapeutic potential of this exciting new hormone."[3] I've discussed the *Atlas of Science* on numerous occasions.[4] In 1987 we officially launched the first section covering pharmacology. In 1988 three new sections on biochemistry, immunology, and animal and plant science will be published.

AIDS Research

AIDS, the disease that has reached frightening proportions worldwide, continues to be an increasingly active research topic. AIDS was first recognized as a new disease entity in the US in 1981. In 1983 research suggested that the causative agent of the disease might be a human retrovirus. In 1983 and 1984 this agent was isolated and called a variety of names including human T-cell lymphotropic virus type III (HTLV-III) and lymphadenopathy-associated virus (LAV).

By 1985 scientists were concentrating on the molecular characteristics of the virus. For example, Mark A. Muesing, Genentech, Inc., San Francisco, California, and colleagues determined the entire nucleotide sequence for the RNA present in HTLV-III virus particles. Their results showed that the AIDS agent is not similar to previously characterized animal and human retroviruses.

After five years of intense research in a variety of AIDS-related fields, scientists needed to step back to assess the research that had been done and plan the direction that future research should take. This is apparent in the number of AIDS-related progress reports that appear in our 1985 most-cited list. These articles do not report new research. Primarily they compile information regarding the status of research data on the disease. For example, a team from the Centers for Disease Control, Atlanta, Georgia, led by James W. Curran, published a paper in *Science* called "The epidemiology of AIDS: current status and future prospects." This article documents the history of the disease in the US, as well as the magnitude of the problem and the state of current research.

The year 1985 also marked the development of an effective screening test for AIDS antibodies. A team led by Stanley H. Weiss, Environmental Epidemiology Branch, NCI, evaluated an enzyme-linked immunosorbent assay (ELISA) that is very specific and sensitive for AIDS antibodies.

While AIDS research has made startling advances in a relatively short period of time, I suspect that this mission-oriented speedy

Table 1: The 1985 and 1986 *SCI®/SSCI®* research fronts that include at least two of the 1985 most-cited life-sciences papers as core documents. A=number of papers in the Bibliography included in the core of each research front. B=total number of core documents. C=total number of 1985 or 1986 citing documents for the year designated by the prefix in the research-front number.

Number	Name	A	B	C
85-1307	Biological activity, receptor distribution, and the systemic and renal hemodynamic effects of ANF	2	45	319
85-1825	Effects of leukemia virus and other retroviruses on human T-cells in patients with leukemia and AIDS	6	56	1,118
86-0192	Characterization and production of human tumor necrosis factor; related cytotoxic activity by macrophages	2	24	377
86-0403	Embryogenesis of *Drosophila* and expression of homeotic genes	2	20	357
86-0494	Analysis of muscular dystrophy and other genetic diseases with prenatal diagnosis using DNA probes	2	35	545
86-0547	Expression and regulation of c-*myc* gene and other oncogenes in human and mouse cells	2	41	945
86-0558	Structure and expression of HTLV-III and other retroviruses associated with AIDS in patients with AIDS and related syndromes	9	54	1,198
86-0633	T-cell antigen receptor gene expression in the activation and function of cytotoxic T-cells	5	59	1,234
86-1290	Specific binding sites and systemic and renal hemodynamic effects of rat and human ANF	8	57	625
86-1983	Protein kinase-C activity, calcium mobilization, and inositol phosphorylation stimulated by phorbol ester receptors	3	45	2,093
86-2283	Pre-messenger RNA splicing *in vitro* and cleavage at splice sites; nucleotide sequences in RNA transcription	4	32	1,200
86-2851	Inhibition of adenylate cyclase activity by guanine nucleotide-binding protein, pertussis toxin, and other proteins	4	33	753
86-3713	Biochemistry, function, and effects of ANF	3	3	212
86-3728	Expression of human *ras* protein and other proteins; their role in transforming genes	2	26	569
86-4303	Expression and structure of platelet-derived growth factor, receptor proto-oncogene feline McDonough sarcoma (FMS), and other cell-transforming growth factors	3	13	694

progress would not have occurred if there had not previously been a burgeoning interest in the immune system over the last 20 years. The present-day AIDS research is indebted to the foundation of immunology knowledge established largely for the simple purpose of furthering basic research.

Our study identifies only two research fronts on AIDS, while there were five fronts included in last year's study of 1984 papers. Although this might suggest that AIDS research is on the decline, that is by no means the case. In the 1984 study, five fronts were cited by about 1,200 papers in 1985.[2] In contrast, the two fronts listed in Table 1 include over 2,300 citing documents. Perhaps more relevant is the number of papers published in 1986 on other aspects of AIDS research, which are not necessarily highlighted by the selections listed above. Were we reporting on everything related to AIDS, there would be dozens of topics that would not fall into the highly selective group of 1986 research topics represented by this particular group of papers.

The largest AIDS front in Table 1 concerns the "Structure and expression of HTLV-III and other retroviruses associated with AIDS in patients with AIDS and related syndromes" (#86-0558). The paper by George M. Shaw, NCI, and colleagues is 1 of 54 "older" core documents identifying this front of current papers. The results from Shaw's study indicate that HTLV-III may have a role in encephalopathy, a form of dementia that occurs in AIDS patients. Cited 201 times, this paper is the third most-cited article in this study.

D. Carleton Gajdusek, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, who coauthored this paper, is one of two Nobelists listed in the Bibliography. Gajdusek shared the 1976 Nobel in physiology or medicine with

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	75	7	Denmark, Finland, France, Israel, Japan, Switzerland
UK	8	0	
Switzerland	6	1	US
Japan	5	2	US
France	3	1	US
Finland	2	1	US
Australia	1	0	
Belgium	1	0	
Canada	1	0	
Denmark	1	1	US
FRG	1	0	
Israel	1	1	US
New Zealand	1	0	
Sweden	1	0	

Table 3: The 25 journals that published the 1985 life-sciences papers most cited in the *SCI®*, 1985-1986. The numbers in parentheses are the 1985 impact factors for the journals. (The 1985 impact factor equals the number of 1985 citations received by the 1983-1984 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 how many papers from each journal appear in the Bibliography.

Journal	Number of Papers
Nature (12.9)	30
Science (10.9)	17
Cell (18.9)	14
N. Engl. J. Med. (19.2)	8
J. Biol. Chem. (6.2)	5
Lancet (12.2)	4
Proc. Nat. Acad. Sci. USA (9.4)	3
Annu. Rev. Biochem. (39.7)	2
Amer. J. Physiol. (3.0)	1
Ann. Intern. Med. (9.5)	1
Biochem. J. (3.7)	1
Ca—A Cancer J. Clin. (3.6)	1
DNA—J. Molec. Biol. (4.7)	1
Endocrine Rev. (9.2)	1
Gene (4.3)	1
Hypertension (4.0)	1
J. Clin. Invest. (6.9)	1
J. Exp. Med. (11.2)	1
JAMA—J. Am. Med. Assn. (4.2)	1
Kidney Int. (4.9)	1
Microbiol. Rev. (28.8)	1
Neuroendocrinology (3.9)	1
Nucl. Acid. Res. (6.1)	1
Plasmid (3.0)	1
Trends Genet. (N/A)	1

Baruch S. Blumberg, Institute for Cancer Research, Philadelphia. Gajdusek's work implicated slow-acting viruses as causal agents in degenerative neurologic disorders.

Walter Gilbert, H.H. Timken Professor of Science, Harvard University, Cambridge, Massachusetts, shared the 1980 Nobel Prize in chemistry with Paul Berg, Stanford University School of Medicine, California, and Frederick Sanger, Laboratory of Molecular Biology, Medical Research Council, Cambridge, UK. Gilbert has become one of America's most visible scientists, and he might be characterized as the prototypic science entrepreneur. With his new company, the Genome Corporation, he hopes not only to map and sequence human genes but also to copyright these discoveries. The ethical and economic issues involved in monopolizing new chemical and biological discoveries have long been controversial. Mapping the human genome only accentuates the ethical dilemma involved.[5]

In addition to the Nobel Prize, the authors in the Bibliography have received other coveted awards. Just to name a few, J. Michael Bishop, professor of microbiology and immunology, University of California, San Francisco, was awarded the Albert Lasker Basic Medical Research Award in 1982. In 1984 he received the Hammer Prize in Cancer and the Gairdner Foundation International Award of Merit. Hiroshi Nikaido, professor of microbiology, University of California, Berkeley, received the Paul Ehrlich-Ludwig Darmstaedter Prize in 1969.

Author Information

Our 1985 list contains 514 unique authors affiliated with 101 institutions from 14 countries. Table 2 provides the number of papers produced by authors affiliated with institutions in each nation. US-affiliated authors appear in 75 papers, 7 of which were coauthored with scientists affiliated with institutions in Denmark, Finland, France, Israel, Japan, and Switzerland.

As in our past studies, the National Institutes of Health (NIH) leads the list, appear-

ing 18 times. Fifteen of these papers are from the NCI division. Most of the papers that include authors from NIH deal with AIDS. Of 17 AIDS papers in the Bibliography, 11 were authored by NIH scientists. The University of California and Harvard appear in the Bibliography 13 and 8 times, respectively.

All but six of the papers in the Bibliography have more than one author. Eighteen papers have two authors, 16 papers have three authors, and 16 papers have four authors. Two papers have 19 authors. Thirty-one authors have more than one paper listed in the Bibliography. The two most prolific authors in our study are AIDS researchers from NCI: Flossie Wong-Staal coauthored 7 papers, while 8 papers were coauthored by Robert C. Gallo.

Noteworthy Papers

The 100 papers in the Bibliography were published in the 25 journals listed in Table 3. As in past studies, over 60 percent of the papers were published in *Nature* (30 papers), *Science* (17 papers), or *Cell* (14 papers). Table 3 also includes 1985 impact factors, calculated by dividing the 1985 citations to 1983 and 1984 articles published in a journal by the number of articles published by that journal in those two years.

In our study of 1984 papers, we highlighted the work of J. Downward, Protein Chemistry Laboratory, Imperial Cancer Research Fund, London, UK, and colleagues.[2] The study showed that the human epidermal growth factor (EGF) receptor has structural or sequence homologies with the tyrosine kinase family of oncogenes.[6] The second most-cited paper in the Bibliography, by A. Ullrich, Departments of Molecular Biology and Protein Biochemistry, Genentech, and colleagues reveals that the human insulin receptor shows amino-acid sequences similar to EGF and the tyrosine kinase family. Understanding the amino-acid sequence of insulin will help to define the molecular mechanisms of insulin action. Cited 228 times, this paper is core to the front on "Expression and structure of platelet-derived growth factor, receptor proto-oncogene feline McDonough sarcoma (FMS), and other cell-transforming growth factors" (#86-4303).

The paper by Alec J. Jeffreys, Department of Genetics, University of Leicester, UK, and colleagues describes the discovery of a DNA "fingerprint" technique that is specific for each individual. The authors note that this technique may "provide a powerful method for paternity and maternity testing, can be used in forensic applications and might also be useful in detecting inbreeding between couples who have had an affected offspring possibly caused by an autosomal recessive gene carried by both parents."[7]

The most-cited paper in this study is by Celeste Yanisch-Perron, Jeffrey Vieira, and Joachim Messing, Department of Biochemistry, University of Minnesota, St. Paul. This paper discusses improvements to a DNA-cloning system that relies on bacteriophage M13 and its host, *Escherichia coli*. The cloning of unmodified DNA and of repetitive sequences was improved by the development of new mutant *E. coli* strains, each of which helps prevent certain previously encountered cloning problems. In addition, the complete nucleotide sequences of two M13 cloning vectors were compiled and published, and full-length M13 clones suitable for sequencing were obtained via a new method.

Conclusion

If we had the resources, it would be gratifying to form a Delphic group to forecast which of the studies we have identified will prove to be the fountainhead of exploitable research areas in years to come. Funding agencies, including governments and investment bankers, would like to know where to invest their funds to maximize scientific employment and wealth opportunities. But there is no certainty in such forecasting. Intuition is often as crucial as market research in these decisions. All that scientometrics can provide today is a more informed basis for decision making. Conservative investors base their decisions on past performance.

High-risk investors look for sleepers. Our annual most-cited lists cover current hot topics and discoveries. Our most-cited studies covering a broader time period include articles with an active past performance as well as some that were once sleepers but have since become active. The *ISI Atlas of Science*, mentioned earlier, draws on our citation-frequency data to map activity in science. This helps both the conservative and high-risk research manager to make informed decisions concerning the best areas to invest funds or expend research effort. Have fun!

* * * * *

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

REFERENCES

1. **Garfield E.** The 1983 articles most cited in 1983 and 1984. 1. Life sciences. *Essays of an information scientist: ghostwriting and other essays.* Philadelphia: ISI Press, 1985. Vol. 8. p. 444-59.
2. ----------. The most-cited 1984 life-sciences articles highlight AIDS research. *Current Contents* (49):3-17, 8 December 1986.
3. **Laragh J H.** Atrial natriuretic peptides. *ISI Atlas of Science: Pharmacology* 1(1):33-9, 1987.
4. **Garfield E.** Launching the *ISI Atlas of Science*: for the new year, a new generation of reviews. *Current Contents* (1):3-8, 5 January 1987.
5. **Roberts L.** Who owns the human genome? *Science* 237(4813):358-61, 1987.
6. **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.
7. **Jeffreys A J, Wilson V & Thein S L.** Hypervariable 'minisatellite' regions in human DNA. *Nature* 314:67-73, 1985.

Bibliography: The 1985 life-sciences articles most cited in the *SCI®*, 1985-1986. Articles are listed in alphabetic order by first author. Research-front numbers indicate the 1985 and 1986 *SCI/SSCI®* research-front specialties for which these are core papers. A=number of 1985 cites. B=number of 1986 cites. C=total number of 1985-1986 cites.

A	B	C	Bibliographic Data
16	54	70	**Aggarwal B B, Kohr W J, Hass P E, Moffat B, Spencer S A, Henzel W J, Bringman T S, Nedwin G E, Goeddel D V & Harkins R N.** Human tumor necrosis factor: production, purification, and characterization. *J. Biol. Chem.* 260:2345-54, 1985. 86-0192
11	60	71	**Arya S K, Guo C, Josephs S F & Wong-Staal F.** *Trans*-activator gene of human T-lymphotropic virus type III (HTLV-III). *Science* 229:69-73, 1985. 86-0558
26	56	82	**Beachy P A, Helfand S L & Hogness D S.** Segmental distribution of bithorax complex proteins during *Drosophila* development. *Nature* 313:545-51, 1985. 86-0403
5	144	149	**Birnstiel M L, Busslinger M & Strub K.** Transcription termination and 3′ processing: the end is in site! *Cell* 41:349-59, 1985. 86-2283
2	85	87	**Bishop J M.** Viral oncogenes. *Cell* 42:23-38, 1985.
17	55	72	**Boeke J D, Garfinkel D J, Styles C A & Fink G R.** Ty elements transpose through an RNA intermediate. *Cell* 40:491-500, 1985. 86-1655
23	72	95	**Brain S D, Williams T J, Tippins J R, Morris H R & MacIntyre I.** Calcitonin gene-related peptide is a potent vasodilator. *Nature* 313:54-6, 1985. 86-0721
11	59	70	**Brody E & Abelson J.** The "spliceosome": yeast pre-messenger RNA associates with a 40*S* complex in a splicing-dependent reaction. *Science* 228:963-7, 1985. 86-2283
14	117	131	**Cantin M & Genest J.** The heart and the atrial natriuretic factor. *Endocrine Rev.* 6:107-27, 1985. 86-3713
16	56	72	**Ceredig R, Lowenthal J W, Nabholz M & MacDonald H R.** Expression of interleukin-2 receptors as a differentiation marker on intrathymic stem cells. *Nature* 314:98-100, 1985. 86-0633
22	68	90	**Cerutti P A.** Prooxidant states and tumor promotion. *Science* 227:375-81, 1985. 86-3901
5	67	72	**Chen E Y & Seeburg P H.** Supercoil sequencing: a fast and simple method for sequencing plasmid DNA. *DNA—J. Molec. Biol.* 4:165-70, 1985.

A	B	C	Bibliographic Data
26	142	168	**Cockcroft S & Gomperts B D.** Role of guanine nucleotide binding protein in the activation of polyphosphoinositide phosphodiesterase. *Nature* 314:534-6, 1985. 86-2851
26	66	92	**Cooper D A, Maclean P, Finlayson R, Michelmore H M, Gold J, Donovan B, Barnes T G, Brooke P & Penny R.** Acute AIDS retrovirus infection. *Lancet* 1:537-40, 1985.
23	66	89	**Croce C M, Isobe M, Palumbo A, Puck J, Ming J, Tweardy D, Erikson J, Davis M & Rovera G.** Gene for α-chain of human T-cell receptor: location on chromosome 14 region involved in T-cell neoplasms. *Science* 227:1044-7, 1985. 86-1364
4	78	82	**Curran J W, Morgan W M, Hardy A M, Jaffe H W, Darrow W W & Dowdle W R.** The epidemiology of AIDS: current status and future prospects. *Science* 229:1352-7, 1985.
29	45	74	**Dale R M K, McClure B A & Houchins J P.** A rapid single-stranded cloning strategy for producing a sequential series of overlapping clones for use in DNA sequencing: application to sequencing the corn mitochondrial 18 S rDNA. *Plasmid* 13:31-40, 1985.
5	109	114	**Dynan W S & Tijian R.** Control of eukaryotic messenger RNA synthesis by sequence-specific DNA-binding proteins. *Nature* 316:774-8, 1985.
15	88	103	**Ebina Y, Ellis L, Jarnagin K, Edery M, Graf L, Clauser E, Ou J-h, Masiarz F, Kan Y W, Goldfine I D, Roth R A & Rutter W J.** The human insulin receptor cDNA: the structural basis for hormone-activated transmembrane signalling. *Cell* 40:747-58, 1985. 86-4303
29	60	89	**Ephrussi A, Church G M, Tonegawa S & Gilbert W.** B lineage-specific interactions of an immunoglobulin enhancer with cellular factors in vivo. *Science* 227:134-40, 1985. 86-1674
12	79	91	**Farrar W L & Anderson W B.** Interleukin-2 stimulates association of protein kinase C with plasma membrane. *Nature* 315:233-5, 1985. 86-1983
5	62	67	**Fauci A S, Masur H, Gelmann E P, Markham P D, Hahn B H & Lane H C.** The acquired immunodeficiency syndrome: an update. *Ann. Intern. Med.* 102:800-13, 1985.
15	71	86	**Feizi T.** Demonstration by monoclonal antibodies that carbohydrate structures of glycoproteins and glycolipids are onco-developmental antigens. *Nature* 314:53-7, 1985.
19	52	71	**Feorino P M, Jaffe H W, Palmer E, Peterman T A, Francis D P, Kalyanaraman V S, Weinstein R A, Stoneburner R L, Alexander W J, Raevsky C, Getchell J P, Warfield D, Haverkos H W, Kilbourne B W, Nicholson J K A & Curran J W.** Transfusion-associated acquired immunodeficiency syndrome: evidence for persistent infection in blood donors. *N. Engl. J. Med.* 312:1293-6, 1985. 85-5421
31	53	84	**Fisher B, Bauer M, Margolese R, Poisson R, Pilch Y, Redmond C, Fisher E, Wolmark N, Deutsch M, Montague E, Saffer E, Wickerham L, Lerner H, Glass A, Shibata H, Deckers P, Ketcham A, Oishi R & Russell I.** Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. *N. Engl. J. Med.* 312:665-73, 1985. 85-1319, 86-0715
51	74	125	**Gonda M A, Wong-Staal F, Gallo R C, Clements J E, Narayan O & Gilden R V.** Sequence homology and morphologic similarity of HTLV-III and visna virus, a pathogenic lentivirus. *Science* 227:173-7, 1985. 85-1825, 86-0558
6	63	69	**Grabowski P J, Seiler S R & Sharp P A.** A multicomponent complex is involved in the splicing of messenger RNA precursors. *Cell* 42:345-53, 1985. 86-2283
12	103	115	**Grynkiewicz G, Poenie M & Tsien R Y.** A new generation of Ca^{2+} indicators with greatly improved fluorescence properties. *J. Biol. Chem.* 260:3440-50, 1985. 86-6190
15	55	70	**Hann S R, Thompson C B & Eisenman R N.** *C-myc* oncogene protein synthesis is independent of the cell cycle in human and avian cells. *Nature* 314:366-9, 1985.
17	53	70	**Hayday A C, Saito H, Gillies S D, Kranz D M, Tanigawa G, Eisen H N & Tonegawa S.** Structure, organization, and somatic rearrangement of T cell gamma genes. *Cell* 40:259-69, 1985. 86-0633
18	72	90	**Hesketh T R, Moore J P, Morris J D H, Taylor M V, Rogers J, Smith G A & Metcalfe J C.** A common sequence of calcium and *p*H signals in the mitogenic stimulation of eukaryotic cells. *Nature* 313:481-4, 1985. 86-1179
28	55	83	**Hirsch M S, Wormser G P, Schooley R T, Ho D D, Felsenstein D, Hopkins C C, Joline C, Duncanson F, Sarngadharan M G, Saxinger C & Gallo R C.** Risk of nosocomial infection with human T-cell lymphotropic virus III (HTLV-III). *N. Engl. J. Med.* 312:1-4, 1985. 86-0762
3	69	72	**Ho D D, Rota T R, Schooley R T, Kaplan J C, Allan J D, Groopman J E, Resnick L, Felsenstein D, Andrews C A & Hirsch M S.** Isolation of HTLV-III from cerebrospinal fluid and neural tissues of patients with neurologic syndromes related to the acquired immunodeficiency syndrome. *N. Engl. J. Med.* 313:1493-7, 1985. 86-0558
18	86	104	**Hood L, Kronenberg M & Hunkapiller T.** T cell antigen receptors and the immunoglobulin supergene family. *Cell* 40:225-9, 1985.
9	58	67	**Horsch R B, Fry J E, Hoffmann N L, Eichholtz D, Rogers S G & Fraley R T.** A simple and general method for transferring genes into plants. *Science* 227:1229-31, 1985. 86-2328
9	69	78	**Huang C-L, Lewicki J, Johnson L K & Cogan M G.** Renal mechanism of action of rat atrial natriuretic factor. *J. Clin. Invest.* 75:769-73, 1985. 86-1290

A	B	C	Bibliographic Data
8	123	131	**Hunter T & Cooper J A.** Protein-tyrosine kinases. *Annu. Rev. Biochem.* 54:897-930, 1985.
12	69	81	**Imboden J B & Stobo J D.** Transmembrane signalling by the T cell antigen receptor. *J. Exp. Med.* 161:446-56, 1985. 86-0633
2	66	68	**Irvine R F, Anggard E E, Letcher A J & Downes C P.** Metabolism of inositol 1,4,5-trisphosphate and inositol 1,3,4-trisphosphate in rat parotid glands. *Biochem. J.* 229:505-11, 1985. 86-1983
10	64	74	**Jacobowitz D M, Skofitsch G, Keiser H R, Eskay R L & Zamir N.** Evidence for the existence of atrial natriuretic factor-containing neurons in the rat brain. *Neuroendocrinology* 40:92-4, 1985. 86-1290
27	70	97	**Jeffreys A J, Wilson V & Thein S L.** Hypervariable 'minisatellite' regions in human DNA. *Nature* 314:67-73, 1985. 86-2192
19	53	72	**Kangawa K, Fukuda A & Matsuo H.** Structural identification of β- and γ-human atrial natriuretic polypeptides. *Nature* 313:397-400, 1985. 86-1290
13	106	119	**Klein G & Klein E.** Evolution of tumours and the impact of molecular oncology. *Nature* 315:190-5, 1985.
1	93	94	**Kornfeld R & Kornfeld S.** Assembly of asparagine-linked oligosaccharides. *Annu. Rev. Biochem.* 54:631-64, 1985. 86-6701
13	54	67	**Kurt-Jones E A, Beller D I, Mizel S B & Unanue E R.** Identification of a membrane-associated interleukin 1 in macrophages. *Proc. Nat. Acad. Sci. USA* 82:1204-8, 1985.
5	67	72	**Landesman S H, Ginzburg H M & Weiss S H.** The AIDS epidemic. *N. Engl. J. Med.* 312:521-4, 1985. 86-7334
31	169	200	**Lang R E, Tholken H, Ganten D, Luft F C, Ruskoaho H & Unger T.** Atrial natriuretic factor: a circulating hormone stimulated by volume loading. *Nature* 314:264-6, 1985. 85-1307, 86-1290
9	61	70	**Lanzavecchia A.** Antigen-specific interaction between T and B cells. *Nature* 314:537-9, 1985. 86-0603
25	115	140	**Lipman D J & Pearson W R.** Rapid and sensitive protein similarity searches. *Science* 227:1435-41, 1985. 86-7486
12	88	100	**Litosch I, Wallis C & Fain J N.** 5-hydroxytryptamine stimulates inositol phosphate production in a cell-free system from blowfly salivary glands. *J. Biol. Chem.* 260:5464-71, 1985. 86-2851
8	59	67	**Lochrie M A, Hurley J B & Simon M I.** Sequence of the alpha subunit of photoreceptor G protein: homologies between transducin, *ras*, and elongation factors. *Science* 228:96-9, 1985. 86-3728
11	97	108	**Maack T, Camargo M J F, Kleinert H D, Laragh J H & Atlas S A.** Atrial natriuretic factor: structure and functional properties. *Kidney Int.* 27:607-15, 1985. 86-3713
8	109	117	**March C J, Mosley B, Larsen A, Cerretti D P, Braedt G, Price V, Gillis S, Henney C S, Kronheim S R, Grabstein K, Conlon P J, Hopp T P & Cosman D.** Cloning, sequence and expression of two distinct human interleukin-1 complementary DNAs. *Nature* 315:641-7, 1985. 86-1365
18	51	69	**Martinez-Arias A & Lawrence P A.** Parasegments and compartments in the *Drosophila* embryo. *Nature* 313:639-42, 1985. 86-0403
23	95	118	**McCord J M.** Oxygen-derived free radicals in postischemic tissue injury. *N. Engl. J. Med.* 312:159-63, 1985. 86-1484
13	69	82	**McLauchlan J, Gaffney D, Whitton J L & Clements J B.** The consensus sequence YGTGTTYY located downstream from the AATAAA signal is required for efficient formation of mRNA 3′ termini. *Nucl. Acid. Res.* 13:1347-68, 1985. 86-2283
15	52	67	**Mishina M, Tobimatsu T, Imoto K, Tanaka K, Fujita Y, Fukuda K, Kurasaki M, Takahashi H, Morimoto Y, Hirose T, Inayama S, Takahashi T, Kuno M & Numa S.** Location of functional regions of acetylcholine receptor α-subunit by site-directed mutagenesis. *Nature* 313:364-9, 1985. 86-0218
14	54	68	**Mitchell R L, Zokas L, Schreiber R D & Verma I M.** Rapid induction of the expression of proto-oncogene *fos* during human monocytic differentiation. *Cell* 40:209-17, 1985. 86-0547
6	64	70	**Monaco A P, Bertelson C J, Middlesworth W, Colletti C-A, Aldridge J, Fischbeck K H, Bartlett R, Pericak-Vance M A, Roses A D & Kunkel L M.** Detection of deletions spanning the Duchenne muscular dystrophy locus using a tightly linked DNA segment. *Nature* 316:842-8, 1985. 86-0494
22	68	90	**Muesing M A, Smith D H, Cabradilla C D, Benton C V, Lasky L A & Capon D J.** Nucleic acid structure and expression of the human AIDS/lymphadenopathy retrovirus. *Nature* 313:450-8, 1985. 86-0558
22	86	108	**Nakamura T & Ui M.** Simultaneous inhibitions of inositol phospholipid breakdown, arachidonic acid release, and histamine secretion in mast cells by islet-activating protein, pertussis toxin. *J. Biol. Chem.* 260:3584-93, 1985. 86-2851

A	B	C	Bibliographic Data
6	92	98	**Needleman P, Adams S P, Cole B R, Currie M G, Geller D M, Michener M L, Saper C B, Schwartz D & Standaert D G.** Atriopeptins as cardiac hormones. *Hypertension* 7:469-82, 1985. 86-3713
12	67	79	**Nikaido H & Vaara M.** Molecular basis of bacterial outer membrane permeability. *Microbiol. Rev.* 49:1-32, 1985. 86-6314
3	89	92	**Nowycky M C, Fox A P & Tsien R W.** Three types of neuronal calcium channel with different calcium agonist sensitivity. *Nature* 316:440-3, 1985. 86-0288
22	48	70	**Poole S J, Kauvar L M, Drees B & Kornberg T.** The *engrailed* locus of Drosophila: structural analysis of an embryonic transcript. *Cell* 40:37-43, 1985.
18	71	89	**Pytela R, Pierschbacher M D & Ruoslahti E.** Identification and isolation of a 140 kd cell surface glycoprotein with properties expected of a fibronectin receptor. *Cell* 40:191-8, 1985. 86-0259
59	112	171	**Ratner L, Haseltine W, Patarca R, Livak K J, Starcich B, Josephs S F, Doran E R, Rafalski J A, Whitehorn E A, Baumeister K, Ivanoff L, Petteway S R, Pearson M L, Lautenberger J A, Papas T S, Ghrayeb J, Chang N T, Gallo R C & Wong-Staal F.** Complete nucleotide sequence of the AIDS virus, HTLV-III. *Nature* 313:277-84, 1985. 85-1825, 86-0558
14	89	103	**Raulet D H, Garman R D, Saito H & Tonegawa S.** Developmental regulation of T-cell receptor gene expression. *Nature* 314:103-7, 1985. 86-0633
23	93	116	**Richards A M, Ikram H, Yandle T G, Nicholls M G, Webster M W I & Espiner E A.** Renal, haemodynamic, and hormonal effects of human alpha atrial natriuretic peptide in healthy volunteers. *Lancet* 1:545-9, 1985. 85-1307, 86-1290
16	105	121	**Roberts A B, Anzano M A, Wakefield L M, Roche N S, Stern D F & Sporn M B.** Type β transforming growth factor: a bifunctional regulator of cellular growth. *Proc. Nat. Acad. Sci. USA* 82:119-23, 1985. 86-0782
1	85	86	**Rosenberg S A, Lotze M T, Muul L M, Leitman S, Chang A E, Ettinghausen S E, Matory Y L, Skibber J M, Shiloni E, Vetto J T, Seipp C A, Simpson C & Reichert C M.** Observations on the systemic administration of autologous lymphokine-activated killer cells and recombinant interleukin-2 to patients with metastatic cancer. *N. Engl. J. Med.* 313:1485-92, 1985. 86-4006
42	82	124	**Sanchez-Pescador R, Power M D, Barr P J, Steimer K S, Stempien M M, Brown-Shimer S L, Gee W W, Renard A, Randolph A, Levy J A, Dina D & Luciw P A.** Nucleotide sequence and expression of an AIDS-associated retrovirus (ARV-2). *Science* 227:484-92, 1985. 85-1825, 86-0558
14	70	84	**Saper C B, Standaert D G, Currie M G, Schwartz D, Geller D M & Needleman P.** Atriopeptin-immunoreactive neurons in the brain: presence in cardiovascular regulatory areas. *Science* 227:1047-9, 1985. 86-1290
30	39	69	**Schupbach J, Haller O, Vogt M, Luthy R, Joller H, Oelz O, Popovic M, Sarngadharan M G & Gallo R C.** Antibodies to HTLV-III in Swiss patients with AIDS and pre-AIDS and in groups at risk for AIDS. *N. Engl. J. Med.* 312:265-70, 1985.
6	68	74	**Schwartz D, Geller D M, Manning P T, Siegel N R, Fok K F, Smith C E & Needleman P.** Ser-Leu-Arg-Arg-atriopeptin III: the major circulating form of atrial peptide. *Science* 229:397-400, 1985. 86-1290
2	67	69	**Serfling E, Jasin M & Schaffner W.** Enhancers and eukaryotic gene transcription. *Trends Genet.* 1:224-30, 1985.
59	142	201	**Shaw G M, Harper M E, Hahn B H, Epstein L G, Gajdusek D C, Price R W, Navia B A, Petito C K, O'Hara C J, Groopman J E, Cho E, Oleske J M, Wong-Staal F & Gallo R C.** HTLV-III infection in brains of children and adults with AIDS encephalopathy. *Science* 227:177-81, 1985. 85-1825, 86-0558
8	110	118	**Sherr C J, Rettenmier C W, Sacca R, Roussel M F, Look A T & Stanley E R.** The c-*fms* proto-oncogene product is related to the receptor for the mononuclear phagocyte growth factor, CSF-1. *Cell* 41:665-76, 1985. 86-4303
18	50	68	**Shirai T, Yamaguchi H, Ito H, Todd C W & Wallace R B.** Cloning and expression in *Escherichia coli* of the gene for human tumour necrosis factor. *Nature* 313:803-6, 1985. 85-0278, 86-0192
11	69	80	**Shtivelman E, Lifshitz B, Gale R P & Canaani E.** Fused transcript of *abl* and *bcr* genes in chronic myelogenous leukaemia. *Nature* 315:550-4, 1985. 86-1906
16	69	85	**Silverberg E.** Cancer statistics, 1985. *Ca—A Cancer J. Clin.* 35:19-35, 1985.
6	68	74	**Smith C D, Lane B C, Kusaka I, Verghese M W & Snyderman R.** Chemoattractant receptor-induced hydrolysis of phosphatidylinositol 4,5-bisphosphate in human polymorphonuclear leukocyte membranes. *J. Biol. Chem.* 260:5875-8, 1985. 86-2851
14	63	77	**Smith K A & Cantrell D A.** Interleukin 2 regulates its own receptors. *Proc. Nat. Acad. Sci. USA* 82:864-8, 1985. 86-3718

A	B	C	Bibliographic Data
33	47	80	**Sodroski J, Rosen C, Wong-Staal F, Salahuddin S Z, Popovic M, Arya S, Gallo R C & Haseltine W A.** *Trans*-acting transcriptional regulation of human T-cell leukemia virus type III long terminal repeat. *Science* 227:171-3, 1985.
11	56	67	**Sodroski J, Patarca R, Rosen C, Wong-Staal F & Haseltine W.** Location of the *trans*-activating region on the genome of human T-cell lymphotropic virus type III. *Science* 229:74-7, 1985. 86-0558
20	92	112	**Sporn M B & Roberts A B.** Autocrine growth factors and cancer. *Nature* 313:745-7, 1985.
23	69	92	**Thompson C B, Challoner P B, Neiman P E & Groudine M.** Levels of c-*myc* oncogene mRNA are invariant throughout the cell cycle. *Nature* 314:363-6, 1985. 86-0547
5	70	75	**Tikkanen I, Metsarinne K, Fyhrquist F & Leidenius R.** Plasma atrial natriuretic peptide in cardiac disease and during infusion in healthy volunteers. *Lancet* 2:66-73, 1985. 86-1290
37	81	118	**Toda T, Uno I, Ishikawa T, Powers S, Kataoka T, Broek D, Cameron S, Broach J, Matsumoto K & Wigler M.** In yeast, *RAS* proteins are controlling elements of adenylate cyclase. *Cell* 40:27-36, 1985. 86-3728
18	75	93	**Truneh A, Albert F, Golstein P & Schmitt-Verhulst A-M.** Early steps of lymphocyte activation bypassed by synergy between calcium ionophores and phorbol ester. *Nature* 313:318-20, 1985. 86-0633
48	180	228	**Ullrich A, Bell J R, Chen E Y, Herrera R, Petruzzelli L M, Dull T J, Gray A, Coussens L, Liao Y-C, Tsubokawa M, Mason A, Seeburg P H, Grunfeld C, Rosen O M & Ramachandran J.** Human insulin receptor and its relationship to the tyrosine kinase family of oncogenes. *Nature* 313:756-61, 1985. 86-4303
20	51	71	**Velcich A & Ziff E.** Adenovirus E1a proteins repress transcription from the SV40 early promoter. *Cell* 40:705-16, 1985.
14	53	67	**Verstraete M, Bory M, Collen D, Erbel R, Lennane R J, Mathey D, Michels H R, Schartl M, Uebis R, Bernard R, Brower R W, de Bono D P, Huhmann W, Lubsen J, Meyer J, Rutsch W, Schmidt W & von Essen R.** Randomised trial of intravenous recombinant tissue-type plasminogen activator versus intravenous streptokinase in acute myocardial infarction. *Lancet* 1:842-7, 1985. 85-0829, 86-1147
46	91	137	**Wain-Hobson S, Sonigo P, Danos O, Cole S & Alizon M.** Nucleotide sequence of the AIDS virus, LAV. *Cell* 40:9-17, 1985. 85-1825, 86-0558
61	72	133	**Weiss S H, Goedert J J, Sarngadharan M G, Bodner A J, AIDS Seroepidemiology Collaborative Working Group, Gallo R C & Blattner W A.** Screening test for HTLV-III (AIDS agent) antibodies. *JAMA—J. Am. Med. Assn.* 253:221-5, 1985. 85-1825
17	51	68	**White R, Leppert M, Bishop D T, Barker D, Berkowitz J, Brown C, Callahan P, Holm T & Jerominski L.** Construction of linkage maps with DNA markers for human chromosomes. *Nature* 313:101-5, 1985. 86-0494
14	60	74	**Williamson J R, Cooper R H, Joseph S K & Thomas A P.** Inositol trisphosphate and diacylglycerol as intracellular second messengers in liver. *Amer. J. Physiol.* 248:C203-16, 1985. 86-1983
11	84	95	**Wong G G, Witek J S, Temple P A, Wilkens K M, Leary A C, Luxenberg D P, Jones S S, Brown E L, Kay R M, Orr E C, Shoemaker C, Golde D W, Kaufman R J, Hewick R M, Wang E A & Clark S C.** Human GM-CSF: molecular cloning of the complementary DNA and purification of the natural and recombinant proteins. *Science* 228:810-5, 1985. 86-1871
3	72	75	**Wong-Staal F & Gallo R C.** Human T-lymphotropic retroviruses. *Nature* 317:395-403, 1985.
24	303	327	**Yanisch-Perron C, Vieira J & Messing J.** Improved M13 phage cloning vectors and host strains: nucleotide sequences of the M13mp18 and pUC19 vectors. *Gene* 33:103-19, 1985. 86-1382