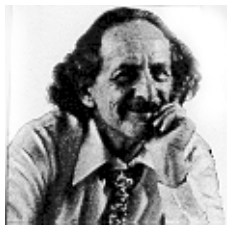
Essays of an Information Scientist, Vol:7, p.313-325, 1984
Current Contents, #41, p.3-15, October 8, 1984



Current Comments®

Introducing the *ISI Atlas of Science: Biotechnology and Molecular Genetics, 1981/82* and Bibliographic Update for 1983/84

Number 41 October 8, 1984

In a poem entitled "A Letter from Caroline Herschel (1750-1848)," the poet and novelist Siv Cedering attributes the following to the sister of astronomer William Herschel:

> I have a way with numbers, so I handle the/necessary reductions and calculations./I also plan every night's observation schedule, for he says my/intuition helps me turn the telescope to discover/star cluster after star cluster....[1]

And so it is at ISI®. We spend our nights and days trying to discover new and meaningful clusters of scientific events. By clustering the core papers, people, journals, or institutions of science, we attempt to find new relationships not otherwise visible in this very multidimensional world of science. By applying citation and co-citation analyses, among other techniques, we have been able to observe order in the seemingly chaotic universe of scientific literature.

The analogy to astronomy is appropriate. As we gaze out into the night sky, we observe a mass of seemingly disconnected stars. But astronomers tell us that these stars are actually organized into a cluster, our galaxy. Moreover, our galaxy is itself part of a cluster of galaxies, one of many such clusters in our universe. One might say that a goal of astronomers is to perceive order in the superficial chaos of the night sky.

Just as these geographers of the sky map the heavens, we information scientists map the continually changing geography of science, as it is reflected in the scientific literature. With hundreds of thousands of scientists publishing millions of articles and books over several centuries, the universe of science often seems chaotic indeed to the untrained observer. This is compounded because of time warp. More literature is now produced in one or two years than in all previous centuries. As Derek J. de Solla Price would say, 90 percent of the scientists who ever lived are alive today. Articles and books from A to Z appear in great profusion. Yet in a process that can be likened to astronomical events, clusters of literature do appear, drawn together by the gravitational pull of their semantic relationships or connectivities.

This may seem like a romanticized way of introducing you to the *ISI Atlas of Science*®. I must confess that finding order in the scientific literature is as moving to me as finding order in the heavens is to my astroscientific friends. From the earliest times, astronomers have been very successful in maintaining public interest in their craft. We hope to be equally successful in conveying the idea that clusters of literature are not only beautiful and interesting, but also useful in the everyday world.

In 1981, we published the *ISI Atlas of Science: Biochemistry and Molecular Biology, 1978/80* as a prototype of a comprehensive encyclopedic *ISI Atlas of Science*.[2] Each of its 102 chapters covered a distinct subspecialty, or re-

Figure 1: List of research fronts or specialties (classified according to "macrogroup") included in the *ISI Atlas of Science®: Biotechnology and Molecular Genetics, 1981/82.*

Gene Expression, Function, and Controls

1. Ultrastructural-studies of chromatin and nuclear-RNP
2. Transcription initiation and termination in eukaryotes
3. Nucleotide-sequence and transforming agents from murine-sarcoma-virus and other sarcoma-viruses
4. Oncogenic transformation by Harvey and Kirsten strains of murine-sarcoma-virus
5. Structure, function and location of HMG non-histone-proteins
6. Sarcoma-virus transforming-proteins
7. Transcription of adenovirus-genes
8. Proviral-DNA of retrovirus, chromosome, integration and RNA-viral-transformation
9. Polyadenylated and non-polyadenylated m-RNA
10. Genetic characterization of pseudogenes
11. Small molecular-weight nuclear RNA
12. Organization, rearrangement and IG gene-expression
13. Organization of repetitive gene-sequences
14. Studies using polyoma-virus DNA
15. Molecular basis of alpha-thalassemia
16. Avian retrovirus-DNA and retrovirus-RNA
17. Endogenous retrovirus-genes
18. Viral DNA, direct repeated-sequences and terminal redundancy
19. B-cell development
20. Stimulation of protein phosphorylation by epidermal growth-factor
21. Codons for termination of translation in eukaryotes
22. Mouse-mammary-tumor-virus DNA and RNA
23. Nucleosome-organization and chromatin-structure
24. Protein-organization of nucleosomes
25. Ubiquitin-protein and HMG-ubiquitin conjugates
26. Structure of isolated chromatin
27. Histones and chromatin-structure
28. Interaction of histones with DNA
29. Association of replicative DNA with the nuclear matrix
30. Eukaryote gene transcription invitro
31. Chromosome localization of single genes
32. Inhibition of DNA-synthesis by aphidicolin and aphidicolin- resistance

DNA Repair and Recombination

33. Site-specific recombination
34. E-coli recA-protein activities
35. Topoisomerases, gyrases and proteins controlling DNA-structure
36. DNA-repair of interstrand cross-linking and mitotic and meiotic recombination in yeast
37. Protein interaction with single-stranded nucleic-acids
38. Control of transcription in bacteriophage-T-3 and bacteriophage-T-7
39. Yeast mating-type genes

DNA Repair Enzymes

40. Xeroderma-pigmentosum and DNA-repair following UV-light
41. DNA-synthesis and DNA-repair in ataxia-telangiectasia
42. Poly-ADP-ribose-polymerase and DNA-repair
43. DNA-repair and 6-methylguanine
44. DNA-repair in xeroderma-pigmentosum
45. DNA glycosylases and other DNA-repair enzymes
46. Enzymes involved in DNA-repair
47. Excision DNA-repair of UV-light induced pyrimidine-dimers

Transposons

48. Bacteriophage-mu genetics and prokaryotic transposons
49. Mechanism of transposons
50. Transposons and IS-1-elements in bacteria and bacteriophages
51. Studies on gene transposition
52. Transposition of IS-1-elements
53. Mechanism of genetic transpositions

Viral Gene Expression

54. DNase-I-sensitive sites in SV-40 nucleoprotein complexes
55. DNA methylation and cellular differentiation
56. SV-40 and polyoma-virus T-antigens

Mitochondrial Genetics

57. Cytochrome-c-oxidase structure and the mitochondrial genome
58. Primary-structure, secondary-structure and function of r-RNA
59. Electrochemical proton-gradients in mitochondria and liposomes
60. Nucleotide-sequences and secondary-structure of r-DNA and r-RNA from mitochondria, chloroplasts and bacteria
61. Mitochondrial genetics of yeast
62. Mitochondrial DNA of yeasts
63. Thermodynamics and mitochondria

Mitochondrial ATPase

64. Nucleotide-binding-sites of chloroplast-coupling-factor-1
65. Nucleotide-sequence of genes coding for ATPase subunits
66. Affinity-labeling with fluorosulfonylbenzoyl-adenosine and adenine-nucleotide analogs
67. Conformational studies of E-coli and mitochondrial ATPase
68. Studies of mitochondrial ATPase

Immunogenetics

69. Immunological diversity of T-cell-response in radiation-chimeras
70. H-2K mice and IR-gene control of cytotoxic T-cells
71. IR genes, IA-antigens, and gene complementation

72. T-cell growth-factor
73. T-cell growth-factor and cell-function
74. Alloreactive T-cell clones
75. T-cell growth-factor interleukin-2
76. Clones of proliferating T-cells
77. Antigen-specific T-cell clones
78. Immunological studies on interleukin-2
79. T-cell-regulation by interleukin-2
80. Production of interleukin-2
81. Invitro growth and maintenance of T-cells

Cytogenetics and Markers of Leukemia and Lymphoma

82. Terminal deoxynucleotidyl-transferase activity
83. Cytogenetics of Burkitts-lymphoma, other lymphomas and other cancers
84. Cytogenetics of preleukemia and acute leukemia
85. Clinical studies of myelogenous and other leukemias
86. Terminal deoxynucleotidyl-transferase during blast crisis in leukemia
87. Cytogenetic markers in acute lymphoblastic leukemia
88. Chromosome-abnormalities in leukemia and lymphoma
89. Cytologic studies on hematopoietic dysplasia

Extrinsic Control of Protein Synthesis

90. *Regulation of eukaryote protein-synthesis by heme, RNA and kinases*
91. Mechanisms of anti-viral activity of interferon

HSV Gene Expression and Organization

92. Characterization of DNA and HSV and *other viruses*
93. Mechanism of anti-HSV activity of acyclovir
94. Eukaryote transformation and transfection by DNA and chromosomes

Individual Specialties

95. Structure and function of elongation-factors and studies with the antibiotic kirromycin
96. Regulation of ribosomal-protein-synthesis
97. Genetics of human complement components
98. Structural studies of fibroblast and leukocyte interferon-genes
99. Molecular-genetics of hepatitis-B-virus
100. Folding and binding of lac-repressor
101. DNA exons and functional domains in protein-structure
102. Conformational studies of DNA and synthetic polynucleotides
103. Monoclonal antibodies
104. Defects in the beta-globin-gene in beta-thalassemia
105. Tumor-promotors and transformation
106. Nucleotide-sequences of influenza-virus genes
107. *Control of bacterial operon-expression*
108. Sister-chromatid-exchange analysis
109. Amplification of dihydrofolate-reductase-genes
110. Studies of plasmids
111. X-linked mental retardation
112. Heat-shock genes and proteins in Drosophila-melanogaster
113. *Mitochondrial DNA-sequences and evolution*
114. Benzopyrene DNA-adducts
115. HLA-antigens and the genetics of diabetes-mellitus
116. Plasmids of Saccharomyces-cerevisiae
117. Photoreactions between psoralen and DNA
118. HY-antigens and gonadal differentiation
119. T-1-plasmid-DNA of agrobacterium and crown-gall-tumors
120. Modification of coronavirus and mouse hepatitis-virus polypeptides
121. Silver staining of nucleoli and nucleolar-organizer-regions
122. *Aflatoxin-B1 DNA-adducts*
123. Plasmids and spontaneous mutagenesis
124. Cell-size mutants of yeast
125. Human genetic-factors in ethanol-metabolism
126. Genetics and protein variation of human rotaviruses
127. Regulation of actin gene-expression

search front, identified by our clustering procedures. Each chapter consisted of four components: a minireview describing the evolution of the research front, a multidimensionally scaled map showing the "connectedness" among the core papers of the research front, a bibliography of these core papers, and a bibliography of current papers ranked by relevance, that is, the number of core papers they cited.

We have now created a second prototype atlas, the *ISI Atlas of Science: Biotechnology and Molecular Genetics, 1981/82*. Its 127 chapters, whose titles are shown in Figure 1, cover the most active research fronts in these fields, where "most active" is defined in terms of publication productivity. Fifty-two of the chapters consist of the same components found in the earlier *Atlas*: a minireview, a cluster map, a bibliography of core papers, and relevance-ranked lists of key papers published in 1981 and 1982 that cite the core.

The remaining 75 chapters simply provide a bibliography of the core publications and lists of the most relevant cur-

rent papers for each research front. These chapters generally cover smaller, still-emerging fields. An example of such an emerging field is protein phosphorylation by epidermal growth factor (EGF), which is covered in Chapter 20. Scientists believe that an understanding of EGF will provide insight into the physiology of cell growth. By extension, EGF will also help elucidate disorders of cell growth, such as cancer. Interest in EGF has grown dramatically since 1981. In that year, five core documents were associated with the EGF specialty. By 1982, this had expanded to 34 core papers. By 1983, 51 core documents were identified.

As an example, the figures that follow illustrate the chapter from the new *Atlas* entitled "Structural studies of fibroblast and leukocyte interferon-genes." Keep in mind that the *Atlas* is an 8½" x 11" volume. The figures that follow have been reduced considerably for reasons of space. Figure 2 presents the minireview of this research front. This minireview summarizes work concerning the determination of the amino acid sequences and gene structures of two types of human interferon: alpha-interferon, from leukocytes (a type of white blood cell), and beta-interferon, from fibroblasts (a cell in connective tissue). As before, the minireviews were written by postdoctoral scientists and then refereed by an average of four experts on each subject. Typically, each essay begins with a definition of the specialty and provides an overview of its evolution. The minireview describes the milestone contributions reported in the core documents. The 1981 and 1982 key citing papers are used as the basis for a discussion of recent research and speculations about future trends.

The minireviews contain no jargon, formulas, or undefined abbreviations and acronyms. Thus, they should be comprehensible to research scientists, science administrators, and graduate students alike. We have gone to great lengths to ensure the accuracy of the minireviews.

Until ISI announced its work on our first *Atlas*, the term "minireview" had not, to my knowledge, been widely used in the literature. Of course, numerous publications had published minireviews of one kind or another. All sorts of journals, such as *Science*, *Nature*, *Trends in Biochemical Sciences*, and others, provide short reviews in their respective styles. We would contend that when one of our minireviews turns out to look like those that are published by more conventional methods, it will be the ultimate validation of the minireview process itself. Indeed, such review articles will automatically move to the top of the list of current relevant papers we retrieve.

While conventional sources of reviewing may collectively overlap our efforts, the unique role of the *Atlas* is to identify and "review" the worldwide research fronts of science in a comprehensive and systematic manner. That is what makes it encyclopedic. And it is our unique and stated purpose to identify those areas that have not previously been reviewed. Selecting highly active fields may sometimes have thwarted this intent in this particular *Atlas*. But we expect eventually to generate minireviews particularly in those areas not yet covered in the standard review literature. Price once suggested to me that reviews would be necessary after 40 new papers are published on a given topic. But this threshold varies widely across the range of scientific disciplines and depends upon many factors.

Figure 3 includes the multidimensionally scaled map for the chapter on fibroblast- and leukocyte-interferon genes. The numbered boxes identify each paper in the bibliography of core papers. To facilitate scanning, the bibliography is arranged alphabetically by first author. Institutional affiliations appear beneath the name of each first author in

Figure 2: Sample minireview reduced to 50 percent of original size.

Specialty 98

Structural Studies of Fibroblast and Leukocyte Interferon-Genes

The interferons are a class of small proteins which protect vertebrate cells from viral infections, in addition to having other effects on the cell growth cycle and the immune response. Efforts to purify and characterize the interferons have been spurred on by the possibility that they might prove useful in the treatment of viral disease and cancer. With the advent of recombinant DNA techniques, researchers became very interested in the structure of the interferon genes, with a view to inserting these genes into microorganisms and inducing them to manufacture interferon on a large scale. The core papers of this specialty describe some of the essential work that has led to the attainment of this goal in addition to providing valuable information on the organization and evolution of the interferon gene family.

The structure of a gene can be investigated in several ways. One can isolate and sequence the gene directly, examine the gene at the level of its messenger RNA copy, or determine the amino acid sequence of the protein encoded by the gene.

Early techniques for the purification of interferon only yielded sufficient material for microsequencing techniques. This limited the sequence analysis to the amino-terminal end of the protein ([9], [10], [17], [22]). Allen and Fantes ([11]) subsequently examined the sequence of other regions of interferons by splitting the protein into small peptides whose sequence was then determined. These investigations revealed considerable sequence heterogeneity among the human interferons. The first major differences were noticed between interferon isolated from leukocytes (called alpha-interferon) and that isolated from fibroblasts (beta-interferon). Further sequence variations were then discovered among the alpha-interferons.

The complete amino acid sequence of both alpha- and beta-interferon proteins was first identified by isolating the messenger RNA molecules that direct the manufacture of interferon in the cell. A 'reverse transcriptase' enzyme was then used to make a DNA copy of the messenger RNA, the nucleotide sequence of this DNA was determined; and, therefore the amino acid sequence of the protein could be deduced ([2], [18], [19]). This approach led to the identification of at least eight distinct chromosomal genes encoding human alpha-interferon ([4], [13], [16]).

These studies identifying the human interferon genes have also yielded interesting information concerning their structure. As would be expected for a secretory protein most of the coding sequences of interferon genes begin with a 'signal peptide' section, marking the protein for transport across the endoplasmic reticulum and out of the cell. Another very interesting finding was that the interferon fibroblast and leukocyte genes do not appear to contain introns, the non-coding sections of DNA found in most eukaryote genes, but not corresponding mRNA, examined to date. Several interferon 'pseudogenes' have also been found. These are interferon genes containing nucleotide alterations in the coding sequence that prevent the genes from producing full-length interferon ([4]).

Comparison of human interferon gene sequences clearly suggests that they have a common ancestry. It has been estimated that the alpha and beta genes probably diverged 500-1000 million years ago, making them as old as the vertebrates([19]). It appears that the alpha gene family probably arose by duplication of the ancestral alpha-interferon gene, beginning 20-80 million years ago (24).

The most studied non-human interferons are those of the mouse. Amino acid sequence analysis has revealed at least two classes of mouse interferon, showing sequence homology with human alpha- and beta-interferon respectively ([12]).

As has already been stated, a major aim of much of the research on interferon genes is to insert these genes into microorganisms and obtain the mass production of interferon for clinical use and further research. Derynck et al.,[1] Goeddel et al. ([3], [5]), Nagata et al. ([12]), Taniguchi et al. ([20]) have inserted interferon genes into *Escherichia coli* and found that the interferon produced was biologically active.

The interferon system is an area of intensive research and much of the recent work has confirmed the conclusions of the earlier core papers. Thus, several research groups have produced evidence supporting the view that interferon genes do not contain introns (4, 5, 9). Gray and Goeddel (30), however, have determined the structure of human gamma-interferon and shown that it has a sequence unrelated to other interferon species and contains three introns.

Recombinant DNA techniques have allowed hybrid interferon genes to be constructed, in which the beginning of one alpha-interferon gene is attached to the end of another[2] (24). A much more extensive control over the structure of interferon genes has been made possible by Edge (1), with the complete chemical synthesis of the gene for human alpha-interferon. These gene synthesis and hybrid gene construction techniques will provide the ability to modify the structure of interferon genes at will, with the expression of the modified genes being obtained by insertion into a suitable microorganism. This ability will no doubt be used to investigate which regions of the genes are important to particular biological functions, and might eventually lead to the design of a more effective product for clinical use.

1. Derynck R, Remaut E, Saman E, Stanssen P, DeClercq E, Content J & Fiers W. Expression of human fibroblast interferon gene in *Escherichia coli*. *Nature* 287 (5779): 193-197, 1980.

2. Weck PK. Antiviral activities of hybrids of two major human leukocyte interferons. *Nucl. Acid R.* 9: 6153, 1981.

the map. We did not include laboratory names in our first *Atlas*. However, it later became obvious that a map without these names was less useful. Even an ordinary world map needs labels for continents, countries, or cities.

Each map is multidimensionally scaled. That is, it depicts the degree of "connectedness" between pairs of papers. Papers that are frequently co-cited, such as those by Mantei (11) and Taniguchi (18) in Figure 3, appear close together on the map. The problems discussed or elucidated in these papers are co-cited for a variety of reasons. Papers less frequently "connected," such as those by Derynck (2) and Houghton (7), are located farther apart on the map.

Undoubtedly, the "meaning" of these maps is one of the most controversial aspects of the *Atlas*. To give greater meaning to the conceptual associations implied by the clustering procedure, we have added generic captions below the maps. It is significant that even within these already specialized but rapidly changing research fronts, the core papers will form "subclusters" that we can easily identify. These subclusters form the profiles for these topics. In Figure 3, papers numbered 2, 18, and 19 discuss the use of a reverse transcriptase enzyme to aid in identifying the amino acid sequence and, later, eight distinct chromosomal genes encoding human alpha-interferon (papers 4, 13, and 16). The captions provide shorthand descriptions of the subdivisions.

It is important to realize that the map is a snapshot of the status of research in 1981, an arbitrary single frame from what is in reality a continuous reel. For example, in the case of the specialty on fibroblast- and leukocyte-interferon genes, by 1982, only 17 of the 22 original core papers continued to be cited at the minimum threshold of 12. By 1983 only eight remained. More will be said about this expansion and contraction of research fronts later.

To facilitate scanning, the list of core references begins on the same page as the map. Each reference includes the institutional affiliation of the first author. The CF number following the entry for each paper indicates the frequency of its citation by 1981 papers. Since the minimum citation threshold was established at 12 when we identified the 1981 core papers, no core paper listed was cited fewer than 12 times in 1981.

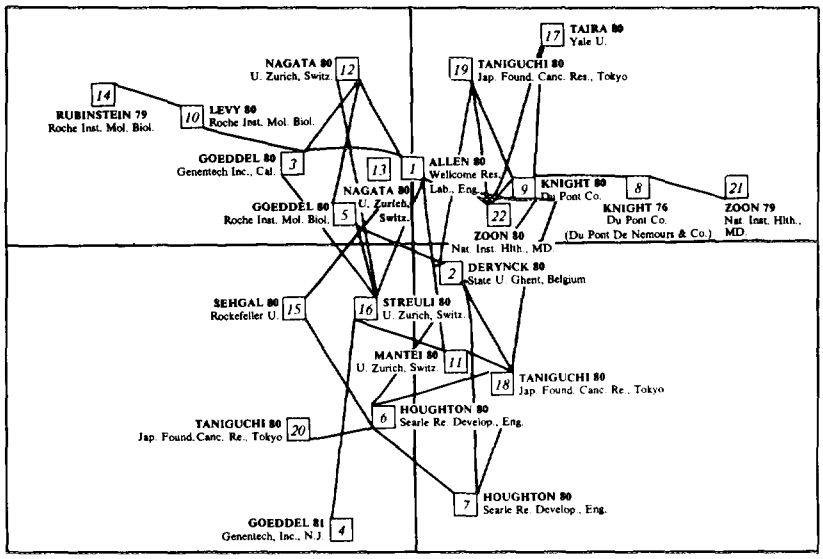
Figure 4 provides part of a list of the most-relevant citing papers from 1981 and 1982. The relevance weight (RW) is shown to the right of each paper. This indicator is the number of core papers cited. For example, Edge *et al.*, ICI Ltd., published a 1981 paper in *Nature* that cited 15 of the core papers. In 1982, Fantes, Wellcome Research Labs, published a review containing 79 references in *Texas Reports in Biology and Medicine*, 19 of which are core papers. There follow more 1982 review papers, by Sehgal, Rockefeller University; Berg, Aarhus University; Dziewanowska, Hoffmann-La Roche, and so on. The system automatically pushes the most-relevant reviews to the top of the list.

Some chapters include a third set of references or footnotes to the minireviews. These are publications that the reviewer or referee believed to merit special mention even though they did not turn up in the core or citing lists. In some cases, they are historically important papers that may no longer be cited explicitly at the minimum threshold required. They might have appeared in clusters for previous years. In the future online version of the *Atlas*, such linkages could be shown.

To test the continuing validity of the core selection, we used the same technique to generate a bibliography of the most up-to-date literature on each topic for 1983 and the first half of 1984. These papers are listed in a supplement to the *Atlas*. In Figure 5, we have listed a few such relevant papers. These 1983-1984

Figure 3: A 50 percent reduced facsimile of a multidimensionally scaled map based on co-citation linkages between core papers. *Numbers in boxes identify core papers in the bibliography. Proximity of boxes to one another is a measure of* similarity or connectivity between core papers.

Specialty 98 — Structural studies of fibroblast and leukocyte interferon-genes



[2, 18, 19] Studies using a reverse transcriptase enzyme to aid in identifying the amino acid sequence and, later, [4, 13, 16] eight distinct chromosomal genes encoding human alpha-interferon.

Cited Core Documents

CF

[1] ALLEN G, FANTES KH — CF 35
A FAMILY OF STRUCTURAL GENES FOR HUMAN LYMPHOBLASTOID (LEUKOCYTE-TYPE) INTERFERON
NATURE 287 408, 1980
WELLCOME RES LABS,DEPT IMMUNOCHEM
BECKENHAM BR3 3BS , KENT , ENGLAND

[2] DERYNCK R, CONTENT J, DECLERCQ E, VOLCKAER, G, TAVERNIE, J, DEVOS R, FIERS W — CF 34
ISOLATION AND STRUCTURE OF A HUMAN FIBROBLAST INTERFERON GENE
NATURE 285 542, 1980
STATE UNIV GHENT,MOLEC BIOL LAB
B-9000 GHENT , BELGIUM

[3] GOEDDEL DV, YELVERTO, E, ULLRICH A, HEYNEKER HL, MIOZZARI G, HOLMES W, SEEBURG PH, DULL T, MAY L, STEBBING N — CF 45
HUMAN LEUKOCYTE INTERFERON PRODUCED BY E-COLI IS BIOLOGICALLY ACTIVE
NATURE 287 411, 1980
GENENTECH INC,DEPT MOLEC BIOL
S SAN FRANCISCO , CA 94080

[4] GOEDDEL DV, LEUNG DW, DULL TJ, GROSS M, LAWN RM, MCCANDLI. R, SEEBURG PH, ULLRICH A, YELVERTO. E, GRAY PW — CF 25
THE STRUCTURE OF 8 DISTINCT CLONED HUMAN LEUKOCYTE INTERFERON CDNAS
NATURE 290 20, 1981
GENENTECH INC,DEPT MOLEC BIOL
S SAN FRANCISCO , CA 94080

[5] GOEDDEL DV, SHEPARD HM, YELVERTO. E, LEUNG D, CREA R, SIOMA A, PESTKA S — CF 29
SYNTHESIS OF HUMAN FIBROBLAST INTERFERON BY E-COLI
NUCL ACID R 8 2885, 1980
GENENTECH INC,DEPT MOLEC BIOL
S SAN FRANCISCO , CA 94080

[6] HOUGHTON M, STEWART AG, DOEL SM, EMTAGE JS, EATON MAW, SMITH JC, PATEL TP, LEWIS HM, PORTER AG, BIRCH JR — CF 15
THE AMINO-TERMINAL SEQUENCE OF HUMAN FIBROBLAST INTERFERON AS DEDUCED FROM REVERSE TRANSCRIPTS OBTAINED USING SYNTHETIC OLIGONUCLEOTIDE PRIMERS
NUCL ACID R 8 1913, 1980
GD SEARLE & CO LTD,SEARLE RES & DEV,DEPT BIOCHEM
HIGH WYCOMBE HP12 4HL , BUCKS , ENGLAND

[7] HOUGHTON M, EATON MAW, STEWART AG, SMITH JC, DOEL SM, CATLIN GH, LEWIS HM, PATEL TP, EMTAGE JS, CAREY NH — CF 12
THE COMPLETE AMINO ACID SEQUENCE OF HUMAN FIBROBLAST INTERFERON AS DEDUCED USING SYNTHETIC OLIGODEOXYRIBONUCLEOTIDE PRIMERS OF REVERSE TRANSCRIPTASE
NUCL ACID R 8 2885, 1980
SEARLE RES & DEV
HIGH WYCOMBE , BUCKS , ENGLAND

[8] KNIGHT E — CF 20
INTERFERON - PURIFICATION AND INITIAL CHARACTERIZATION FROM HUMAN DIPLOID CELLS
P NAS US 73 520, 1976
DUPONT CO,EXPTL STN,DEPT CENT RES & DEV
WILMINGTON , DE 19898

[9] KNIGHT E, HUNKAPIL. M, KORANT BD, HARDY RWF, HOOD LE — CF 40
HUMAN FIBROBLAST INTERFERON - AMINO ACID ANALYSIS AND AMINO TERMINAL AMINO ACID SEQUENCE
SCIENCE 207 525, 1980
DUPONT CO,DEPT CENT RES & DEV
WILMINGTON , DE 19898

[10] LEVY WP, SHIVELY J, RUBINSTE. M, DELVALLE U, PESTKA S — CF 14
AMINO-TERMINAL AMINO ACID SEQUENCE OF HUMAN LEUKOCYTE INTERFERON
P NAS BIOL 77 5102, 1980
ROCHE INST MOLEC BIOL
NUTLEY , NJ 07110

Figure 3 *(cont.)*

Cited Core Documents *(cont.)*

		CF
11	MANTEI N, SCHWARZS. M, STREULI M, PANEM S, NAGATA S, WEISSMAN. C THE NUCLEOTIDE SEQUENCE OF A CLONED HUMAN LEUKOCYTE INTERFERON CDNA *GENE* 10:1, 1980 UNIV ZURICH,INST MOLEK BIOL 1 CH-8093 ZURICH , SWITZERLAND	32
12	NAGATA S, TAIRA H, HALL A, JOHNSRUD L, STREULI M, ECSODI J, BOLL W, CANTELL K, WEISSMAN. C SYNTHESIS IN E-COLI OF A POLYPEPTIDE WITH HUMAN LEUKOCYTE INTERFERON ACTIVITY *NATURE* 284:316, 1980 UNIV ZURICH,INST MOLEK BIOL 1 CH-8093 ZURICH , SWITZERLAND	52
13	NAGATA S, MANTEI N, WEISSMAN. C THE STRUCTURE OF ONE OF THE 8 OR MORE DISTINCT CHROMOSOMAL GENES FOR HUMAN INTERFERON-ALPHA *NATURE* 287:401, 1980 UNIV ZURICH,INST MOLEK BIOL 1 CH-8093 ZURICH , SWITZERLAND	54
14	RUBINSTE.M, RUBINSTE. S, FAMILLET P, MILLER RS, WALDMAN AA, PESTKA S HUMAN LEUKOCYTE INTERFERON - PRODUCTION, PURIFICATION TO HOMOGENEITY, AND INITIAL CHARACTERIZATION *P NAS US* 76:640, 1979 ROCHE INST MOLEC BIOL NUTLEY , NJ 07110	34
15	SEHGAL PB, SAGAR AD HETEROGENEITY OF POLY(I).POLY(C)-INDUCED HUMAN FIBROBLAST INTERFERON MESSENGER RNA SPECIES *NATURE* 288:95, 1980 ROCKEFELLER UNIV NEW YORK , NY 10021	16
16	STREULI M, NAGATA S, WEISSMAN. C AT LEAST 3 HUMAN TYPE-ALPHA INTERFERONS - STRUCTURE OF ALPHA-2 *SCIENCE* 209:1343, 1980 UNIV ZURICH,INST MOLEK BIOL 1 CH-8093 ZURICH , SWITZERLAND	33
17	TAIRA H, BROEZE RJ, JAYARAM BM, LENGYEL P, HUNKAPIL. M, HOOD LE MOUSE INTERFERONS - AMINO TERMINAL AMINO ACID SEQUENCES OF VARIOUS SPECIES *SCIENCE* 207:528, 1980 YALE UNIV,DEPT MOLEC BIOPHYS & BIOCHEM NEW HAVEN , CT 06520	17
18	TANIGUCH.T, OHNO S, FUJIIKUR. Y, MURAMATS. M THE NUCLEOTIDE SEQUENCE OF HUMAN FIBROBLAST INTERFERON CDNA *GENE* 10:11, 1980 JAPANESE FDN CANC RES,INST CANC,DEPT BIOCHEM TOKYO 170 , JAPAN	31
19	TANIGUCH.T, MANTEI N, SCHWARZS. M, NAGATA S, MURAMATS. M, WEISSMAN. C HUMAN LEUKOCYTE AND FIBROBLAST INTERFERONS ARE STRUCTURALLY RELATED *NATURE* 285:547, 1980 JAPANESE FDN CANC RES,INST CANC,DEPT BIOCHEM TOKYO 170 , JAPAN	35
20	TANIGUCH.T, GUARENTE L, ROBERTS TM, KIMELMAN D, DOUHAN J, PTASHNE M EXPRESSION OF THE HUMAN FIBROBLAST INTERFERON GENE IN ESCHERICHIA-COLI *P NAS BIOL* 77:5230, 1980 JAPANESE FDN CANC RES,INST CANC,TOSHIMA KU TOKYO 170 , JAPAN	12
21	ZOON KC, SMITH ME, BRIDGEN PJ, NEDDEN DZ, ANFINSEN CB PURIFICATION AND PARTIAL CHARACTERIZATION OF HUMAN LYMPHOBLASTOID INTERFERON *P NAS US* 76:5601, 1979 NIAMDD,CHEM BIOL LAB BETHESDA , MD 20205	12
22	ZOON KC, SMITH ME, BRIDGEN PJ, ANFINSEN CB, HUNKAPIL. M, HOOD LE AMINO TERMINAL SEQUENCE OF THE MAJOR COMPONENT OF HUMAN LYMPHOBLASTOID INTERFERON *SCIENCE* 207:527, 1980 NIAMDD,CHEM BIOL LAB BETHESDA , MD 20205	31

Figure 4: 1981 and 1982 key citing papers ranked by relevance. For reasons of space, all 48 key citing papers cannot be shown.

Key Citing Documents

	1981	RW
1	EDGE MD, ATKINSON TC, GREENE AR, HEATHCLI.GR, MARKHAM AF, MEACOCK PA, NEWTON CR, SCANLON DB, SCHUCH W TOTAL SYNTHESIS OF A HUMAN-LEUKOCYTE INTERFERON GENE *NATURE* 292:756, 1981 55R ICI LTD,DIV PHARMACEUT MACCLESFIELD SK10 4TG , CHESHIRE , ENGLAND	15
2	GOEDDEL DV, DULL TJ, GRAY PW, GROSS M, LAWN RM, LEUNG DW, MCCANDLI.R, SEEBURG PH, ULLRICH A, YELVERTO.E THE STRUCTURE OF 8 DISTINCT CLONED HUMAN-LEUKOCYTE INTERFERON CDNAS *NATURE* 290:20, 1981 47R GENENTECH INC,DEPT MOLEC BIOL SAN FRANCISCO , CA 94080	15
3	GORDON J, MINKS MA THE INTERFERON RENAISSANCE - MOLECULAR ASPECTS OF INDUCTION AND ACTION *MICROBIOL R* 45:244, 1981 R 263R FRIEDRICH MIESCHER INST CH-4002 BASEL , SWITZERLAND	15
4	HOUGHTON M, BARBER C, CAREY NH, CATLIN GH, DOEL SM, JACKSON IJ, PORTER AG THE ABSENCE OF INTRONS WITHIN A HUMAN FIBROBLAST INTERFERON GENE *NUCL ACID R* 9:247, 1981 51R GD SEARLE & CO LTD,SEARLE RES & DEV,DEPT MOLEC GENET,POB 53,LANE END RD HIGH WYCOMBE HP12 4HL , BUCKINGHAMSHIRE , ENGLAND	13
5	TAVERNIE J, DERYNCK R, FIERS W EVIDENCE FOR A UNIQUE HUMAN FIBROBLAST INTERFERON (IFN-BETA-1) CHROMOSOMAL GENE, DEVOID OF INTERVENING SEQUENCES *NUCL ACID R* 9:461, 1981 36R STATE UNIV GHENT,MOLEC BIOL LAB B-9000 GHENT , BELGIUM	13

	1982	RW
23	FANTES KH INTERFERONS - CHEMICAL PROPERTIES *TEX REP BIO* 41:240, 1982 R 79R WELLCOME RES LABS,DEPT VIROL RES & DEV BECKENHAM BR3 3BS, KENT, ENGLAND	19
24	SEHGAL PB THE INTERFERON GENES *BIOC BIOP A* 695:17, 1982 R 108R ROCKEFELLER UNIV NEW YORK, NY 10021	17
25	BERG K PURIFICATION AND CHARACTERIZATION OF MURINE AND HUMAN INTERFERONS - A REVIEW OF THE LITERATURE OF THE 1970S *ACT PAT M C* 1982 1, 1982 R 334R AARHUS UNIV,INST MED MICROBIOL DK-8000 AARHUS C, DENMARK	16
26	DZIEWANO.ZE, PESTKA S THE HUMAN INTERFERONS *MED RES REV* 2:325, 1982 R 166R HOFFMANN LA ROCHE INC,DEPT MED ONCOL & IMMUNOL NUTLEY, NJ 07110	16
27	LENGYEL P BIOCHEMISTRY OF INTERFERONS AND THEIR ACTIONS *ANN R BIOCH* 51:251, 1982 R 257R YALE UNIV,DEPT MOLEC BIOPHYS & BIOCHEM NEW HAVEN, CT 06511	16
28	RUBINSTE.M THE STRUCTURE OF HUMAN INTERFERONS *BIOC BIOP A* 695:5, 1982 73R WEIZMANN INST SCI IL-76100 REHOVOT, ISRAEL	16
29	RUBINSTE.M PURIFICATION AND STRUCTURAL ANALYSIS OF INTERFERON *PHI T ROY B* 299:39, 1982 51R WEIZMANN INST	15

Figure 5: 1983 and 1984 key citing papers included in the supplemental bibliography, ranked by relevance. For reasons of space, all 23 key citing papers cannot be shown.

Specialty (98)

Structural Studies of Fibroblast and Leukocyte Interferon-Genes

Key Citing Documents

	1983	RW
1	PESTKA S THE HUMAN INTERFERONS - FROM PROTEIN-PURIFICATION AND SEQUENCE TO CLONING AND EXPRESSION IN BACTERIA - BEFORE, BETWEEN, AND BEYOND *ARCH BIOCH* 221:1, 1983 R 174R ROCHE INST MOLEC BIOL NUTLEY, NJ 07110	18
2	DWORKINR.E, DWORKIN MB, SWETLY P MOLECULAR-CLONING OF HUMAN ALPHA-INTERFERON AND BETA-INTERFERON GENES FROM NAMALWA CELLS *J INTERF R* 2:575, 1982 47R ERNST BOEHRINGER INST ARZNEIMITTELFORSCH,BIOCHEM LAB, DR BOEHRINGER GASSE 5-11 A-1121 VIENNA, AUSTRIA	12
3	MCCULLAG.KG, CATLIN GH, DAVIES JA, DAWSON KM, DOEL SM, HOUGHTON M, ONEILL GJ, SIM IS BIOLOGICAL PROPERTIES OF HUMAN INTERFERON BETA-1 SYNTHESIZED IN RECOMBINANT BACTERIA *J INTERF R* 3:97, 1983 N 48R SEARLE RES & DEV,DEPT BIOL,POB 53,LANE END RD HIGH WYCOMBE HP12 4HL, BUCKS, ENGLAND	12
4	ATTALLAH AM, JOHNSON RP, PETRICCI.JC, YEATMAN TJ BIOLOGICAL RESPONSE MODIFIERS AND THEIR PROMISE IN CLINICAL MEDICINE *PHARM THERA* 19:435, 1982 R 148R US BUR BIOL,BLDG 29,ROOM 507,8800 ROCKVILLE PIKE BETHESDA, MD 20205	11
5	WEISSMAN.C THE ALPHA-INTERFERONS - SOME ANSWERS AND MANY QUESTIONS *HARVEY LECT* 1983:129, 1983 R 69R UNIV ZURICH,INST MOLEKULARBIOL 1 CH-8006 ZURICH, SWITZERLAND	11
6	WILSON V, BARRIE PA, BOSELEY PG, BURKE DC, EASTON A, JEFFREYS AJ, SLOCOMBE PM A COMPARISON OF VERTEBRATE INTERFERON GENE FAMILIES DETECTED BY HYBRIDIZATION WITH HUMAN INTERFERON DNA *J MOL BIOL* 166:457, 1983 61R UNIV LEICESTER,DEPT GENET LEICESTER LE1 7RH, ENGLAND	10
7	HAYNES J, WEISSMAN.C CONSTITUTIVE, LONG-TERM PRODUCTION OF HUMAN INTERFERONS BY HAMSTER-CELLS CONTAINING MULTIPLE COPIES OF A CLONED INTERFERON GENE *NUCL ACID R* 11:687, 1983 56R UNIV ZURICH,INST MOLEK BIOL 1 *CH-8093 ZURICH, SWITZERLAND*	9
8	KELKER HC, ANDERSON P, VILCEK J, YIP YK EFFECTS OF GLYCOSIDASE TREATMENT ON THE PHYSICO-CHEMICAL PROPERTIES AND BIOLOGICAL-ACTIVITY OF HUMAN INTERFERON-GAMMA *J BIOL CHEM* 258:8010, 1983 40R NYU,SCH MED,DEPT MICROBIOL NEW YORK, NY 10016	9

	1984	RW
12	MENGE U, KULA MR PURIFICATION TECHNIQUES FOR HUMAN INTERFERONS *ENZYME MICR* 6:101, 1984 R 142R GESELL BIOTECHNOL FORSCH MBH,MASCHERODER WEG 1 D-3300 BRUNSWICK, FED REP GER	10
13	BOWDEN DW, GILL T, HSIAO K, LILLQUIS.JS, MAO JI, TESTA D, VOVIS GF CLONING OF EUKARYOTIC GENES IN SINGLE-STRAND PHAGE VECTORS - THE HUMAN INTERFERON GENES *GENE* 27:87, 1984 37R COLLABORAT RES INC,128 SPRING ST LEXINGTON, MA 02173	9
14	YONEHARA S JA)) RECEPTOR SYSTEM FOR INTERFERON *SEIKAGAKU* 56:184, 1984 R 49R TOKYO METROPOLITAN INST MED SCI,BIOPHYLAXIS SECT, BUNKYO KU TOKYO 113, JAPAN	8
15	KHESIN YE, AMCHENKO.AM, GULEVICH NE, NAROVLYA.AN, VORONINA FV RS)) GENETIC MECHANISMS OF THE HUMAN INTERFERON SYSTEM AS A FACTOR OF THE MAINTENANCE OF CELLULAR HOMEOSTASIS *VA MED NAUK* 80, 1984 R 75R NF GAMALEYA EPIDEMIOL & MICROBIOL INST MOSCOW, USSR	7
16	DIJKEMA R, DEREUS A, POUWELS P, SCHELLEK H STRUCTURE AND EXPRESSION IN ESCHERICHIA-COLI OF A CLONED RAT INTERFERON-ALPHA GENE *NUCL ACID R* 12:1227, 1984 34R TNO,MED BIOL LAB,POB 45 2280 AA RIJSWIJK, NETHERLANDS	6
17	KELLEY KA, DANDOY F, DEMAEYER E, DEMAEYER J, KOZAK CA, PITHA PM, SKUP D, SOR F, WINDASS JD MAPPING OF MURINE INTERFERON-ALPHA GENES TO CHROMOSOME-4 *GENE* 26:181, 1983 36R JOHNS HOPKINS UNIV,SCH MED,CTR ONCOL BALTIMORE, MD 21205	6
18	OSHEROFF PL, CHIANG TR, TAHARA SM MONOCLONAL ANTIBODIES TO A RECOMBINANT HUMAN-LEUKOCYTE INTERFERON TRIFN-ALPHA-B *CLIN IMMUN* 30:188, 1984 20R HOFFMANN LA ROCHE INC,ROCHE RES CTR,BIOPOLYMER RES DEPT,340 KINGSLAND ST NUTLEY, NJ 07110	6
19	BRUNDA MJ, ROSENBAU.D *MODULATION OF MURINE NATURAL-KILLER CELL* ACTIVITY INVITRO AND INVIVO BY RECOMBINANT HUMAN INTERFERONS *CANCER RES* 44:597, 1984 35R HOFFMANN LA ROCHE INC,DEPT EXPTL & APPL BIOL NUTLEY, NJ 07110	5

papers are also ranked by relevance, that is, the number of core papers they cited.

The *Atlas* also includes a foldout "global" map of all 127 specialties, a clustering of clusters. Each research front or specialty is identified in the map by its name and cluster number. We created this map using "residual links." A residual link occurs when two core papers from different specialties are co-cited, but not frequently enough to place them in the same cluster. In this way we can cluster groups of research fronts.

We have also included a number of indexes to make the information contained in the *Atlas* readily retrievable. The author index includes all authors and coauthors of papers included in the

Atlas. There is also an alphabetic keyword index to the names or titles of the research fronts, and an alphabetic listing of all the significant words from every document title. Finally, we have added an institutional index organized by country and city.

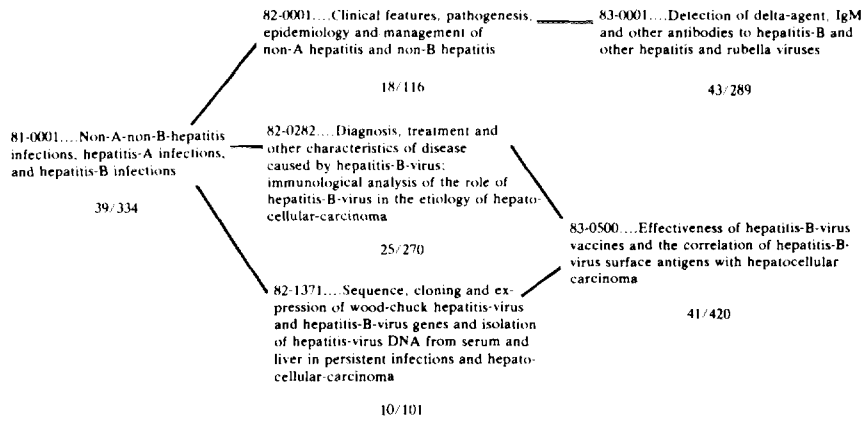
We have also included a 1981 to 1983 chronology for the 52 most-active research fronts to illustrate the dynamic processes of expansion and contraction within the research universe. As was mentioned here earlier, we deliberately chose to minireview the "hottest" fields, and most of these 52 fronts have dramatically changed in terms of core papers, volume of publication, and nomenclature. Thus, having identified a particular 1981 research front in the main *Atlas*, you can observe where that research front had moved in 1982 and 1983.

For example, Figure 6 shows the 1981-1983 chronology for research front #81-0001, which is Specialty 99 in the *Atlas*. The six-digit code number identifies the specialty in the *Index to Research Fronts in ISI/BIOMED®, 1983*. In 1981, this research front, entitled "Non-A-Non-B-Hepatitis-Infections, Hepatitis-A-Infections, and Hepatitis-B-Infections," consisted of 39 core papers and 334 citing papers. By 1982, it split into three separate research fronts. Research front #82-0001 deals with the clinical diagnosis and management of hepatitis infections. It included 18 core papers and 116 citing papers. By 1983, this research front contained 43 core papers and 289 citing papers on the immunological aspects of hepatitis as well as rubella viruses.

The other two 1982 research fronts focus on the connection between hepatitis B virus and hepatocellular cancer. Research front #82-0282, which concentrates on the diagnosis, treatment, and immunological features of hepatitis B virus, included 25 core papers and 270 citing papers. Research front #82-1371 contained 10 core papers and 101 citing papers on the sequence, cloning, and expression of hepatitis genes. By 1983, these two research fronts merged and included 41 core papers and 420 citing papers.

In addition to research directors, we anticipate that educators, graduate students, and scientists will be the principal users of the *Atlas*. Historians of science, administrators, and librarians will also find it useful. Teachers can use the lists

Figure 6: Sample 1981-1983 chronology for Specialty 99 in the *Atlas*.



of core documents and key citing documents as the basis for preparing reading lists. By using these bibliographies, they can be certain that they've included the papers that have had the greatest impact on the particular topic under discussion. In addition to the bibliographic information, the minireviews could be used when assigning reading for seminars or thesis topics.

In the near future, we will be announcing further developments in the evolution of the *Atlas*. In 1985, we plan to make the same type of encyclopedic information available online. Eventually, we expect to create several thousand minireviews each year. Together with the reference lists for the core and current literature for each research front, the minireviews will become a dynamic, up-to-date account of any topic you choose.

There is a kind of Matthew effect not only with respect to authors[3] but also to subjects. One of the commentators to whom I sent the preliminary *Atlas* material suggested that we were emphasizing those subjects that were already widely discussed in the literature. This is in fact implicit in our definition of "most active" since we chose the first 52 topics to be minireviewed on the basis of the number of articles published. Presumably, there is a large current interest in these topics, because publication productivity is high. However, we realize that less popular topics need reviewing as much as the "hot" ones. We intend to stress such topics in our online *Atlas*.

However, if we restricted our minireviewing to the least "popular" topics, it would diminish the value of our exercise in scientography. In a sense, we would be limiting our discussion to the unexplored parts of the world and omitting world-class science. It would be a strange and perverse type of encyclopedism to begin by reviewing *only* the partially explored areas of science.

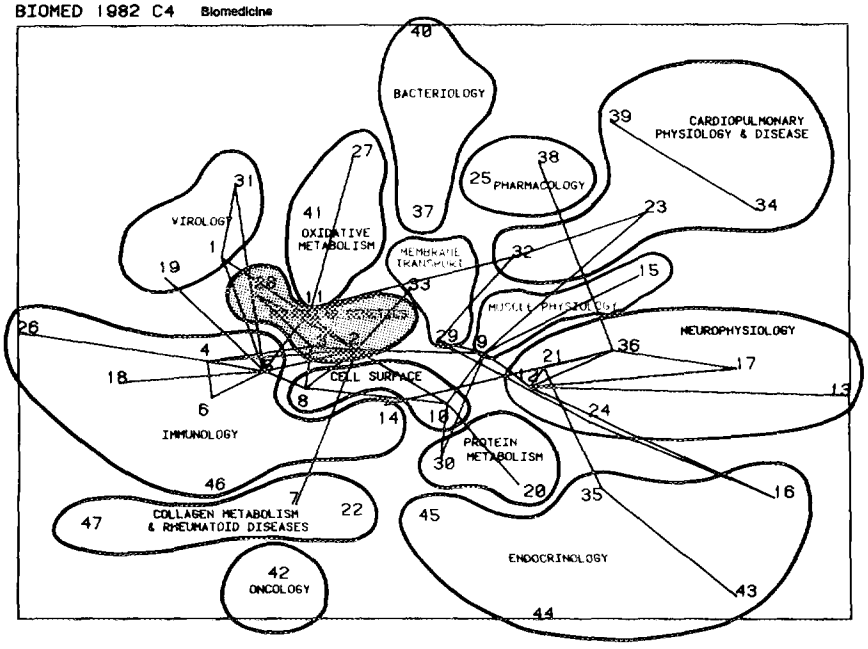
The advantage of an online version of the *Atlas* is that lists of references can literally become up-to-the-minute. By combining this information with our *Automatic Subject Citation Alert* (*ASCA*®) service, we can regularly provide weekly bibliographic supplements to the minireviews. In fact, this is how we added the 1983/84 supplement to the *Atlas* just a few weeks ago. We have been able to overcome many of the time limitations involved in printing a volume of more than 700 pages. However, no printed edition can match the ultimate timeliness of an electronic version of the *Atlas*.

Figure 7 shows our so-called "C4 level" map of the 1982 world of biomedicine. The territory covered by the *Atlas* primarily falls into the gray-shaded area. Don't be deceived by the relatively small size of this area. It requires an 11" x 21" foldout map, included with the *Atlas*, to detail all the research fronts associated with this rather large and active area of science. The territories we have marked off have no physical significance, that is, they do not measure the size of the field in terms of publications. The research area subtended by each is a measure of distance in a mathematical sense.

We have provided you with examples of both superstar and less brilliant research areas. Among the thousands of areas yet to be minireviewed are stars of varying brilliance. In a reasonable time we hope to have online at least those of maximal brightness. And with the software we are developing, you will eventually be able to zoom in on the faintest of stars in the Universe of Science.

The *ISI Atlas of Science: Biotechnology and Molecular Genetics 1981/82* (ISSN: 0278-2898; ISBN: 0-941708-01-2) including the Bibliographic Update for 1983/84 can now be ordered directly from Jim Shea, ISI, 3501 Market Street, Philadelphia, PA 19104. We expect the first copies of the *Atlas* to be delivered in November. If you are not familiar with

Figure 7: Map of 1982 clusters in the *ISI BIOMED*® database at the C4 level showing the grand divisions of bioscience. The shaded area represents the territory covered in the *ISI Atlas of Science*®: *Biotechnology and Molecular Genetics, 1981/82*. A = number identifying C3 cluster. B = cluster names.



Each C3 cluster is a cluster of C2 clusters that in turn is a cluster of C1 research fronts. Each forms part of the hierarchy from discipline to subspecialty to core paper.

A	B
1	Immunology and treatment of viral hepatitis
2	DNA structure and factors controlling gene expression
3	Histone and non-histone nuclear proteins
4	Immunoglobulin expression and regulation of the immune response
5	Cellular immunity and diseases of the immune response
6	Chromosome abnormalities and immune response in Hodgkins disease, leukemia and other malignant diseases
7	Collagen genes and collagen synthesis
8	Cell surface composition and effects of various agents on cancer cells
9	Contractile proteins, membrane dynamics, neuronal development and effects of calcium
10	Effects of peptide hormones on cell surface receptors and metabolism
11	Cytotoxicity of oxygen free radicals, macrophages and other substances
12	Peptide hormones and release factors, neurotransmitters and opioid peptides in the CNS
13	Nociception
14	Chemotaxis, histamine release, and purine and pyrimidine metabolism
15	Myosin isoenzymes and innervation patterns in muscle
16	Hypothalamic obesity and the control of food intake
17	Amino acid neurotransmitters
18	Allergies, immunotherapy and cimetidine treatment
19	Regulation of protein synthesis with interferon and other methods in virus infected cells
20	Lipoproteins
21	Receptors for neurotransmitters
22	Collagen metabolism in rheumatoid arthritis and fibroblasts
23	Assessment of ventricular function and management of ventricular disease
24	Hypertension

25 Management of ulcers and other gastrointestinal disorders
26 Cyclophosphamide therapy and delayed-type hypersensitivity
27 Lipid peroxidation and oxygen free radical metabolism in liver
28 DNA repair and anti-cancer drugs
29 Treatment of infections, and prostaglandins and related compounds and kidney function
30 Proteases, amino acid metabolism and protein degradation
31 Herpes simplex virus and infections of homosexual men
32 Adult respiratory distress syndrome and pulmonary vascular injuries
33 Protein and proton translocation across membranes
34 Respiration
35 Pituitary hormones
36 Adenosine and GABA receptors and drug analogs
37 Bacterial toxins and diseases of *E-coli* and other enteric bacteria
38 Theophylline and pharmacokinetics of drug therapy in the elderly
39 Sudden infant death syndrome, sleep apnea and esophageal disorders
40 Treatment of infective endocarditis and staphylococcal infections
41 Cytochrome-P-450 and metabolism of cytotoxic aromatic hydrocarbons
42 Treatment of cancer using methotrexate and other drugs
43 Steroid hormones in the pituitary and effects on development and sexual behavior
44 Management of diabetes
45 Hyperparathyroidism and regulation of protein secretion
46 Importance of dietary zinc
47 HLA systems in rheumatic diseases and lupus erythematosus

the earlier *Atlas of Biochemistry*, we can send you a brochure that describes it. The *ISI Atlas of Science: Biochemistry and Molecular Biology, 1978/80* (ISSN: 0278-2898; ISBN: 0-941708-00-4) can still be purchased for $90 while the supply lasts. The new *ISI Atlas of Science: Biotechnology and Molecular Genetics, 1981/82* is priced at $250. Each includes the maps and indexes described earlier.

* * * * *

My thanks to Brad Schepp for his help in the preparation of this essay.

REFERENCES

1. **Cedering S.** A letter from Caroline Herschel (1750-1848). (Poem.) *Science 84* 5(5):65, 1984.
2. **Garfield E.** Introducing the *ISI Atlas of Science: Biochemistry and Molecular Biology, 1978/80*. *Essays of an information scientist*. Philadelphia: ISI Press, 1983. Vol. 5, p. 279-87.
3. **Merton R K.** The Matthew effect in science. *Science* 159:56-63, 1968.