## **Current Comments®**

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Science Watch: ISI's Highly Cited Newsletter Shows How Quantitative Assessments of the Literature Can Contribute to R&D Management, Policymaking, and Strategic Analysis

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At the beginning of this year, ISI® embarked on a new venture with the publication of *Science Watch* TM, a monthly eightpage newsletter that combines scientometrics with the expertise of insiders to track trends and performance in basic research.

When I announced Science Watch to Current Contents ® (CC ®) readers last January,1 I said that it would be a unique publication. That's because Science Watch bases all its stories on quantitative assessments of the scientific literature, both in the form of publication and citation statistics. That perspective on scientific research activity is available nowhere else. In particular, by analyzing significant patterns of citations-to a paper, a field, or an institution—Science Watch is able to reflect accurately the scientific community's collective judgment on what are the hot and emerging areas, as well as on which institutions and which researchers are leading the way in those areas.

During almost a year of publication, Science Watch has already become an authoritative source for information on trends and performance in scientific research. What's more, this information is showing a widening audience something of the benefits that scientometrics can bring to their professional lives. It provides a new kind of intelligence about scientific activity.

To date, scientometrics has been chiefly the domain of academics and some science policy analysts. But *Science Watch* has consciously tried to bring scientometrics to a broader audience, including R&D managers and administrators, marketing and strategic analysts in industry, financial analysts who track science-based industries, venture capitalists who invest in those businesses, as well as science journalists.

Industry is increasingly turning to quantitatively based science indicators to help plan their business strategies—to better understand how a particular company is deploying its research resources, which ones are making the most significant contributions in a certain area, or whether a firm might be overlooking an important, emerging topic.

Journalists certainly have picked up on Science Watch, as evidenced by frequent quotation of the newsletter in national newspapers such as the Wall Street Journal, the New York Times, the Washington Post, Newsday, the Toronto Globe and Mail, and publications like Nature, Science, New Scientist, The Scientist ®, the British Medical Journal, Asia Technology, and many others. The reason these well-respected publications are quoting Science Watch is plain: it is providing a unique, global view on the scientific scene, and that view is both interesting and relevant to a broad audience.

In the following pages, we are reprinting three stories from past issues of Science Watch to give CC readers a taste for the types of analyses found in Science Watch. The first lists the top 10 papers in biology, based on current levels of citations, and highlights the impressive record of Howard Hughes Medical Institute investigators in fielding hot papers. Science Watch gleans this information from ISI's Hot Papers database, which records papers published during the last three years that are attracting more citations than other papers of the same type and vintage. (Incidentally, in 1991 CC readers will find in these pages expanded coverage of both hot papers and research fronts.) The second focuses on an intriguing new discovery in clinical medicine: a link

between a bacterium and peptic ulcer disease. This story relies on ISI's Research-Front Database, an annual compilation of some 8,000 significant and currently active specialty areas based on patterns of co-citation analysis. The last, on the 10 US universities that have exhibited the greatest improvement in citation impact (mean citations per paper) of their science papers, draws on the Science Indicators database, a custom in-house file that is a subset of ISI's Science Citation Index ©.

These three databases—the Science Indicators file, the Research-Front Database, and the Hot Papers file—are state-of-the-art tools that permit ISI to conduct analyses that are beyond the capability of any other organization.

In that context I should mention as well that these resources are available to others through ISI's Research Department, which conducts custom contract research for government agencies here and abroad, universities, independent labs, and science-based businesses, such as pharmaceutical and biotechnology firms and scientific equipment manufacturers.

If the following stories whet your appetite for *Science Watch*, I invite you to fill out the order form at the end of this essay. Those who subscribe before 1991 are entitled to a special charter subscription rate of \$245.00, which is \$50.00 off the regular subscription rate of \$295.00.

If you wish to examine Science Watch in greater detail and would like a recent sample issue, please write to the editor, David A. Pendlebury, Research Department, 3501 Market Street, Philadelphia, Pennsylvania 19104, or call him at 1-800-523-1850, ext. 1411. Inquiries regarding custom contract research should be directed to either David or to Henry Small, director of the Research Department, at ext. 1307.

#### REFERENCE

 Garfield E. Announcing Science Watch: a unique newsletter tracking trends and performance in scientific research. Current Contents (4):3-7, 22 January 1990.

Reprinted from Science Watch 1(8):5, September 1990.



### **Cell Signaling, Gene Expression Dominate Biology Top Ten**

Two major themes and one impressive statistic stand out in the current list of the hottest papers in biology. The themes are signal transduction and transcription. The statistic is that four of these 10 papers are by Howard Hughes Medical Institute (HHMI) investigators.

Science Watch turned to W. Maxwell Cowan, Vice President and Chief Scientific Officer of HHMI, for a perspective on these papers and his reaction to the strong showing by HHMI scientists.

"The list reflects the great current interest in two principal areas," says Cowan. "The first is how cells send signals to each other, which involves both cell surface receptors and how these receptors activate intracellular signaling mechanisms. The second major area is gene regulation. The tie-in between the two is that many of the signaling mechanisms result in the activation of factors that either bind to DNA or bind to proteins which have already bound to DNA. An example of a paper that brings these themes together is #9. These two areas, signal transduction and transcription, are among the hottest fields in molecular biology today."

In the last list of hot papers in biology (see *Science Watch*, 1[7]:5, July-August 1990), three were by HHMI researchers. This time there are four. To obtain a broader view of the contribution of HHMI investigators to the best of biology today, *Sci*-

WHAT'S HOT IN BIOLOGY.		
Paper	Citations This Period (May-June 90)	Rank Last Period (Mar-Apr 90)
Y. Nishizuka, "The molecular heterogeneity of protein kinase C and its implications for cellular regulation," <i>Nature</i> , 334(6184):661-5, 25 August 1988. [Kobe U. Sch. Med., Kobe, Japan]	2	
R.M. Evans, "The steroid and thyroid-hormone receptor su- perfamily," <i>Science</i> , 240(4854):889-95, 13 May 1988. [How- ard Hughes Med. Inst., Salk Inst. Biol. Studies, La Jolla, Calif.]	68	3
W.H. Landschulz, P.F. Johnson, S.L. McKnight, "The leucine zipper: a hypothetical structure common to a new class of DNA-binding proteins," <i>Science</i> , 240(4860):1759-64, 24 June 1988. [Howard Hughes Med. Inst., Dept. Embryol., Carnegie Inst. Washington, Baltimore, Md.]	5	
P.J. Mitchell, R. Tjian, "Transcriptional regulation in mamma- lian cells by sequence specific DNA-binding proteins," <i>Sci-</i> <i>ence</i> , 245(4916):371-8, 28 July 1989. [Howard Hughes Med. Inst., U. Calif., Berkeley]	54	*
S.K. Hanks, A.M. Quinn, T. Hunter, "The protein kinase family: Conserved features and deduced phylogeny of the catalytic domains," <i>Science</i> , 241(4861):42-52, 1 July 1988. [Salk Inst. Biol. Studies, La Jolla, Calif.]	51	10
M. Ptashne, "How eukaryotic transcriptional activators work," Nature, 335(6192):683-9, 20 October 1988. [Harvard U., Cambridge, Mass.]	50	7
M.J. Berridge, R.F. Irvine, "Inositol phosphates and cell sig- naling," <i>Nature</i> , 341(6239):197-205, 21 September 1989. [A.F.R.C., Cambridge, U.K.]	44	*
M. Beato, "Gene regulation by steroid hormones," <i>Cell,</i> 56(3):335-44, 10 February 1989. [Inst. Molekular Biol. & Tumorforsch., Marburg, F.R.G.]	37	4
R. Chiu, W.J. Boyle, J. Meek, T. Smeal, T. Hunter, M. Karin, "The c-Fos protein interacts with c-Jun/AP-1 to stimulate transcription of AP-1 responsive genes," <i>Cell</i> , 54(4):541-52, 12 August 1988. [U. Calif., San Diego Sch. Med.; and Salk Inst. Biol. Studies, La Jolla, Calif.]	34	*
M.M. Davis, P.J. Bjorkman, "T-cell antigen receptor genes and T-cell recognition," <i>Nature</i> , 334(6181):395-402, 4 August 1988. [Howard Hughes Med. Inst. and Dept. Microbiol. & Im- munol., Stanford U. Sch. Med., Stanford, Calif.]	32	*
	Paper  Y. Nishizuka, "The molecular heterogeneity of protein kinase C and its implications for cellular regulation," <i>Nature</i> , 334(6184):661-5, 25 August 1988. [Kobe U. Sch. Med., Kobe, Japan]  R.M. Evans, "The steroid and thyroid-hormone receptor superfamily," <i>Science</i> , 240(4854):889-95, 13 May 1988. [Howard Hughes Med. Inst., Salk Inst. Biol. Studies, La Jolla, Calif.]  W.H. Landschulz, P.F. Johnson, S.L. McKnight, "The leucine zipper: a hypothetical structure common to a new class of DNA-binding proteins," <i>Science</i> , 240(4860):1759-64, 24 June 1988. [Howard Hughes Med. Inst., Dept. Embryol., Carnegie Inst. Washington, Baltimore, Md.]  P.J. Mitchell, R. Tjian, "Transcriptional regulation in mammalian cells by sequence specific DNA-binding proteins," <i>Science</i> , 245(4916):371-8, 28 July 1989. [Howard Hughes Med. Inst., U. Calif., Berkeley]  S.K. Hanks, A.M. Quinn, T. Hunter, "The protein kinase family: Conserved features and deduced phylogeny of the catalytic domains," <i>Science</i> , 241(4861):42-52, 1 July 1988. [Salk Inst. Biol. Studies, La Jolla, Calif.]  M. Ptashne, "How eukaryotic transcriptional activators work," <i>Nature</i> , 335(6192):683-9, 20 October 1988. [Harvard U., Cambridge, Mass.]  M.J. Berridge, R.F. Irvine, "Inositol phosphates and cell signaling," <i>Nature</i> , 341(6239):197-205, 21 September 1989. [A.F.R.C., Cambridge, U.K.]  M. Beato, "Gene regulation by steroid hormones," <i>Cell</i> , 56(3):335-44, 10 February 1989. [Inst. Molekular Biol. & Tumorforsch., Marburg, F.R.G.]  R. Chiu, W.J. Boyle, J. Meek, T. Smeal, T. Hunter, M. Karin, "The c-Fos protein interacts with c-Jun/AP-1 to stimulate transcription of AP-1 responsive genes," <i>Cell</i> , 54(4):541-52, 12 August 1988. [U. Calif., San Diego Sch. Med.; and Salk Inst. Biol. Studies, La Jolla, Calif.]	Y. Nishizuka, "The molecular heterogeneity of protein kinase C and its implications for cellular regulation," <i>Nature</i> , 334(6184):661-5, 25 August 1988. [Kobe U. Sch. Med., Kobe, Japan]  R.M. Evans, "The steroid and thyroid-hormone receptor superfamily," <i>Science</i> , 240(4854):889-95, 13 May 1988. [Howard Hughes Med. Inst., Salk Inst. Biol. Studies, La Jolla, Calif.]  W.H. Landschulz, P.F. Johnson, S.L. McKnight, "The leucine zipper: a hypothetical structure common to a new class of DNA-binding proteins," <i>Science</i> , 240(4860):1759-64, 24 June 1988. [Howard Hughes Med. Inst., Dept. Embryol., Carnegie Inst. Washington, Baltimore, Md.]  P.J. Mitchell, R. Tijian, "Transcriptional regulation in mammalian cells by sequence specific DNA-binding proteins," <i>Science</i> , 245(4916):371-8, 28 July 1989. [Howard Hughes Med. Inst., U. Calif., Berkeley]  S.K. Hanks, A.M. Quinn, T. Hunter, "The protein kinase family: Conserved features and deduced phylogeny of the catalytic domains," <i>Science</i> , 241(4861):42-52, 1 July 1988. [Salk Inst. Biol. Studies, La Jolla, Calif.]  M. Ptashne, "How eukaryotic transcriptional activators work," <i>Nature</i> , 335(6192):683-9, 20 October 1988. [Harvard U., Cambridge, Mass.]  M.J. Berridge, R.F. Irvine, "Inositol phosphates and cell signaling," <i>Nature</i> , 341(6239):197-205, 21 September 1989.  [A.F.R.C., Cambridge, U.K.]  R. Chiu, W.J. Boyle, J. Meek, T. Smeal, T. Hunter, M. Karin, "The c-Fos protein interacts with c-Jun/AP-1 to stimulate transcription of AP-1 responsive genes," <i>Cell</i> , 54(4):541-52, 12 August 1988. [U. Calif., San Diego Sch. Med.; and Salk Inst. Biol. Studies, La Jolla, Calif.]  M.M. Davis, P.J. Bjorkman, "T-cell antigen receptor genes and T-cell recognition," <i>Nature</i> , 334(6181):395-402, 4 August 1988. [Howard Hughes Med. Inst. and Dept. Microbiol. & Im-

### SOURCE: ISI's Hot Papers Database

NB. Only papers published since May 1988 are tracked. An asterisk indicates that the paper was not ranked in the top ten during the last period. In the event that two or more papers collected the same number of citations in the most recent bimonthly period, total citations to date determine the rankings.

ence Watch searched ISI's Hot Papers Database, which as of May-June 1990 contained some 1,250 papers representing a variety of disciplines. These papers were all published since the beginning of 1987 and have been cited much more frequently than papers of a similar type. Of the 894 representing biology broadly defined, nearly one in 10 is by an HHMI investigator. HHMI currently sponsors about 220 U.S. scientists.

Science Watch found, by comparison, that 84 papers in the Database were the work of researchers in the intramural programs at NIH and NIMH. The fact that some 220 HHMI investigators have fielded roughly the same number of hot papers as all NIH and NIMH intramural researchers, who number perhaps 10 times that of the HHMI group, suggests to Science Watch that HHMI's recruitment and research decisions are now highly influential in shaping the future of U.S. biology and biomedicine.

"I think you'd have to say that at this moment the voice Hughes exerts in the community in the areas of basic research in which it is involved is on the same level as the intramural program at NIH," Phillip A. Sharp of the Center for Cancer Research at MIT and an advisor to HHMI tells Science Watch. "But remember that the intramural program at NIH has responsibility for clinical and basic sciences, areas that Hughes does not have."

Sharp is quick to add, too, that these statistics should not be interpreted to mean that "all we have to do is find the top 2% of the scientific community and support

# HHMI Investigators Fielded Nearly 10% of the Hottest Biology Papers, 1987-90

No. of biology papers in ISI's Hot Papers Database published since 1987 894
·
No. by HHMI investigators 82
Percent by HHMI investigators9.2
HHMI investigators ranked by number of hot papers published since 1987:
Robert Tjian (UC Berkeley)10
Ronald M. Evans (Salk Inst.)
John W. Kappler & Philippa Marrack (Natl.
Jewish Ctr. for Immunol.
& Resp. Med.) 4
Robert J. Lefkowitz (Duke U.)4
Stephen L. McKnight (Carnegie Inst.) 4
Lewis T. Williams (UCSF)4
Graeme I. Bell (U. Chicago)3
Francis S. Collins (U. Michigan)
Corey S. Goodman (UC Berkeley)3
Lily Y. Jan & Yuh Nung Jan (UCSF)3
Daniel Nathans (Johns Hopkins U.)3
Don C. Wiley (Harvard U.)3

them." Rather, he says that HHMI's selection process has given it a leadership role.

"There are leaders in science, and Hughes by and large has identified many of them in the areas it is supporting, but it hasn't really been active long enough to establish those people as leaders," Sharp says. "So the question is, how will Hughes exert its leadership in the future? If Hughes can be more innovative than NIH in pushing science forward because it has fewer restrictions, then I think Hughes is justifiable as an organization. That's the challenge for Hughes."

Reprinted from Science Watch 1(4):7, April 1990.

### **Evidence Mounts on Bacterium's Role in Peptic Ulcer Disease**

In 1983, Australian researchers J. Robin Warren and Barry J. Marshall published the surprising findings that a bacterium (first identified as *Campylobacter pylori*, but renamed *Helicobacter pylori* last October) was strongly associated with gastritis, a common inflammation of gastric mucosa. Later studies by these and other investigators have shown that *H*.

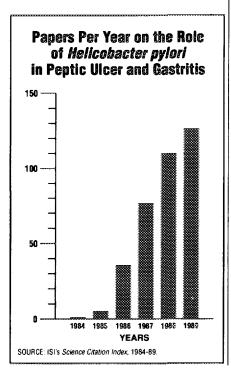
*pylori* probably plays a causative or a contributory role in peptic ulcer disease.

The hypothesis that an infectious agent may lead to gastritis and ulcer has sparked considerable controversy, since it runs counter to long-held ideas about the pathogenesis of gastrointestinal disease. Researchers now generally accept that *H. pylori* is the causative agent of

gastritis, and more and more are coming around to accept its "essential role" in peptic ulcer disease.

Science Watch searched ISI's Science Citation Index database for the years 1984-1989 and identified papers published each year that had the name of the bacterium (Campylobacter pylori or, more recently, Helicobacter pylori, or variant spellings of those names) and the terms ulcer or gastritis in their titles. The results appear in the histogram below. Research on this topic has clearly taken off, and experts tell Science Watch that the pace of research shows no signs of slowing.

"It's a hot field in GI, definitely," says Nicholas Talley of the Mayo Clinic in Rochester, Minnesota. "Some are convinced—and I am becoming more convinced—that H. pylori is an essential player [in peptic ulcer]. If you remove that essential player, you may halt the disease process, and if that's the case, then it has enormous implications for therapy and will eventually revolutionize the whole field of duodenal ulcer treatment."



"Right now we clearly need more data. Also, there's no good therapy at the moment for eradicating *H. pylori*, so there's a difficulty with treatment that hasn't been overcome. That combination of factors makes many of us reticent to change what we do now, but I can foresee in the next decade a dramatic change."

#### **Antibacterial Treatment**

Talley says that he treats patients who have an ordinary ulcer with traditional anti-secretory agents like Zantac or Tagamet. "At present, traditional therapy heals ulcers as well as anything, and these drugs will probably still be used even if H. pylori is found to be important, which I think it is. But for the patients with severe relapsing duodenal ulcer disease, we have recommended that one heal the ulcer with traditional therapy and then consider trying to eradicate the organism at that time. It has not been absolutely proven that antibacterial therapy promotes ulcer healing, although it probably does.

The current strategy for eradicating *H. pylori* goes under the name "triple therapy" and uses two antibiotics and bismuth. "You have to use combination therapy, because nothing on its own works terribly well," says Talley. He points out, however, that triple therapy can have significant toxicity.

David Y. Graham, of Baylor University and the Veterans Administration Medical Center in Houston, Texas, is also cautious about the antibiotic-bismuth combination treatment.

"It's not yet a prime-time therapy," he tells Science Watch. "It has about a 60-70% success rate, with some side effects. On the other hand, the traditional methods are very effective and very safe. So we're telling people that Helicobacter pylori is the future, but stick with the present. Heal the ulcer and ignore the infection."

Another reason he hesitates to use antibacterial therapy at the moment is that failure of the treatment will likely leave the patient with very resistant organisms. "Then, three years from now, when you have a safe and effective therapy, you might not be able to cure them, so you might do them a great disservice."

	Helicobacter pylori: Where the Action Was in 1989						
Rank	Nation	Percent	Institution	Percent			
1	United Kingdom	26.0	Middlesex Hosp., London	5.1			
2	United States	16.2	Hammersmith Hosp., London	4.7			
3	Italy	9.8	Univ. Turin, Italy	3.1			
4	France	8.6	Hop. St. Andre, Bordeaux	2.4			
5	U.S.S.R.	6.3	Falun Cent. Hosp., Sweden 2				
6	Australia	4.8	St. James Univ. Hosp., Leeds 2.				
7	The Netherlands	4.2	Royal Perth Hosp., Australia				
8	All Others	24.1	All Others	78.4			
SOUR	CE: ISI's Science Citation	<i>Index</i> , 1989.	[n=127]				

Some, like Marshall, are recommending antibacterial therapy for all ulcer patients with the infection and even for those with dyspepsia (indigestion). But that is still a minority view. Generally, the clinical community is waiting for results from further studies before switching over to antibacterial treatments.

Research on *H. pylori* and its role in gastritis, dyspepsia, and peptic ulcer continues on many fronts. "There's work ongoing to look at what this bug does to the mucosa, on how it damages mucosa. Others are working on the bacterium itself to learn more about its genetics and how it attaches. In regard to ulcer disease, there are trials underway to see whether eliminating the bacterium

changes the course of the disease," says Talley. "And there's a lot of epidemiological work to see how common it is—who has disease and who doesn't. Overall, it's a multidisciplinary approach."

### New Drugs in Late 1990s

The pharmaceutical industry is also showing interest, Karl Habermas, a drug analyst at Sanford C. Bernstein in New York, tells *Science Watch*. "Companies are beginning to take notice and a few are developing compounds that they hope will target *H. pylori*." Habermas says that new ulcer treatments that include an antibacterial component will probably appear in the second half of the 1990s.

Reprinted from Science Watch 1(3):8, March 1990.

Congratulations to the University of South Alabama in Mobile. Its scientific papers showed the most improved performance, as measured by citation impact, for 1981-1988 as compared to 1973-1988, according to a recent survey conducted by ISI's Research Department.

The citations-per-paper rate for scientific articles from the University of South Alabama for 1973-1988 was 10.72, which was 76.1% of the average for the U.S. portion of ISI's Science Indicators file during this 16-year period (14.09). But for the period 1981-1988, the University of South Alabama's citation impact

(8.77) jumped to 92.5% of the U.S. file average (9.48). That gave the University an increase, in percentage terms, of 21.6% over its former rate and made it the top up-and-coming U.S. university in science among 100 surveyed.

"Certainly we are aware that we're making good progress, and it hasn't come accidentally," Charles M. Baugh, Dean of the Medical School and a long-time faculty member at the University of South Alabama tells Science Watch.
"There has been a push [for improvement] here, both to facilitate research and to recruit quality people. Good

# Up-And-Comers: 10 Most Improved U.S. Universities in Science

Rank	University	Increase in Impact 81-88 vs. 73-88	Impact 81-88	Rank 81-88
1	University of South Alabama Mobile, Ala.	21.6%	8.77	58
2	University of Houston Houston, Tex.	19.1%	9.02	51
3	Brigham Young University Provo, Utah	16.0%	8.02	78
4	Virginia Commonwealth University Richmond, Va.	15.4%	8.65	63
5	College of William and Mary Williamsburg, Va.	13.8%	8.12	75
6	Syracuse University Syracuse, N.Y.	12.5%	8.06	76
7	University of Massachusetts Amherst, Mass.	12.4%	9.12	47
8	Univ. California, Santa Barbara Santa Barbara, Calif.	12.0%	12.30	18
9	Creighton University Omaha, Neb.	10.1%	8.37	70
10	University of Vermont Burlington, Vt.	9.9%	8.29	72

SOURCE: ISI's Science Indicators File, 1973-88 and 1981-88.

faculty members are what makes this happen, of course, so we look at each faculty position as a very precious resource. At the Medical School we've been very cognizant of the importance of doing everything possible to help young people accomplish their research goals. In others words, we don't just recruit them and stick them in four walls. We try to get at least the minimal equipment necessary for them to be productive."

It is important to emphasize that this analysis measures each university against itself. In absolute terms, the University of South Alabama ranked 58th in citation impact for the period 1981-1988 and slightly below the average of the file. The only university among the 10 featured here that exhibited an above-average performance in citation impact for 1981-1988 is the University of California, Santa Barbara, which ranked 18th.