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Current Comments®

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A Citationist Perspective on Xenobiotics Research, 1981-1992: The Highest Impact Papers, Institutions, and Authors

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Abstract

A citation analysis of the xenobiotics literature published and cited from 1981 through 1992 is presented. It is based on 45 ISI® indexed journals, representing 123,063 research papers, reviews, and technical notes that received 986,375 citations. The papers, institutions, and authors with the highest current impact on xenobiotics research are identified.

Introduction

Last June, Laurence S. Kaminsky, New York State Department of Health, Wadsworth Center for Laboratories and Research, Albany, invited me to participate in the annual meeting of the International Society for the Study of Xenobiotics in Bal Harbour, Florida, from November 2 to November 6. I was happy to accept because it was a challenge to speak from the perspective of someone who knows next to nothing about the topic—xenobiotics.

Al Welljams-Dorof, ISI®'s director of corporate communications, spoke with Kaminsky to discuss appropriate topics and prepare the required data. They decided the audience would be most interested in a citationist perspective on current research in the field. That is, an analysis of the most-cited papers, institutions, and authors in xenobiotics. This essay is a condensed version of the Florida presentation.

What Xenobiotics Is: The Humpty Dumpty Syndrome

The first task was to find out what xenobiotics is. The easiest option is to consult a dictionary, which gave a brief and uninformative definition—a chemical compound foreign to living organisms. Another option is to ask someone, and Kaminsky gave us a good idea of what a specialist in the field thinks xenobiotics is all about.

However, from 40 years of experience with citation and linguistic analyses, I've learned that subjects are not always what people say they are. It is like what Humpty Dumpty said to Alice—"When I use a word it means just what I choose it to mean, neither more nor less." In fact, xenobiotics or anything else is not necessarily what you *say* but rather what you *do*.

So the 1991 compact disc edition of the *Science Citation Index®* (*SCI®*) was searched by article title,[1] and over 100 papers with "xenobiotics" in their titles were identified. It was obvious that xenobiotics is closely connected with the problem of drug metabolism, as Kaminsky had confirmed. In addition, a search of authors' addresses was done, which quickly identified several explicitly named xenobiotics labs—including the Academy of Medical Sciences, Novosibirsk, Russia; the Institut National de la Recherche Agronomique, Toulouse, France; the National Institute of Hygiene Science, Tokyo, Japan; and the University of Grenoble, France (also called Joseph Fourier University).

We then selected the journal title search option of the *SCI* CD-ROM to identify

those with "xenobiotics" in the title. This identified *Xenobiotica*, published by Taylor & Francis, London. But when we examined the titles of its 1991 papers, the Humpty Dumpty Syndrome was confirmed. Out of 148 papers, only 12 had xenobiotics or drug metabolism in their titles.

Lastly, the 1990 *SCI Journal Citation Reports®* (*JCR®*) was consulted to see what journals were cited by *Xenobiotica* and, conversely, what journals cited it. Not surprisingly, there was considerable overlap between both lists, and journals of drug metabolism, toxicology, and carcinogenesis dominated. The lists also showed that xenobiotics was related to pharmacology in general, as well as the larger journals of biochemistry and molecular biology.

The Basis of the Study

Kaminsky examined ISI-indexed journals in these fields and selected 45 that were most suitable for a citation analysis of xenobiotics research. As it turned out, more than half of the journals on this expert-derived list also appeared on the *JCR* lists for *Xenobiotica*. This illustrates how citation data can serve as an expert system using artificial intelligence to define xenobiotics or other research areas. That is, by computer analysis of citations in a single relevant journal, a list of core journals can be derived that agrees with expert opinion.

Using the expert-derived list of 45 journals, we created a xenobiotics database for 1981-1992. It included 123,063 papers published in this 12-year period. These included original research articles, reviews, and technical notes only. That is, editorials, letters to the editor, meeting abstracts, and other "source items" were excluded.

These papers received 986,375 citations during 1981-1992. It should be noted that papers published in 1981 would generally have received more citations than those in 1991 or 1992. Dividing citations by papers, the average xenobiotics paper was cited 8.0 times. This represents the 12-year "baseline" citation impact for the study.

Most-Cited Papers

From this database, ranked lists of the most-cited and highest impact papers, institutions, and authors were derived. Table 1 lists 18 papers published from 1981 through 1992 that received at least 350 citations during this period. Complete bibliographic information is provided.

The 18 papers were published in eight journals. The *Journal of Pharmacology and Experimental Therapeutics* accounted for five papers, followed by the *European Journal of Pharmacology* (four), *Molecular Pharmacology* (three), and *Antimicrobial Agents and Chemotherapy* (two). The following journals accounted for one paper each: *Biochemical Pharmacology*, *British Journal of Pharmacology*, *Journal of Pharmacobio-Dynamics*, and *Journal of Medicinal Chemistry*. Not surprisingly, they are among the highest impact pharmacology journals, as indicated in the 1990 *JCR*.

Twenty institutions were involved in producing the most-cited xenobiotics papers. Of these, 10 are in the US, the UK accounts for 3, and Belgium for 2. Five additional nations each accounted for one paper: Denmark, France, Japan, Sweden, and Switzerland.

Of these institutions, 15 are universities, hospitals, and government or independent research institutes. The remaining five are corporations. This indicates a strong industrial orientation in xenobiotics research, which is not surprising when you realize that the field can be considered a branch of the pharmaceutical sciences. In the impact rankings discussed below, separate lists for universities/institutes and corporations are presented.

One interesting observation about Table 1 is that the only journal named *Xenobiotica* is not represented. In fact, the most-cited paper from that journal was published in 1982 and has been cited 133 times to date. Authored by F.P. Guengerich, Vanderbilt University, Nashville, and colleagues, the paper described the purification and characterization of microso-

Table 1: 1981-1992 *SCI®* xenobiotics papers cited at least 350 times.

Cites	Bibliographic Information
761	**Leysen J E, Niemegeers C J E, Van Nueten J M & Laduron P M.** H-3 labeled ketanserin (R 41 468), a selective H-3 labeled ligand for serotonin-2 receptor binding sites: binding properties, brain distribution, and functional role. *Mol. Pharmacol.* 21:301-14, 1982. Janssen Pharmaceut., Beerse, Belgium
708	**Yamaoka K, Tanigawara Y, Nakagawa T & Uno T.** A pharmacokinetic analysis program (MULTI) for microcomputer. *J. Pharmacobio-Dynam.* 4:879-85, 1981. Kyoto Univ., Japan
632	**Iorio L C, Barnett A, Leitz F H, Houser V P & Korduba C A.** SCH-23390, a potential benzazepine anti-psychotic with unique interactions on dopaminergic systems. *J. Pharmacol. Exp. Ther.* 226:462-8, 1983. Schering Plough Corp., Bloomfield, NJ
581	**Martin W, Villani G M, Jothianandan D & Furchgott R F.** Selective blockade of endothelium dependent and glyceryl trinitrate induced relaxation by hemoglobin and by methylene blue in the rabbit aorta. *J. Pharmacol. Exp. Ther.* 232:708-16, 1985. SUNY—Downstate Med. Ctr., Brooklyn, NY
552	**Van Nueten J M , Janssen P A J, Van Beek J, Xhonneux R, Ver Beuren T J & Van Houtte P M.** Vascular effects of ketanserin (R-41-468), a novel antagonist of 5-HT2 serotonergic receptor S. *J. Pharmacol. Exp. Ther.* 218:217-30, 1981. Janssen Pharmaceut., Beerse, Belgium; Univ. Antwerp, Wilrijk, Belgium
548	**Middlemiss D N & Fozard J R.** 8-hydroxy-2-(di-normal propylamino)-tetralin discriminates between subtypes of the 5-HT1 recognition site. *Eur. J. Pharmacol.* 90:151-3, 1983. Merrell Intl., Strasbourg, France
507	**Daly J W.** Adenosine receptors: targets for future drugs. *J. Med. Chem.* 25:197-207, 1982. NIADDKD, Bethesda, MD
505	**Anis N A, Berry S C, Burton N R & Lodge D.** The dissociative anesthetics, ketamine and phencyclidine, selectively reduce excitation of central mammalian neurons by N-methyl aspartate. *Brit. J. Pharmacol.* 79:565-75, 1983. Univ. London, Roy. Vet. Coll., England
486	**Hyttel J.** SCH-23390: the first selective dopamine D-1 antagonist. *Eur. J. Pharmacol.* 91:153-4, 1983. H. Lundbeck & Co., Copenhagen, Denmark
482	**Von Voigtlander P F, Lahti R A & Ludens J H.** U-50,488: a selective and structurally novel non-mu-(kappa)-opioid agonist. *J. Pharmacol. Exp. Ther.* 224:7-12, 1983. Upjohn Co., Kalamazoo, MI
475	**Ignarro L J , Lippton H, Edwards J C, Baricos W H, Hyman A L, Kadowitz P J & Gruetter C A.** Mechanism of vascular smooth muscle relaxation by organic nitrates, nitrites, nitroprusside and nitric oxide: evidence for the involvement of S-nitrosothiols as active intermediates. *J. Pharmacol. Exp. Ther.* 218:739-49, 1981. Tulane Univ. Sch. Med., New Orleans, LA
445	**McGrath J C.** Evidence for more than one type of post-junctional alpha-adrenoreceptor. *Biochem. Pharmacol.* 31:467-84, 1982. Univ. Glasgow, Scotland
408	**Wolfson J S & Hooper D C.** The fluoroquinolones: structures, mechanisms of action and resistance, and spectra of activity in vitro. *Antimicrob. Agents Chemother.* 28:581-6, 1985. Massachusetts Gen. Hosp., Boston, MA
401	**Delean A, Hancock A A & Lefkowitz R J.** Validation and statistical analysis of a computer modeling method for quantitative analysis of radioligand binding DNA for mixtures of pharmacological receptor subtypes. *Mol. Pharmacol.* 21:5-16, 1982. Duke Univ. Med. Ctr., Durham, NC
382	**Squires R F, Casida J E, Richardson M & Saederup E.** (S-35)-butylbicyclophosphorothionate binds with high affinity to brain specific sites coupled to gamma-aminobutyric acid-A and ion recognition sites. *Mol. Pharmacol.* 23:326-36, 1983. Rockland Res. Inst., Orangeburg, NY; Univ. California, Berkeley, CA
368	**Lundberg J M, Franco-Cereceda A, Hua X, Hokfelt T & Fischer J A.** Co-existence of substance P and calcitonin gene-related peptide-like immunoreactivities in sensory nerves in relation to cardiovascular and bronchoconstrictor effects of capsaicin. *Eur. J. Pharmacol.* 108:315-9, 1985. Karolinska Inst., Stockholm, Sweden; Univ. Zurich, Switzerland
366	**Wise R, Andrews J M & Edwards L J.** In vitro activity of BAY-09867, a new quinoline derivative, compared with those of other antimicrobial agents. *Antimicrob. Agents Chemother.* 23:559-64, 1983. Dudley Road Hosp., Birmingham, England
351	**Handa B K, Lane A C, Lord J A H, Morgan B A, Rance M J & Smith C F C.** Analogs of beta-LPH61-64 possessing selective agonist activity at mu-opiate receptors. *Eur. J. Pharmacol.* 70:531-40, 1981. SUNY, Buffalo, NY

Table 2: Highest impact institutions in xenobiotics, 1981-1992 *SCI*®, which produced at least 100 papers. A = Impact. B = Citations. C = Papers.

Rank	Institution	A	B	C
1.	NIADDKD Bethesda, MD	27.3	3380	124
2.	SUNY— Downstate Med. Ctr. Brooklyn, NY	22.3	2279	102
3.	Massachusetts Gen. Hosp. Boston, MA	20.1	2574	128
4.	NINCDS Bethesda, MD	18.7	2484	133
5.	NIMH Rockville, MD	18.1	5626	311
	Univ. Amsterdam The Netherlands	18.1	3669	203
7.	Flinders Univ. Adelaide & Bedford Park, Australia	17.2	2224	129
8.	Dudley Road Gen. Hosp. Birmingham, England	17.1	3086	181
9.	Univ. Aberdeen Scotland	16.9	2232	132
10.	Emory Univ. Atlanta, GA	16.8	3738	222
11.	Univ. California Berkeley, CA	16.7	2477	148
12.	Graz Univ. Austria	16.4	3158	193
13.	Columbia Univ. New York, NY	15.9	4815	302
14.	San Francisco Gen. Hosp. San Francisco, CA	15.8	1600	101
15.	Karolinska Inst. Stockholm, Sweden	15.7	9381	596
16.	NHLBI Bethesda, MD	15.5	2733	176
	Univ. Colorado Boulder & Denver, CO	15.5	6289	407
18.	Mayo Clinic & Mayo Fdn. Rochester, MN	15.4	5318	346
	Univ. California San Diego, CA	15.4	5003	326
	Univ. Freiburg Germany	15.4	4487	291
21.	Univ. Leicester England	15.3	1929	126
22.	Duke Univ. Durham, NC	15.2	7727	510
23.	Univ. Cagliari Italy	15.0	1969	131
	Yale Univ. New Haven, CT	15.0	6000	401
25.	Catholic Univ. Louvain Belgium	14.5	7402	511
	NCI Bethesda, MD	14.5	9557	658
27.	Univ. Essen Gesamthochschule, Germany	14.4	3097	215
	Vanderbilt Univ. Nashville, TN	14.4	7152	498
29.	Johns Hopkins Univ. Baltimore, MD	14.3	7965	557
30.	New England Med. Ctr. Hosp. Boston, MA	14.2	1678	118
	St. Louis Univ. St. Louis, MO	14.2	1445	102
32.	Chem. Ind. Inst. Toxicol. Research Triangle Park, NC	14.1	2502	178
33.	Rockefeller Univ. New York, NY	14.0	1474	105
34.	Univ. Sherbrooke Quebec, Canada	13.7	2153	157
35.	CUNY Mt. Sinai Sch. Med. New York, NY	13.6	2826	208
	Univ. Chicago Chicago, IL	13.6	3356	247
37.	Tulane Univ. New Orleans, LA	13.4	2439	182
	Univ. Virginia Charlottesville, VA	13.4	2538	189
39.	MIT Cambridge, MA	13.3	1405	106
	Stanford Univ. Stanford, CA	13.3	5438	409
41.	St. Georges Hosp. & Med. Sch. London, England	13.2	1454	110
	Univ. Strasbourg 1 France	13.2	1447	110
43.	Huddinge Univ. Hosp. Huddinge, Sweden	13.1	1761	134
44.	Queen's Univ. Ontario, Canada	12.9	1441	112
45.	Univ. Lund Lund, Sweden	12.8	2897	226
46.	Inst. Pasteur Paris, Lille & Lyons, France	12.7	2989	236
	NIDA Rockville, MD	12.7	2389	188
	Univ. Pennsylvania Philadelphia, PA	12.7	4334	342
49.	Univ. Arizona Tucson, AZ	12.6	7501	595
50.	Univ. Bonn Bonn, Germany	12.5	4051	324

mal cytochrome P-450s.[2] As it happens, Kaminsky is a coauthor of this paper.

Highest Impact Institutions

Table 2 identifies the 50 highest impact universities, hospitals, and government or independent research institutes in the 1981-1992 xenobiotics database. Only those institutions which produced at least 100 papers during this period are included.

The National Institutes of Health dominates the list. The National Institute of Arthritis, Digestive, Diabetes, and Kidney Diseases (NIADDKD) ranks first with an impact of 27.3. Under the NIH reorganization in 1986, the NIADDKD became two separate institutes. In addition, five other US national institutes are listed—the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS, 18.7); National Institute of Mental Health (NIMH, 18.1); National Heart, Lung, and Blood Institute (NHLBI, 15.5); National Cancer Institute (NCI, 14.5); and National Institute of Drug Abuse (NIDA, 12.7).

Of the 50 institutions listed here, 31 are based in the US. The UK is represented by four institutions, and Sweden and Germany account for three each. France and Canada each have two, and the following account for one each: Australia; Austria; Belgium; Italy; and The Netherlands.

Highest Impact Corporations

The highest impact corporations are shown in Table 3. The list includes some of the largest multinational pharmaceutical corporations as well as comparatively smaller companies.

Of the 53 corporations listed, 23 are based in the US, followed by Japan with 16. France, Germany, and the UK account for three each. It should be noted that Wellcome Research Labs is based both in the US and UK, and Rhone Poulenc-Rorer is located in France and the US. Italy, Sweden, and Switzerland are represented by two corporations each, and Belgium by one.

Japan's dominance in corporate research is interesting to note. No Japanese universities appeared among the impact rankings in Table 2, but Japanese companies represent 30 percent of the corporations in Table 3. This no doubt reflects the internal structure of Japanese science, where most research has traditionally been done at corporations rather than universities. Also, Japanese university research has tended to be more applied than basic—in general, applied research papers are typically less frequently cited than basic science.

Most-Cited Institutions and Corporations

In terms of absolute citations as distinct from impact, the most-cited institutions and corporations were: Merck Sharp & Dohme, Rahway, New Jersey, and West Point, Pennsylvania (13,746 citations); Univ. California, San Francisco (10,690); NCI (9,557); Karolinska Institute, Stockholm, Sweden (9,381); Univ. North Carolina, Chapel Hill and Charlotte (8,381); Univ. Michigan, Ann Arbor (8,177); Harvard Univ., Cambridge, Massachusetts (8,028); Johns Hopkins Univ., Baltimore, Maryland (7,965); Hoffmann La Roche, Nutley, New Jersey (7,792); Univ. Washington, Seattle (7,781); Wellcome Research Labs, Beckenham, England, and Research Triangle Park, North Carolina (7,750); Duke Univ., Durham, North Carolina (7,727); and Univ. Arizona, Tucson (7,501).

Most Productive Institutions and Corporations

In terms of productivity, those that published at least 650 papers were: Univ. Tokyo, Japan (1,249); Merck Sharp & Dohme (1,125); Kyoto Univ., Japan (951); Univ. California, San Francisco (883); Osaka Univ., Japan (809); Kyushu Univ., Fukuoka, Japan (780); Univ. Minnesota, Minneapolis-St. Paul (747); Tohuku Univ., Miyagi, Japan (692); Univ. Michigan (688); Univ. North Carolina (680); Hoffmann La Roche (679); NCI (658); and Harvard (651).

The dominance of Japanese universities in the productivity rankings is fairly obvious. Of the 52 universities and corpora-

Table 3: Highest impact corporations in xenobiotics, 1981-1992 *SCI*®, which produced at least 100 papers. A = Impact. B = Citations. C = Papers

Rank	Corporation	A	B	C
1.	Sandoz Ltd. Basel, Switzerland	23.5	6638	282
2.	Synthelabo Res. Paris & Bagneux, France	18.8	3701	197
3.	Astra Lakemedel AB Sodertalje, Sweden	16.9	2710	160
4.	Merrell Dow Pharmaceut. & Res. Inst. Cincinnati, OH	16.1	6892	427
5.	Janssen Pharmaceut. & Res. Inst. Beerse, Belgium	16.0	5326	333
6.	Wellcome Res. Labs Beckenham, England Research Triangle Park, NC	15.9	7750	488
7.	Glaxo Grp. Res. Ltd. England (several sites)	14.9	4926	330
8.	Bayer AG Levekusen & Wuppertal, Germany	13.6	3106	229
9.	A. Menarini Pharmaceut. Florence, Italy	12.9	2097	163
10.	SmithKline & French Labs. Philadelphia, PA (now SmithKline Beecham)	12.6	6423	511
11.	ICI PLC England (several sites)	12.3	5798	470
12.	Merck Sharp & Dohme Ltd. Rahway, NJ West Point, PA	12.2	13,746	1125
13.	Eli Lilly & Co. Indianapolis, IN	11.9	7422	626
14.	Hoffmann La Roche Nutley, NJ	11.5	7792	679
15.	Ciba Geigy Corp. Summit, NJ	11.2	2950	263
	Schering Plough Corp. Bloomfield, Kenilworth & Union, NJ	11.2	2973	266
17.	SRI Intl. Menlo Park, CA	11.0	1240	113
18.	Ciba Geigy AG Basel, Switzerland	10.7	3031	283
	DuPont Co. Wilmington, DE	10.7	1556	146
20.	Burroughs Wellcome Co. Research Triangle Park, NC	10.3	2216	216
21.	Warner Lambert-Parke Davis Ann Arbor, MI	9.9	3335	337
22.	Syntex Inc. & Res. Corp. Palo Alto, CA	9.7	2669	274
23.	Bristol Myers-Squibb Co. US (several sites)	9.5	6820	717
24.	Upjohn Co. Kalamazoo, MI	8.7	5460	629
25.	AB Hassle Molndal, Sweden	8.6	1411	165
	Dr. Karl Thomae GmbH Biberach, Germany	8.6	1119	130
	Pfizer Inc. Groton, CT	8.6	2052	239
28.	Takeda Chem. Ind. Ltd. Osaka, Japan	7.7	3417	445
29.	Abbott Labs. Abbott Park & North Chicago, IL	7.5	2603	347
30.	Yamanouchi Pharmaceut. Ibaraki, Japan	7.2	1169	162
31.	Nippon Kayaku Co. Tokyo, Japan	7.1	907	127
32.	Wyeth-Ayerst Labs. Princeton, NJ Philadelphia, PA	7.0	2707	389
33.	American Cyanamid Co. Pearl River, NY Princeton, NJ Stamford, CT	6.9	1574	229
	Boehringer & Ingelheim Ridgefield, CT	6.9	2042	297
35.	Fujisawa Pharmaceut. Co. Ibaraki & Osaka, Japan	6.8	2156	319
36.	Farmitalia Carlo Erba Milan, Italy	6.5	1171	180
37.	G.D. Searle & Co. Skokie, IL	6.3	1385	219
	Hoechst AG Frankfurt, Germany	6.3	1604	254
	Roussel Uclaf Paris & Romainville, France	6.3	694	110
40.	Sterling-Winthrop Rensselaer, NY Malvern, PA	6.2	1113	179
41.	Shionogi & Co. Osaka & Shiga, Japan	5.9	2759	469
42.	Kyowa Hakko Kogyo Co. Shizuoka & Tokyo, Japan	5.5	1448	264
	Meiji Seika Kaisha Kanagawa & Yokohama, Japan	5.5	898	162
44.	Sankyo Co. Tokyo, Japan	5.4	1676	312
45.	Mitsubishi Kasei Co. & Inst. Tokyo & Yokohama, Japan	5.2	853	163

Table 3 (continued)

Rank	Corporation	A	B	C
46.	Dainippon Pharmaceut. Co. Osaka, Japan	5.1	1085	211
47.	Chugai Pharmaceut. Co. Shizuoka & Tokyo, Japan	5.0	653	130
48.	Rhone Poulenc-Rorer Vitry, France King of Prussia, PA	4.9	794	162
49.	Eisai & Co. Gifu, Ibaraki & Tokyo, Japan	4.5	907	201
50.	Kanebo Co. Osaka, Japan	4.2	603	145
	Tanabe Seikayu Co. Osaka & Saitama, Japan	4.2	1187	281
52.	Daiichi Seikayu Co. Tokyo, Japan	4.1	1129	273
	Otsuka Pharmaceut. Co. Tokushima, Japan	4.1	441	107

tions that produced at least 400 papers, 17 (33 percent) are based in Japan—15 universities and 2 corporations. However, only 4 Japanese universities rank among the top 50 in terms of citations—Univ. Tokyo (7,262); Kyoto Univ. (6,147); Kyushu Univ. (4,548); and Osaka Univ. (4,055). And none appears in the impact rankings in Table 2. Thus, while Japanese universities are comparatively highly productive in xenobiotics research, their absolute citation frequency and average impact are relatively low. As noted earlier, this may be due to a more applied than basic orientation in Japanese university research.

Highest Impact Authors

From the 1981-1992 database of about 123,000 papers, data on the number of papers, citations, and impact were compiled for *all* authors—not just first authors in the byline. About 460,000 surnames were identified, which include homographs—that is, two or more authors with the same last name and initials.

Only those authors who published at least 20 papers in the 12-year period of this study were ranked. Some authors may achieve high impact rankings on the basis of having published just one or two highly cited papers. For example, L.J. Edwards of Dudley Road General Hospital, Birmingham, England, had an impact of 366.0 based on a single paper,[3] which is listed in Table 1. Thus, by setting a threshold of at least 20 papers, the impact rankings identify authors who have consistently published throughout the time period of this study.

Table 4 identifies 51 authors with an impact of at least 32.5 for the period 1981-1992. The list excludes homographs, which were identified by checking current author addresses. When two or more institutional affiliations were consistently listed for an author's name, it was purged from the list.

The impact of these 51 authors was between four and nine times as great as the average for the field. And they rank among the 99.99th percentile of all author names in the 1981-1992 xenobiotics database.

It is interesting to note that one of the authors who shares the 35th rank is Jacques Benveniste, University of Paris Sud and INSERM, France. He is perhaps better known today for his controversial "homeopathic" work suggesting that a substance could remain biologically active at dilutions that preclude the presence of even a single molecule of active ingredient.[4] But this work does not account for his high ranking. Rather, his less controversial work on platelet aggregation and activating factors contributed to his high citation frequency.

Their Institutional Affiliation

The table also shows the current institutional affiliation for each author. Twenty-one authors were based in the US. The UK is represented by 10, followed by France and Switzerland, each with 4. Three were based in Belgium, and the following nations accounted for two each: Austria, Germany, and Sweden. One author each was based in Denmark, Japan, and The Netherlands.

In terms of institutions rather than nations, four authors were based at Sandoz Ltd., Basel, Switzerland, and three at the NCI. Two each were at Janssen Research Foundation, Beerse, Belgium; Karolinska Institute; Merck Sharp & Dohme; Reckitt

Table 4: Highest impact authors in xenobiotics, 1981-1992 *SCI*®, who published at least 20 papers. A = Impact. B = Citations. C = Papers.

Rank	Author	A	B	C
1.	Kosterlitz H W Univ. Aberdeen Scotland	71.2	1496	21
2.	Palmer R M J Wellcome Res. Labs Beckenham, England	70.3	1688	24
3.	Ignarro L J Univ. California Los Angeles, CA	69.2	1384	20
4.	Hoyer D Sandoz Ltd. Basel, Switzerland	67.8	2713	40
5.	Kalkman H O Sandoz Ltd. Basel, Switzerland	62.1	1365	22
6.	Snyder S H Johns Hopkins Univ. Baltimore, MD	59.5	2498	42
7.	Van Meel J C A Dr. Karl Thomae GmbH Biberach, Germany	54.0	1134	21
8.	Salmon J A Wellcome Res. Labs Beckenham, England	53.1	1062	20
9.	Barnett A Schering Plough Corp. Bloomfield, NJ	51.3	1077	21
10.	Martin W Univ. Glasgow Scotland	50.3	1458	29
11.	Kadowitz P J Tulane Univ. New Orleans, LA	50.1	1352	27
12.	Fozard J R Sandoz Ltd. Basel, Switzerland	47.9	1580	33
	Moncada S Wellcome Res. Labs Beckenham, England	47.9	2777	58
14.	Lodge D Univ. London England	47.6	1047	22
15.	Broder S NCI Bethesda, MD	46.7	1354	29
16.	Hokfelt T Karolinska Inst. Stockholm, Sweden	46.5	929	20
17.	Saria A Univ. Innsbruck Austria	44.5	1068	24
18.	Dejonge A Duphar BV Weesp, The Netherlands	44.1	1765	40
19.	Palacios J M Sandoz Ltd. Basel, Switzerland	43.0	1119	26
20.	Middlemiss D N Merck Sharp & Dohme Ltd. Harlow, England	42.3	1185	28
21.	Laduron P M Rhone Poulenc-Rorer Vitry, France	41.8	1631	39
22.	Harden T K Univ. North Carolina Chapel Hill, NC	41.2	1112	27
23.	Glossmann H Univ. Innsbruck Austria	40.8	1265	31
	Labthavikul P Columbia Univ. New York, NY	40.8	898	22
25.	Levin W Hoffmann La Roche Nutley, NJ	40.6	812	20
26.	Hyttel J H. Lundbeck & Co. Copenhagen, Denmark	40.3	968	24
27.	Leysen J E Janssen Res. Fdn. Beerse, Belgium	39.3	1730	44
28.	Johns D G NCI Bethesda, MD	37.9	1098	29
29.	Kazda S Bayer AG Wuppertal, Germany	37.7	830	22
30.	Yamaoka K Kyoto Univ. Japan	36.9	959	26
31.	Wolfe B B Georgetown Univ. Washington, DC	36.8	920	25
32.	Von Voigtlander P F Upjohn Co. Kalamazoo, MI	36.4	838	23
33.	Creese I Rutgers Univ. Newark, NJ	35.8	931	26
	Schoemaker H Synthelabo Res. Bagneux, France	35.8	894	25
35.	Benveniste J Univ. Paris Sud Clamart, France	35.1	807	23
	Lefkowitz R J Duke Univ. Durham, NC	35.1	912	26

Table 4 (continued)

Rank	Author	A	B	C
37.	Bockaert J CNRS Ctr. Pharmacol. Endocrinol. Montpellier, France	35.0	1261	36
38.	Pauwels R Catholic Univ. Louvain Belgium	34.8	835	24
39.	Johnson K M Univ. Texas Galveston, TX	34.6	726	21
40.	Roach A G Reckitt & Colman PLC Hull, England	34.4	791	23
41.	Weston A H Univ. Manchester England	34.3	1234	36
42.	Niemegeers C J E Janssen Res. Fdn. Beerse, Belgium	34.2	1435	42
43.	Triggle D J SUNY Buffalo, NY	33.8	1755	52
44.	Lundberg J M Karolinska Inst. Stockholm, Sweden	33.6	1982	59
45.	Wood P L G.D. Searle-Monsanto Co. St. Louis, MO	33.1	827	25
46.	Cooney D A NCI Bethesda, MD	33.0	924	28
	Van Houtte P M Baylor Coll. Med. Houston, TX	33.0	2346	71
48.	Casida J E Univ. California Berkeley, CA	32.9	657	20
49.	Ward S J Sterling Drug. Inc. Rensselaer, NY	32.8	655	20
50.	Ulm E H Merck Sharp & Dohme West Point, PA	32.7	916	28
51.	Doxey J C Reckitt & Colman PLC Hull, England	32.6	716	22

& Colman PLC, Hull, England; Wellcome Research Labs; and the University of Innsbruck, Austria.

Most-Cited Authors

Another way to rank authors is by absolute citations rather than impact. Both types of rankings have their advantages and disadvantages. For example, impact rankings might include the occasional graduate student or lab assistant who coauthored a few papers with very highly cited senior authors. On the other hand, total citation rankings might include very prolific authors whose papers are cited at or even below the average for the field.

Table 5 shows 55 authors whose 1981-1992 papers received at least 1,350 citations in this period. As in the impact ranking, only those authors who published at least 20 papers are included.

Not surprisingly, there is some overlap between the lists of most-cited and highest impact authors. Of the 55 most-cited authors in the database, 18 also ranked among the 51 highest impact authors. They are indicated by asterisks.

Twenty-one of the 55 most-cited authors were based in the US. The UK accounted for 10 authors, followed by Belgium with 6. Germany is represented by four authors, and three authors each were based in France, The Netherlands, and Switzerland. The following nations each accounted for one author: Austria, Canada, Italy, Japan, and Sweden.

Most Productive Authors

Table 6 lists 32 authors who published at least 100 papers in the xenobiotics database from 1981 to 1992. Japan dominates, accounting for 12 of the 32 most productive authors (38 percent). The UK follows with eight, and the US accounts for six. Two are based in The Netherlands, and one each is from Belgium, France, Germany, and Italy.

Fifteen of the authors in Table 6 also appeared on the list of most-cited authors. They are indicated by asterisks. However, none of the most prolific authors were included in the list of highest impact authors. This typically is the case not just in xenobiotics but virtually any field or specialty. The number of publications has been a traditional criterion for evaluating researchers for promotion or tenure. But the recent trend is towards identifying what one considers

Table 5: Most-cited authors in xenobiotics, 1981-1992 *SCI®*, who published at least 20 papers. Asterisks indicate authors who also appear on Table 4. A = Citations. B = Papers. C = Impact.

Rank	Author	A	B	C
1.	Greenblatt D J Tufts Univ. Boston, MA	3313	312	10.6
2.	Langer S Z Synthelabo Res. Bagneux, France	3295	133	24.8
3.	Declercq E Catholic Univ. Louvain Belgium	3255	177	18.4
4.	Timmermans P B M W M DuPont-Merck Pharmaceut. Co. Wilmington, DE	3207	102	31.4
5.	Wise R Dudley Road Gen. Hosp. Birmingham, England	3084	173	17.8
6.	Van Zwieten P A Univ. Amsterdam The Netherlands	2918	116	25.2
7.	*Moncada S Wellcome Res. Labs. Beckenham, England	2777	58	47.9
8.	*Hoyer D Sandoz Ltd. Basel, Switzerland	2713	40	67.8
9.	Neu H C Columbia Univ. New York, NY	2662	120	22.2
10.	*Snyder S H Johns Hopkins Univ. Baltimore, MD	2498	42	59.5
11.	*Van Houtte P M Baylor Coll. Med. Houston, TX	2346	71	33.0
12.	Klaassen C D Univ. Kansas Kansas City, KS	2227	115	19.4
13.	Burnstock G Univ. London England	2150	82	26.2
14.	Yamamura H I Univ. Arizona Tucson, AZ	2019	82	24.6
15.	Breimer D D Leiden Univ. The Netherlands	2018	151	13.4
16.	Shader R I Tufts Univ. Boston, MA	1992	139	14.3
17.	*Lundberg J M Karolinska Inst. Stockholm, Sweden	1982	59	33.6
18.	Reid J L Univ. Glasgow Scotland	1945	216	9.0
19.	Balzarini J Catholic Univ. Louvain Belgium	1944	81	24.0
20.	Mitsuhashi S Gunma Univ. Sch. Med. Episome Inst. Gunma, Japan	1870	105	17.8
21.	Takemori A E Univ. Minnesota Minneapolis, MN	1794	82	21.9
22.	Regoli D Univ. Sherbrooke Quebec, Canada	1787	92	19.4
23.	*Dejonge A Duphar BV Weesp, The Netherlands	1765	40	44.1
24.	Maggi C A A. Menarini Pharmaceut. Florence, Italy	1763	120	14.7
25.	*Triggle D J SUNY Buffalo, NY	1755	52	33.8
26.	Daly J W NIDDK Bethesda, MD	1752	71	24.7
27.	Starke K Univ. Freiburg Germany	1742	76	22.9
28.	*Leysen J E Janssen Res. Fdn. Beerse, Belgium	1730	44	39.3
29.	Lembeck F Graz Univ. Austria	1726	62	27.8
30.	Janssen P A J Janssen Res. Fdn. Beerse, Belgium	1718	72	23.9
31.	*Palmer R M J Wellcome Res. Labs. Beckenham, England	1688	24	70.3
32.	Ruffolo R R SmithKline Beecham Pharmaceut. King of Prussia, PA	1660	86	19.3
33.	Abernethy D R Brown Univ. Providence, RI	1651	133	12.4
34.	*Laduron P M Rhone Poulenc-Rorer Vitry, France	1631	39	41.8
35.	Barnes P J NHLI Bethesda, MD	1629	99	16.5

Table 5 (continued)

Rank	Author	A	B	C
36.	Van Nueten J M Janssen Res. Fdn. Beerse, Belgium	1625	15	108.3
37.	*Fozard J R Sandoz Ltd. Basel, Switzerland	1580	33	47.9
38.	Eichelbaum M Dr. Margarete Fischer Bosch Inst. Clin. Pharmacol. Stuttgart, Germany	1554	71	21.9
39.	Gothert M Univ. Bonn Germany	1547	58	26.7
40.	Portoghese P S Univ. Minnesota Minneapolis, MN	1517	77	19.7
41.	Andrews J M Dudley Road Gen. Hosp. Birmingham, England	1509	89	17.0
42.	Skolnick P NIDDK Bethesda, MD	1501	68	22.1
43.	*Kosterlitz H W Univ. Aberdeen Scotland	1496	21	71.2
44.	Janis R A Miles Inst. Preclin. Pharm. New Haven, CT	1474	14	105.3
45.	Scatton B Synthelabo Res. Bagneux, France	1460	54	27.0
46.	*Martin W Univ. Glasgow Scotland	1458	29	50.3
47.	*Niemegeers C J E Janssen Res. Fdn. Beerse, Belgium	1435	42	34.2
48.	*Ignarro L J Univ. California Los Angeles, CA	1384	20	69.2
49.	Park B K Univ. Liverpool England	1378	138	10.0
50.	Paul S M NIMH Rockville, MD	1366	46	29.7
51.	*Kalkman H O Sandoz Ltd. Basel, Switzerland	1365	22	62.1
52.	Nahorski S R Univ. Leicester England	1360	57	23.9
53.	Herz A Max Planck Inst. Psychiat. Martinsreid, Germany	1358	62	21.9
54.	*Broder S NCI Bethesda, MD	1354	29	46.7
55.	*Kadowitz P J Tulane Univ. New Orleans, LA	1352	27	50.1

to be his or her most significant work. Indeed, researchers have contacted us to obtain personal citation profiles to help them do just that.

Current Xenobiotics Research Fronts

In a sense, the data reviewed so far are "demographic"—that is, they give aggregated statistics on large populations of papers, authors, and institutions. ISI's data can also be used to indicate the "psychographics" of research. That is, we can identify particular topics within a specialty that are attracting high current interest.

This is achieved by applying co-citation analysis and multidimensional scaling methods to ISI's database. Co-citation analysis is complex and has been described in previous publications.[5,6] Explained simply, it involves tracking *pairs* of papers that are cited together in the source articles we index. When the same pairs of papers are co-cited with other papers by many authors, a *cluster* of research begins to form. The co-cited papers in these clusters share some common topic, subject area, or method.

Indeed, the papers at the "core" of these clusters can be considered the foundation or key publications of a particular research specialty since they are highly cited by researchers currently working at the forefront of that specialty. In fact, that is why we refer to the citing papers as constituting the current "research front." The research front is automatically "named" by using the most frequent words and phrases the citing authors themselves provide in the titles of their papers.

Table 6: Most productive authors in xenobiotics who produced at least 100 papers, 1981-1992 *SCI*®. Asterisks indicate authors who also appear in Table 5. A = Papers. B = Citations. C = Impact.

Rank	Author	A	B	C
1.	*Greenblatt D J Tufts Univ. Boston, MA	312	3313	10.6
2.	*Reid J L Univ. Glasgow Scotland	216	1945	9.0
3.	Omura S Kitasato Univ. Tokyo, Japan	194	1259	6.5
4.	*Declercq E Catholic Univ. Louvain Belgium	177	3255	18.4
5.	*Wise R Dudley Road Gen. Hosp. Birmingham, England	173	3084	17.8
6.	*Breimer D D Leiden Univ. The Netherlands	151	2018	13.4
7.	Yoshimura H Kyushu Univ. Fukuoka, Japan	150	576	3.8
8.	*Shader R I Tufts Univ. Boston, MA	139	1992	14.3
9.	*Park B K Univ. Liverpool England	138	1378	10.0
10.	*Abernethy D R Brown Univ. Providence, RI	133	1651	12.4
	*Langer S Z Synthelabo Res. Bagneux, France	133	3295	24.8
12.	Mutschler E Univ. Frankfurt Germany	126	844	6.7
13.	Naganawa H Microbial Chem. Res. Fdn. Tokyo, Japan	123	837	6.8
	Nishioka I Kyushu Univ. Fukuoka, Japan	123	848	6.9
15.	Takayanagi I Toho Univ. Chiba, Japan	122	492	4.0
	Turner P St. Bartholomew's Hosp. London, England	122	657	5.4
17.	*Maggi C A A. Menarini Pharmaceut. Florence, Italy	120	1763	14.7
	*Neu H C Columbia Univ. New York, NY	120	2662	22.2
19.	Hanano M Univ. Tokyo Japan	119	649	5.5
	McDevitt D G Univ. Dundee Scotland	119	705	5.9
21.	Okuda T Okayama Univ. Japan	116	887	7.7
	*Van Zwieten P A Univ. Amsterdam The Netherlands	116	2918	25.2
23.	*Klaassen C D Univ. Kansas Kansas City, KS	115	2227	19.4
24.	Elliott H L Univ. Glasgow Scotland	110	746	6.8
	Kato R Keio Univ. Tokyo, Japan	110	1091	9.9
	Sugiyama Y Univ. Tokyo Japan	110	681	6.2
27.	Kitagawa I Osaka Univ. Japan	108	1122	10.4
28.	Iga T Univ. Tokyo Hosp. Japan	107	644	6.0
29.	Breckenridge A M Univ. Liverpool England	106	965	9.1
30.	*Mitsuhashi S Gunma Univ. Sch. Med. Episome Inst. Gunma, Japan	105	1870	17.8
31.	*Timmermans P B M W M DuPont-Merck Pharmaceut. Wilmington, DE	102	3207	31.4
32.	Shanks R G Queen's Univ. Belfast North Ireland	101	569	5.6

Table 7 identifies six 1991 research fronts that included variants of "xenobiotic" or "drug metabolism" in their titles. They are ranked by the number of 1991 published—that is, *citing*—papers they include. The first research front contains 500 citing papers and 5 core or cited publications. Specialists in the field would recognize a key

Table 7: 1991 ISI® research fronts on xenobiotics and drug metabolism.

Citing Papers	Core Papers	Research Front Name
500	5	Liver microsomal cytochrome P-450; hepatic drug metabolizing activity in rats; mono-oxygenase pathway
181	18	Xenobiotic metabolizing enzymes; St. Clair River; marine fish; polycyclic aromatic hydrocarbons; hepatic cytochrome P-450; Black Rock Harbor carcinogens
162	6	Microsomal cytochrome P-450 in rat liver; in vivo intestinal metabolism; hepatic mono-oxygenases; primary cultures; xenobiotic induction; IIIA subfamily
126	5	Induction of cytochrome P-450; microsomal drug metabolizing enzymes; porcine ciliary epithelium
91	10	Insecticide resistance; gene amplification; xenobiotic metabolism; soluble esterases
36	2	Hepatic cytochrome P-450 system; xenobiotic metabolizing enzymes; pyrolized tobacco product; rat lung; sea star Asterias Rubens L; rabbit liver

phrase directly relevant to xenobiotics research that was mentioned earlier—"Cytochrome P-450." The P-450s are important enzymes that metabolize a wide range of xenobiotics, including most drugs, pesticides, and carcinogens. The P-450 enzymes have been intensively researched because they can further our understanding of the events triggering cell death, toxic reactions, and carcinogenesis.

Not surprisingly, then, with one exception, all of the research fronts shown here include P-450 in their "titles." These are computer-created descriptions based on the titles of all citing papers involved. The exception is the fifth research front on the list—nevertheless, its relevance to our subject is indicated by the title phrase, "Xenobiotic Metabolism."

Conclusion

This concludes our citationist perspective on the xenobiotics literature. Citation analysis can provide a unique and interesting view of research, enabling one to identify the leading papers, research fronts, authors, institutions, and nations in a particular field. But these "scientometric" applications are in addition to the fundamental purpose of the *SCI*—to enable researchers to navigate the flood of literature in their fields. This is especially useful in a specialty like xenobiotics, where the literature is scattered among a wide range of journals in a variety of fields.

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