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Editorial

Shaping the Transformation of Pharmaceutical Science

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This final issue of *Pharmaceutical Research* in 2008 is dedicated to the celebration of the journal's 25th anniversary. This particular issue is a collage of (a) selected invited papers for the symposium entitled, "25th Anniversary of *Pharmaceutical Research*: Impact on Drug Development and Roadmap to Future Innovations" at the AAPS meeting in Atlanta and (b) contributions from the authors at large whose work collectively defines the future direction of *Pharmaceutical Research*. The themed sections are illustrative of the indispensable role of integrated research in modern science and of the translation of basic research to disease management.

Pharmaceutical science is translational by its very nature. My goal as editor-in-chief was to position *Pharmaceutical Research* as the forum of choice for assuring the scientific quality as well as for archiving translational research in pharmaceutical science. In my view, the journal is a rich source of information and case studies on the integration of fundamental principles in chemistry, biology, and engineering for creating and evaluating innovative products or protocols that meet the needs of a healthy society.

Transport, formulation, biopharmaceutics and pharmacokinetics, simulation and mathematical modeling, and drug delivery are the building blocks of *Pharmaceutical Research*. They comprise the tool kit for creating innovative solutions to challenging entities. These entities range from small organic molecules to stem cells, which are on their way to becoming life-enrichment medicine. The top 25 papers from 1984 to the present, listed in Table I, span the area defined by the keywords mentioned earlier. The range of average citations per year is from 8.95 to 48.29. All but two of these papers were published in the decade of 1990–1999; the other two papers were published in 1998 (ranked no. 15) and in 2002 (ranked no. 22).

Pharmaceutical Research continues to flourish because of your support. To date, 13,985 authors have published in a total of 6,018 papers in the journal. Over 50% of the work was conducted in the laboratories of the 25 investigators listed in Table II. The top five contributors in this group are R.H Guy. G.L. Amidon, Y. Sugiyama, R. Borchardt, and V. Shah in that order. Table II also lists the top 25 institutions as well as the top 25 countries in number of papers published. The US Food and Drug Administration and three pharmaceutical companies (Upjohn, Genentech, and Pfizer) are sharing the top 25 institutions with universities in the United States, Japan, Israel. Sweden, and the Netherlands. In terms of countries, the United States contributes more than half of the published papers, followed by Japan (11.6%), and England (5.42%). The up and coming countries in Asia (South Korea, China, India, Singapore and Taiwan) together account for 4% of all published manuscripts in *Pharmaceutical Research* (Table III).

The pharmaceutical world is dynamic, and realignment in the lineup of major contributors, institutions, and countries to the top-tiered has already started. Although the United States and Japan together still contribute to 60% of all published manuscripts in recent years (2003–present) (Table II), only one of the top five most cited work is from the United States. The underlying cause and the strategy to reverse such a trend are very much needed.

With 676 citations to date, the paper by Amidon *et al.* (paper no. 1 in Table I), which formalized the biopharmaceutic drug classification (known for short as BCS), is the most highly cited paper in the history of the journal. This citation classic presented an elegant way to select the fundamental drug properties deemed important in bioavailability. The lesson learned from such a strategy undoubtedly will exert a profound impact on the strategy of drug product development by drug manufacturers and on the approach adopted by drug regulators to examine drug applications. In so doing, the BCS concept serves as an effective interface between the business sector and the government agency charged with safeguarding the health of the public from drug misadventures. Other topics that are on the more recent top 25 list include protein formulations; drug transporters; prediction, experimental evaluation, and modification of epithelial drug permeability; and polymeric carriers for oligonucleotides and genes.

We are living in a world of unprecedented change. Change knows no geographical, disciplinary or national boundaries. First, the internet has created a cost effective way for sharing information with anyone, anywhere, anytime. It is already changing the business model of publishing. Second, the confluence of biotechnology, nanotechnology, and informational technology has enabled scientists to tackle complex scientific questions. Discovery of disease subtypes, hence the need for more sophisticated treatment, may be on the rise. Third, the resolution of such questions as well as an improved understanding of disease at the genetic, cellular and molecular levels will accelerate the development of personalized

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Table I. Rank Order of Top 25 Papers Published in *Pharmaceutical Research* Since Its Launch in 1984

Rank	Paper in *Pharmaceutical Research*	Total 98,336	Average citations per year 3,933.44
1	*Author(s)*: Amidon, GL; Lennernas, H; Shah, VP; *et al.* *Title*: A theoretical basis for a biopharmaceutic drug classification—the correlation of *in-vitro* drug product dissolution and *in-vivo* bioavailability *Source*: Pharmaceutical Research, 12 (3): 413–420 Mar 1995	676	48.29
2	*Author(s)*: Davies, B; Morris, T *Title*: Physiological-parameters in laboratory-animals and humans *Source*: Pharmaceutical research, 10 (7): 1093–1095 Jul 1993	674	42.12
3	*Author(s)*: Cohen, S; Yoshioka, T; Lucarelli, M; *et al.* *Title*: Controlled delivery systems for proteins based on poly(lactic glycolic acid) microspheres *Source*: Pharmaceutical Research, 8 (6): 713–720 Jun 1991	433	24.06
4	*Author(s)*: Potts, RO; Guy, RH *Title*: Predicting skin permeability *Source*: Pharmaceutical Research, 9 (5): 663–669 May 1992	390	22.94
5	*Author(s)*: Shah, VP; Midha, KK; Dighe, S; *et al.* Title: Analytical methods validation—bioavailability, bioequivalence and pharmacokinetic studies *Source*: Pharmaceutical Research, 9 (4): 588–592 Apr 1992	290	17.06
6	*Author(s)*: Artursson, P; Lindmark, T; Davis, SS; *et al.* *Title*: Effect of chitosan on the permeability of monolayers of intestinal epithelial-cells (caco-2) *Source*: Pharmaceutical Research, 11 (9): 1358–1361 Sep 1994	276	18.4
7	*Author(s)*: Kim, RB; Wandel, C; Leake, B; *et al.* *Title*: Interrelationship between substrates and inhibitors of human CYP3A and P-glycoprotein *Source*: Pharmaceutical Research, 16 (3): 408–414 MAR 1999	273	27.3
8	*Author(s)*: Illum, L; Farraj, NF; Davis, SS *Title*: Chitosan as a novel nasal delivery system for peptide drugs *Source*: Pharmaceutical Research, 11 (8): 1186–1189 Aug 1994	265	17.67
9	*Author(s)*: Fischer, D; Bieber, T; Li, YX; *et al.* *Title*: A novel non-viral vector for DNA delivery based on low molecular weight, branched polyethylenimine: effect of molecular weight on transfection efficiency and cytotoxicity *Source*: Pharmaceutical Research, 16 (8): 1273–1279 Aug 1999	262	26.2
10	*Author(s)*: Hilgers, AR; Conradi, RA; Burton, PS *Title*: Caco-2 cell monolayers as a model for drug transport across the intestinal-mucosa *Source*: Pharmaceutical Research, 7 (9): 902–910 Sep 1990	252	13.26
11	*Author(s)*: Palm, K; Stenberg, P; Luthman, K; *et al.* *Title*: Polar molecular surface properties predict the intestinal absorption of drugs in humans *Source*: Pharmaceutical Research, 14 (5): 568–571 May 1997	248	20.67
12	*Author(s)*: Hancock, BC; Shamblin, SL; Zografi, G *Title*: Molecular mobility of amorphous pharmaceutical solids below their glass-transition temperatures *Source*: Pharmaceutical Research, 12 (6): 799–806 Jun 1995	244	17.43
13	*Author(s)*: Yee, SY *Title*: *In vitro* permeability across Caco3 cells (colonic) can predict *in vivo* (small intestinal) absorption in man—fact or myth *Source*: Pharmaceutical Research, 14 (6): 763–766 Jun 1997	232	19.33
14	*Author(s)*: Legendre, JY; Szoka, FC *Title*: Delivery of plasmid DNA into mammalian-cell lines using pH-sensitive liposomes—comparison with cationic liposomes *Source*: Pharmaceutical Research, 9 (10): 1235–1242 Oct 1992	231	13.59
15	*Author(s)*: Audus, KL; Borchardt, RT *Title*: Characterization of an *in vitro* blood–brain-barrier model system for studying drug transport and metabolism *Source*: Pharmaceutical Research, 3 (2): 81–87 Apr 1986	218	9.48
16	*Author(s)*: Williams, AC; Barry, BW *Title*: Terpenes and the lipid protein partitioning theory of skin penetration enhancement *Source*: Pharmaceutical Research, 8 (1): 17–24 Jan 1991	210	11.67
17	*Author(s)*: Kawabata, K; Takakura, Y; Hashida, M *Title*: The fate of plasmid DNA after intravenous-injection in mice-involvement of scavenger receptors in its hepatic-uptake *Source*: Pharmaceutical Research, 12 (6): 825–830 Jun 1995	198	14.14

Table I. (continued)

Rank	Paper in *Pharmaceutical Research*	Total	Average citations per year
		98,336	3,933.44
18	*Author(s)*: Kier, LB; Hall, LH *Title*: An electrotopological-state index for atoms in molecules *Source*: Pharmaceutical Research, 7 (8): 801–807 Aug 1990	195	10.26
19	*Author(s)*: Kelder, J; Grootenhuis, PDJ; Bayada, DM; *et al.* *Title*: Polar molecular surface as a dominating determinant for oral absorption and brain penetration of drugs *Source*: Pharmaceutical Research, 16 (10): 1514–1519 Oct 1999	194	19.4
20	*Author(s)*: Desai, MP; Labhasetwar, V; Amidon, GL; *et al.* *Title*: Gastrointestinal uptake of biodegradable microparticles: effect of particle size *Source*: Pharmaceutical Research, 13 (12): 1838–1845 Dec 1996	191	15.92
21	*Author(s)*: Jeffery, H; Davis, SS; Ohagan, DT *Title*: The preparation and characterization of poly(lactide-*co*-glycolide) microparticles. 2. The entrapment of a model protein using a (water-in-oil)-in-water emulsion solvent evaporation technique *Source*: Pharmaceutical Research, 10 (3): 362–368 Mar 1993	188	11.75
22	*Author(s)*: Schipper, NGM; Olsson, S; Hoogstraate, JA; *et al.* *Title*: Chitosans as absorption enhancers for poorly absorbable drugs. 2. Mechanism of absorption enhancement *Source*: Pharmaceutical Research, 14 (7): 923–929 Jul 1997	180	15
23	*Author(s)*: Quintana, A; Raczka, E; Piehler, L; *et al.* *Title*: Design and function of a dendrimer-based therapeutic nanodevice targeted to tumor cells through the folate receptor *Source*: Pharmaceutical Research, 19 (9): 1310–1316 Sep 2002	172	24.57
24	*Author(s)*: Erbacher, P; Zou, SM; Bettinger, T; *et al.* *Title*: Chitosan-based vector/DNA complexes for gene delivery: biophysical characteristics and transfection ability *Source*: Pharmaceutical Research, 15 (9): 1332–1339 Sep 1998	171	15.55
25	*Author(s)*: Lee, WA; Gu, L; Miksztal, AR; *et al.* *Title*: Bioavailability improvement of mycophenolic-acid through amino ester derivatization *Source*: Pharmaceutical Research, 7 (2): 161–166 Feb 1990	170	8.95

Source of data was ISI Web of Knowledge.

medicine. The blockbuster model—the current industry standard—may have to make room for the targeted therapeutics model. Because we are in a better position to identify risk, manage, and communicate risk, more and more new drug products may undergo a similar shift. Open access to information is a revolutionary change that will happen eventually. Should *Pharmaceutical Research* shape that evolution?

Pharmaceutical Research must reach out to keep pace with change. In the past 25 years, *Pharmaceutical Research* is generally considered by many as an icon of quality and leadership. Having a paper published in *Pharmaceutical Research* is a statement of achievement in the pharmaceutical community. That must not change, and I am honored to have played a role in during the formative years of *Pharmaceutical Research.*

Table II. The Top 25 Contributing Authors, Institutions, and Countries to *Pharmaceutical Research* from 1984 to Present and from 2003 to Present

	1984–present		2003–present		1984–present		2003–present		1984–present		2003–present	
Rank	Author	No. of papers	Author	No. of papers	Institution	No. of papers	Institution	No. of papers	Country	No. of papers	Country	No. of papers
1	Guy, RH	72	Hennink, WE	7	Univ Calif San Francisco	179	Univ Utrecht	14	USA	3,384	USA	252
2	Amidon, GL	64	Ghandehari, H	6	Univ Michigan	164	Univ Michigan	13	Japan	699	Japan	54
3	Sugiyama, Y	60	Storm, G	6	Univ Kansas	145	Univ Utah	13	England	326	England	40
4	Borchardt, RT	55	Brayden, DJ	5	Univ Minnesota	118	Univ Maryland	12	Germany	282	Netherlands	29
5	Shah, VP	40	Chan, HK	5	Univ Utah	110	Univ Kentucky	11	France	272	Germany	27
6	Hashida, M	38	Guy, RH	5	Univ Kentucky	108	Bristol Myers Squibb Co.	9	Netherlands	249	Canada	21
7	Au, JLS	37	Park, K	5	Univ n Carolina	106	Natl Univ Singapore	9	Canada	217	South Korea	17
8	Mitra, AK	37	Shah, VP	5	Purdue Univ	104	Northeastern Univ	8	Switzerland	190	Australia	15
9	Couvreur, P	36	Tamai, I	5	US FDA	100	Rutgers State Univ	8	Sweden	167	France	15
10	Lee, VHL	35	Terasaki, T	5	Kyoto Univ	86	Univ Bath	8	Belgium	97	Peoples R China	15
11	Crommelin, DJA	34	Lee, VHL	4	Ohio State Univ	81	Univ Groningen	8	Israel	91	Switzerland	13
12	Davis, SS	33	Maeda, T	4	Univ Wisconsin	81	US FDA	8	Australia	89	Singapore	11
13	Inui, k	32	Ohtsuki, S	4	SUNY Buffalo	80	Amgen inc	7	South Korea	70	Sweden	11
14	Benet, LZ	31	Pardridge, WM	4	Univ So Calif	79	Seoul Natl Univ	7	Denmark	69	Belgium	10
15	Jusko, WJ	31	Taylor, LS	4	Univ Florida	76	Univ Sydney	7	Italy	67	India	9
16	Otagiri, M	31	Torchilin, VP	4	Univ Tokyo	72	Univ Wisconsin	7	Spain	61	Italy	9
17	Suryanarayanan, R	31	Williams, RO	4	Upjohn Co	71	GlaxoSmithKline Inc	6	Finland	58	Finland	8
18	Langer, R	30	Yu, LX	4	Univ Utrecht	70	Ohio State Univ	6	Peoples R China	51	Ireland	7
19	Dressman, JB	29	Amidon, GL	3	Hebrew Univ Jerusalem	67	Pfizer Inc	6	India	49	Denmark	6
20	Tsuji, A	29	Aso, Y	3	Leiden Univ	66	Purdue Univ	6	Greece	47	Austria	5
21	Deluca, PP	28	Bae, YH	3	Univ Illinois	65	SUNY Buffalo	6	Singapore	40	Spain	5
22	Kissel, T	28	Banga, AK	3	Univ Uppsala	61	Tohoku Univ	6	Taiwan	39	Greece	4
23	Macheras, P	28	Boado, RJ	3	Genentech Inc	58	Tokyo Univ Sci	6	Wales	35	New Zealand	4
24	Sadee, W	28	Byun, Y	3	Pfizer Inc	56	Univ Minnesota	6	Fed Rep Ger	34	Scotland	4
25	Bodor, N	27	Chaumeil, JC	3	Univ Maryland	56	Univ n Carolina	6	Austria	31	Taiwan	4

Table III. Rank Order of Top 25 Papers Published in *Pharmaceutical Research* from 2003–present Since Its Launch in 1984

Rank	Paper in *Pharmaceutical Research*	Total	Average Citations per Year
		6,993	1,398.6
1	*Author(s)*: Wu, CY; Benet, LZ *Title*: Predicting drug disposition via application of BCS: transport/absorption/elimination interplay and development of a biopharmaceutics drug disposition classification system *Source*: Pharmaceutical Research, 22 (1): 11–23 Jan 2005	129	32.25
2	*Author(s)*: Huang, M; Khor, E; Lim, LY *Title*: Uptake and cytotoxicity of chitosan molecules and nanoparticles: effects of molecular weight and degree of deacetylation *Source*: Pharmaceutical Research, 21 (2): 344–353 Feb 2004	73	14.6
3	*Author(s)*: Smith, J; Wood, E; Dornish, M *Title*: Effect of chitosan on epithelial cell tight junctions *Source*: Pharmaceutical Research, 21 (1): 43–49 Jan 2004	57	11.4
4	*Author(s)*: Kondo, C; Suzuki, H; Itoda, M; *et al.* *Title*: Functional analysis of SNPs variants of BCRP/ABCG2 *Source*: Pharmaceutical Research, 21 (10): 1895–1903 Oct 2004	54	10.8
5	*Author(s)*: Jeong, WS; Kim, IW; Hu, R; *et al.* *Title*: Modulatory properties of various natural chemopreventive agents on the activation of NF-kappa B signaling pathway *Source*: Pharmaceutical Research, 21 (4): 661–670 Apr 2004	48	9.6
6	*Author(s)*: Forrest, ML; Meister, GE; Koerber, JT; *et al.* *Title*: Partial acetylation of polyethylenimine enhances *in vitro* gene delivery *Source*: Pharmaceutical Research, 21 (2): 365–371 Feb 2004	48	9.6
7	*Author(s)*: Havelund, S; Plum, A; Ribel, U; *et al.* *Title*: The mechanism of protraction of insulin detemir, a long-acting, acylated analog of human insulin *Source*: Pharmaceutical Research, 21 (8): 1498–1504 Aug 2004	46	9.2
8	*Author(s)*: Martanto, W; Davis, SP; Holiday, NR; *et al.* *Title*: Transdermal delivery of insulin using microneedles *in vivo* *Source*: Pharmaceutical Research, 21 (6): 947–952 Jun 2004	43	8.6
9	*Author(s)*: Thomas, M; Ge, Q; Lu, JJ; *et al.* *Title*: Cross-linked small polyethylenimines: while still nontoxic, deliver DNA efficiently to mammalian cells *in vitro* and *in vivo* *Source*: Pharmaceutical Research, 22 (3): 373–380 Mar 2005	41	10.25
10	*Author(s)*: Hermeling, S; Schellekens, H; Crommelin, DJA; *et al.* *Title*: Micelle-associated protein in epoetin formulations: A risk factor for immunogenicity? *Source*: Pharmaceutical Research, 20 (12): 1903–1907 Dec 2003	41	8.2
11	*Author(s)*:*Author(s)*: Kaul, G; Amiji, M *Title*: Tumor-targeted gene delivery using poly(ethylene glycol)-modified gelatin nanoparticles: *in vitro* and *in vivo* studies *Source*: Pharmaceutical Research, 22 (6): 951–961 Jun 2005	40	10
12	*Author(s)*: Ito, K; Houston, JB *Title*: Comparison of the use of liver models for predicting drug clearance using *in vitro* kinetic data from hepatic microsomes and isolated hepatocytes *Source*: Pharmaceutical Research, 21 (5): 785–792 May 2004	40	8
13	*Author(s)*: Yazdanian, M; Briggs, K; Jankovsky, C; *et al.* *Title*: The "high solubility" definition of the current FDA Guidance on Biopharmaceutical Classification System may be too strict for acidic drugs *Source*: Pharmaceutical Research, 21 (2): 293–299 Feb 2004	38	7.6
14	*Author(s)*: Ito, K; Houston, JB *Title*: Prediction of human drug clearance from *in vitro* and preclinical data using physiologically based and empirical approaches *Source*: Pharmaceutical Research, 22 (1): 103–112 Jan 2005	37	9.25
15	*Author(s)*: Galindo-Rodriguez, S; Allemann, E; Fessi, H; *et al.* *Title*: Physicochemical parameters associated with nanoparticle formation in the salting-out, emulsification–diffusion, and nanoprecipitation methods *Source*: Pharmaceutical Research, 21 (8): 1428–1439 Aug 2004	36	7.2
16	*Author(s)*: Hirouchi, M; Suzuki, H; Itoda, M; *et al.* *Title*: Characterization of the cellular localization, expression level, and function of SNP variants of MRP2/ABCC2 *Source*: Pharmaceutical Research, 21 (5): 742–748 May 2004	35	7

Table III. (continued)

Rank	Paper in *Pharmaceutical Research*	Total	Average Citations per Year
		6,993	1,398.6
17	*Author(s)*: Kalantzi, L; Goumas, K; Kalioras, V; *et al.* *Title*: Characterization of the human upper gastrointestinal contents under conditions simulating bioavailability/bioequivalence studies *Source*: Pharmaceutical Research, 23 (1): 165–176 Jan 2006	34	11.33
18	*Author(s)*: Kang, HM; DeLong, R; Fisher, MH; *et al.* *Title*: Tat-conjugated PAMAM dendrimers as delivery agents for antisense and siRNA oligonucleotides *Source*: Pharmaceutical Research, 22 (12): 2099–2106 Dec 2005	34	11.33
19	*Author(s)*: Shenoy, D; Little, S; Langer, R; *et al.* *Title*: Poly(ethylene oxide)-modified poly(beta-amino ester) nanoparticles as a pH-sensitive system for tumor-targeted delivery of hydrophobic drugs: part 2. *In vivo* distribution and tumor localization studies *Source*: Pharmaceutical Research, 22 (12): 2107–2114 Dec 2005	33	11
20	*Author(s)*: Begat, P; Morton, DAV; Staniforth, JN; *et al.* *Title*: The cohesive-adhesive balances in dry powder inhaler formulations I: direct quantification by atomic force microscopy *Source*: Pharmaceutical Research, 21 (9): 1591–1597 Sep 2004	33	6.6
21	*Author(s)*: Zhang, SZ; Yang, XN; Morris, ME *Title*: Combined effects of multiple flavonoids on breast cancer resistance protein (ABCG2)-mediated transport *Source*: Pharmaceutical Research, 21 (7): 1263–1273 Jul 2004	33	6.6
22	*Author(s)*: Trehin, R; Krauss, U; Muff, R; *et al.* *Title*: Cellular internalization of human calcitonin derived peptides in MDCK monolayers: A comparative study with Tat(47–57) and penetratin(43–58) *Source*: Pharmaceutical Research, 21 (1): 33–42 Jan 2004	32	6.4
23	*Author(s)*: Jeong, WS; Kim, IW; Hu, R; *et al.* *Title*: Modulation of AP-1 by natural chemopreventive compounds in human colon HT-29 cancer cell line *Source*: Pharmaceutical Research, 21 (4): 649–660 Apr 2004	31	6.2
24	*Author(s)*: Opanasopit, P; Yokoyama, M; Watanabe, M; *et al.* *Title*: Block copolymer design for camptothecin incorporation into polymeric micelles for passive tumor targeting *Source*: Pharmaceutical Research, 21 (11): 2001–2008 Nov 2004	30	6
25	*Author(s)*: Porter, CJH; Kaukonen, AM; Boyd, BJ; *et al.* *Title*: Susceptibility to lipase-mediated digestion reduces the oral bioavailability of danazol after administration as a medium-chain lipid-based microemulsion formulation *Source*: Pharmaceutical Research, 21 (8): 1405–1412 Aug 2004	30	6

Source of data was ISI Web of Knowledge