

Terminology and the Construction of Scientific Disciplines: The Case of Pharmacogenomics

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This article explores the way in which social explanations underpin the names of particular disciplines. Taking the example of pharmacogenomics (a spin-off from the Human Genome Project), it shows how this term has been constructed since it appeared in 1997, the differences and similarities between it and its precursor, pharmacogenetics, and the way in which commercial interests underpin this new term. Drawing on the idea of visions and the sociology of expectation, the article shows how different actors compete to have their preferred definitions of the term accepted by the world at large.

Keywords: genetics; expectations; biotechnology; industry

How important are names in the social construction of particular technologies? Does it matter what we call a discipline or research area; does it affect how it develops and expands—how influential it becomes? This article presents a case study of a technological discipline arising from modern genetic research: pharmacogenomics, the study of genetic differences between people that affect drug metabolism. As a topic, it brings together a number of different technologies as well as different interest groups (patients, health care funders, regulators, industry). It could also have significant impact on society; pharmacogenomics is interesting as a locus of sociological research and policy importance. This article's central claim is that rather than strictly representing an area of research, the term *pharmacogenomics* can be seen as a rhetorical device used to gain support among policy makers and funders for

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particular research topics and technologies. By tapping into the interest and “hype” surrounding the word *genomics*, pharmacogenomics links into a number of future scenarios about the impact of genomic technology on health care systems and society as a whole.

The term *pharmacogenomics* is a modern variation on the term *pharmacogenetics*, used since 1959 to describe the study of genetic variation in drug response. Within any given human population, there are a number of different possible reactions to a drug, from no response through the speedy metabolism of the drug to clinical usefulness or even harm or death. Current drugs are marketed and prescribed on a “one-size-fits-all” basis, but genetic difference between individuals means that this is rarely the case. Since 1997, the term *pharmacogenomics* has appeared in the scientific literature, often contrasted with *pharmacogenetics*, yet clearly, they are related. If *pharmacogenetics* has been in use as a term for over forty years, it is sensible to ask why we are coming to talk about pharmacogenomics rather than pharmacogenetics and what is it about modern science that makes us talk about pharmacogenomics now?

The two main technologies involved in pharmacogenomics are single-nucleotide polymorphisms (SNPs) and DNA chips. SNPs are tiny but identifiable differences between people’s genetic makeups (genomes), which can be mapped out and linked to particular features, such as diseases or reactions to drugs. DNA chips are testing kits that allow one to test thousands of bits of DNA at the same time, thus reducing the cost per polymorphism tested. In this sense, pharmacogenomics is a spin-off from the Human Genome Project (HGP), the international research program that has spent the past ten years sequencing the human genome. But as this article suggests, the development of pharmacogenomics is about more than just technological advance.

Discussions surrounding pharmacogenetics and pharmacogenomics claim that these disciplines will revolutionize medical practice in the near future. This will allow the prescription of drugs that are more likely to work and less likely to result in adverse drug reactions (ADRs), which are claimed to be between the fourth and the sixth biggest killers in the United States (Lazarou, Pomeranz, and Corey 1998). Developments in pharmacogenetics are interesting not just as a further example of the social shaping of technology but as a possible intervention in an area of public health.

Explanatory Structures

Science and technology studies has long been interested in scientific disciplines as a topic of study (see Golinski 1999 for a historical review), and

this in turn has given rise to the concept of “boundary work,” whereby scientists distinguish one discipline from another (Gieryn 1995). The role of specific terms in the construction and control of disciplines was examined by Balmer and Sharp (1993), who discussed the institutional disputes that surrounded the term *biotechnology* in the United Kingdom in the 1980s (see also Bud 1993). Rawling’s (1994) work shows how terms become topics for dispute, representing different positions relating to scientific priority, as does Misa’s (1992) research on the meaning of the words *steel* and *iron*. In a broader way, Jane Calvert (2000) showed how the term *basic research* has been used by scientists in a rhetorical way to acquire prestige and resources. What these studies show is the importance of what we call things. The names we use to label particular disciplines have a role in structuring them, and this in turn affects the uptake of particular technologies.

One theoretical approach to explain the development and use of the term *pharmacogenomics* is the social construction of technology, a critique of technological determinism that has provided insights into the development of a huge range of technologies, from bicycles through washing machines to the M-16 rifle and rocket guidance systems (MacKenzie and Wajcman 1999). Work in this area has also covered the pharmaceutical and biotechnology industries, including their regulation (Abraham 1995) and the development of the gene therapy industry (Martin 1995, 1999). Within this framework, the idea that the name of a research topic plays a rhetorical role in building support for that research is highly plausible, with the term *rhetoric* being used here in a neutral, nonderogatory sense (Myers 1990b, 25-34; Guice 1999, 84).

Rhetoric’s importance is enhanced by modern science policy and funding, which has “created a ‘space’ in which promises can be floated: generally to whoever is willing to listen, and specifically directed towards sponsors of R&D who have an interest in promising areas of science” (van Lente and Rip 1998, 222). In their discussion of the rise of membrane technology in the 1980s, van Lente and Rip suggested that in the early stages, it is important for a promising area of research to have the right labels to aid network building and resource allocation (p. 224). Although these labels are chosen by participants, they also reflect past institutional commitments and broader responses to social and economic change (Balmer and Sharp 1993). I suggest that pharmacogenomics fits this model of promissory science, particularly the issue of using the right labels, tying into the work of Jon Guice (1999), who has mapped out how protagonists’ arguments serve to promote specific fields of study. Guice claimed that one of the ways in which proponents of particular technologies gain support for their ideas is through self-fulfilling prophecies: “by supposing something to exist, one makes it exist in collective

imagination . . . one lends support to a particular view of the issue and defines it as an issue in the first place” (p. 84).¹

Another author who has addressed the issue of self-fulfilling prophecies is Donald MacKenzie (1996), in his work on the development of supercomputers and the limits to their processing speed. One risk of promoting a particular area of science through such prophecies is that claims will come across as hype, which is “purely emotional and promotional, makes sweeping claims, and lacks evidence” (Guice 1999, 85). But as Guice pointed out, drawing a sharp distinction between hype and genuine scientific promotion is fruitless. Scientific promotion always carries some appeal to emotion, and hype, although low on content, does serve to relate developments in a particular field to a social context (p. 85).

In this article, I build on this idea of promissory science by suggesting that participants in discussions surrounding pharmacogenomics and pharmacogenetics are putting forward what we might call “visions.” The concept of a technological vision was used by Paul Martin (1999) to describe discursive constructions that “act as both a means of enrolling support and resources into the emerging socio-technical network and as a guide to the physical design of artefacts” (p. 520).² In the area of gene therapy, Martin (1995, 166) noted how firms try to construct markets for products while they are still designing technologies, shaping both the use and the development of their products prior to their appearance.

A similar thing is happening in the pharmacogenomics industry. Through their writings, commentators are shaping the regulatory structure of pharmacogenomics through discussion of changes to clinical trials (e.g., the number of participants required for an adequate trial), the market environment within which pharmacogenomics is adopted through discussing changes to health care systems (particularly the role and funding of genetic tests in clinics), and the positions of their own firms within the future market in terms of those technologies most likely to produce results (e.g., the number of SNPs required for an adequate pharmacogenomic map). As I show in Section 4, there is no internal, technical reason for the use of the term *pharmacogenomics*; one can coherently define *pharmacogenetics* to cover the same issues. But the word *pharmacogenomics* has a rhetorical strength to it, and in sketching out visions of how they think this technology will develop, authors are enlisting the word *genomics* and the technologies it implies to contrast with old-fashioned genetics.

The idea of a technological vision helps explain the empirical information presented in the first half of this article, in which data from the ISI’s *Science Citation Index (SCI)* database sets the scene and highlights trends in research publication on the topics of pharmacogenetics and pharmacogenomics. I am

not making statistical claims for this research, nor am I carrying out an exhaustive analysis of research groups, co-citations, and interest networks (e.g., Garfield 1979). But although it is traditional to view qualitative sociology of science as quite separate from scientometrics (van den Besselaar 2001), a number of studies have shown that graphs and database searches can provide useful material for qualitative analysis (Callon, Law, and Rip 1986; Rawling 1994). This article provides another example of this, with the second half analyzing the implications of the trends outlined in Section 3.

In defense of this method, it is important to note that the usual criticisms leveled against the use of the ISI's database focus on the study of citations, that is, how authors reference other scientists, the networks this produces, and the explanations for such citations (e.g., Gilbert and Woolgar 1974; Woolgar 1991). Most of these objections—for example, the noncitation of central influences, the nonrepresentative nature of co-citations, and the strategic noncitation of competitors (Edge 1979)—are simply not relevant if we are considering research simply looking at how a often specific term is mentioned. Edge mentioned two possible broader objections from a constructivist perspective that might be relevant: first, that quantitative methods focus on the formal published literature, promoting a rationalized ideal of scientific processes that are most in need of analysis, and second, that quantitative methods promote a positivist view of the way science “really” is, diverting attention from the social aspects of scientists' lives, which may provide alternative perspectives on the science in question (p. 108).

I understand both these concerns about quantitative research as a whole but again suggest that they do not apply to the very basic approach I adopt in this article. I accept that the use of the term *pharmacogenomics* occurs outside the written literature and that it started circulating informally as a term sometime (perhaps a year) before it was ever published in a journal. Yet this does not undermine the use of the *SCI* to “track” the appearance of this term in the literature, its uptake by researchers and promoters of this technology. The quantitative data are simply a starting point for the qualitative research. Without these data, it would be impossible to ask why *pharmacogenomics* “appeared” in 1997, why authors from commercial backgrounds are so attracted to its use, and why it tends to appear in reviews rather than research articles. Nor does tracking this term in this way imply that there is a concrete, objective, realist *pharmacogenomics*, which exists independently of its social context. As this article attempts to show, the flexible, contingent nature of this term supports many of the constructivist assumptions underpinning my work.

An example of the value of mixing qualitative and quantitative research can be found by comparing Nelkin and Lindee's (1995) work on the cultural

representation of genetics with Celeste Condit's research (Condit 1999a, 1999b; Condit, Ofulue, and Sheedy 1998), which tests many of their ideas and finds some of their claims lacking. For example, Condit disputed the idea that media representations of genetics are more deterministic now than they have been in the past, a fact beyond dispute for Nelkin and Lindee. Through a quantitative sampling of magazine articles over the whole of the twentieth century, Condit, Ofulue, and Sheedy showed that modern reporting on genetics is in many ways more sophisticated and less deterministic than it has been previously. Nelkin and Lindee were vigorously nonquantitative, claiming that their

intention was to explore many different forms of popular culture. Although we can show that images have changed through time, we have not compiled quantitative data and do not think it would have been appropriate or meaningful to do so. (P. ix)

Even if we accept that it is possible to convincingly prove such changes without showing how representative the examples used are, such work is always at the mercy of quantitative studies, which can sample more broadly. It is not that Nelkin and Lindee's (1995) analysis of the cultural representation of genetics is flawed—far from it. In many ways, it is a prime example of the way in which popular culture can be drawn on as a research resource. The problems came when Nelkin and Lindee went beyond their data and drew conclusions about the representation of genetics in other time periods, for which they presented no evidence. I hope that my combination of basic quantitative data on the use of the term *pharmacogenomics*, followed by a qualitative analysis of examples of that usage, allows me to draw tentative conclusions about the rhetorical role such a term plays, without overstating my case.

Database Information

These data were drawn from the ISI's *SCI* and *Social Science Citation Index*, noting the number of publications in which the specific term (e.g., *pharmacogenetic* or *pharmacogenetics*) appears in the title, abstract, or key words of an article.³ Obviously, a number of assumptions underpin this method; the first is that there is some sort of relationship between published literature and research carried out. I accept that not all research related to pharmacogenetics or pharmacogenomics could be included in this database search; there may be influential research articles that do not contain these terms.⁴ In addition, important research carried out by industry might not

result in published articles.⁵ But because of the value systems underpinning the scientific enterprise, people doing research are also people who publish it (Merton 1973). In this sense, publications mentioning these terms are indicators of research activity or at the very least interest (Balmer and Martin 1991).

Pharmacogenetics

Figure 1 compares the appearance of the words *pharmacogenetic* or *pharmacogenetics* and *pharmacogenomic* or *pharmacogenomics* from the beginning of the ISI's Web database in 1981 to 2000. In the case of *pharmacogenetic* or *pharmacogenetics*, there were three distinct time periods: 1981 to 1990 (an average of 16.3 publications per year), 1991 to 1997 (an average of 65.7 publications per year), and 1998 to 2000 (an average of 191.3 publications per year). What happened to cause these jumps?

An obvious explanation for the jump from 1990 to 1991 is that it occurred at the same time as the United States and other governments announced funding for their human genome projects (Balmer and Martin 1991). With more money going into molecular genetics as whole, associated disciplines such as pharmacogenetics might have seen increases in research grants and hence articles published. There are a number of problems with this explanation. The first is the time lag that occurs between funding, research, and publication. With funding in this area starting in 1990, it is unlikely that enough ground would have been covered to produce this jump. In addition, none of the articles in the period from 1990 to 1991 mention the HGP in their titles, abstracts, or key words.⁶ This does not mean of course that there was no pharmacogenetic research influenced by the expansion in human genetics, but one would expect any direct influence to be acknowledged. Similarly, if the HGP was a direct driving force behind such an increase in publications, one would expect some citation of articles laying out the HGP or outlining its structure. Although a number of such articles were present in the literature before 1991,⁷ none of them were cited in any of the sixty-six articles on pharmacogenetics that were published in 1991. One solution to this problem was offered up by Balmer and Martin, who noted that in the early years of the project, *genome mapping* was the term used to describe this research rather than *human genome project*. In addition, they noted that at least in the United States, there was a surge in the number of articles discussing genome mapping before funding for the HGP was announced: "There is a possibility that major research initiatives may not always *give rise to* an increase in the volume of research and published output, but may instead *follow* such an increase" (p. 376).⁸

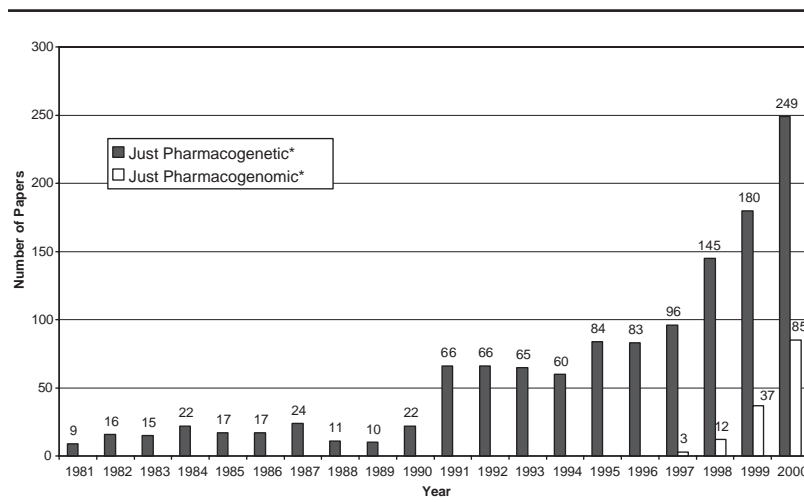


Figure 1. Pharmacogenetics and pharmacogenomics.

The second jump in Figure 1 comes between 1997 and 1998, tying into the focus of the next section, the arrival of the term *pharmacogenomics*. Briefly, the reasons behind this increase in research into pharmacogenetics lie in increased industry interest in a discipline that was previously restricted to academia (Regalado 1999, 42). For the moment, I simply want to note that the three time periods had different proportions of authors and coauthors of articles with commercial connections (Table 1).

As it stands, these figures note nothing more than the well-acknowledged fact that the biological sciences are becoming increasingly commercialized (Krimsky, Ennis, and Weissman 1991; Kenney 1998). But as this article shows, in pharmacogenetics, the role of the pharmaceutical industry is vital in terms of how the discipline is developing and changing into pharmacogenomics. What is clear from the literature on pharmacogenetics is how resolutely uncommercial its concerns were until the mid-1990s. A typical review such as Meyer's (1990) outlines the history, successes, and techniques of pharmacogenetics, without once speculating about the effect of developments in pharmacogenetics on the pharmaceutical industry or health care systems. Some discussion of these topics was provided by Kalow (1990), but even a review by the same author in 1997 did not set pharmacogenetics in an industrial context, the way pharmacogenomics has always been seen (Kalow 1997).

Table 1. Papers Authored or Coauthored by Someone from a Commercial Source

<i>Date</i>	<i>Percentage</i>	<i>Number</i>
Pharmacogenetics		
1981 to 1990	4	6/163
1991 to 1997	8	36/460
1998 to 2000	17	96/574
Pharmacogenomics		
1997 to 2000	21	29/137

NOTE: The ISI's database allows one to search according to an author's affiliation. A search can be run to include commercial indicators such as *Inc.* or *Ltd.*, as well as the names of firms that do not use such indicators (e.g., Astrazeneca). Test searches showed that such a search includes all commercial authors while excluding articles with no commercial links. Percentages are rounded up.

Pharmacogenomics

The term *pharmacogenomics* has no existence in the ISI's database before 1997, when it got three mentions. One of these was a news item describing the commercial alliance between Genset (a French firm with large genetic databases) and Abbott Labs (a large U.S. pharmaceutical company with an interest in genetic testing) (Marshall 1997a). The other two articles looked at the commercial and scientific backgrounds of pharmacogenomics (Jordan 1997; Marshall 1997b). The appearance of the term *pharmacogenomics* corresponded with the second jump in references to pharmacogenetics, suggesting that the causes for these two events may have been the same.

The news report that first mentioned the word *pharmacogenomics* was published in the September 1997 issue of *Nature Biotechnology* and was called "Genset-Abbott Deal Heralds Pharmacogenomics Era." The author, Andrew Marshall (1997a), discussed an alliance between the two firms to create a detailed map of the human genome, focusing on those sections that are associated with drug response. At least one commentator suggested that the term *pharmacogenomics* "emerged from the bowels of the genomics industry to prominence [only] with the announcement of the Genset-Abbott alliance" (Regalado 1999, 40). The Genset-Abbott deal followed a commercial genomics "open season" in April and May 1997 that saw a number of alliances between companies developing tests and those with large amounts of genetic data, as well as a conference in Monte Carlo in May 1997 that brought together interested parties from industry and academia (Brower 1997; Jordan 1997).⁹

Confirmation of the role of the Genset-Abbott alliance in promoting the term *pharmacogenomics* comes from reviewing the newsletter of the biotechnology industry, *Genetic Engineering News (GEN)*. *GEN* has been published since the early 1980s and is currently a bimonthly trade paper covering technical developments in the biotech industry; commercial changes (such as buyouts, mergers, and alliances); and all the news, gossip, and conference reports one would expect from such a journal. *GEN*'s searchable, Web-based database lists the first mention of *pharmacogenomics* in an article title at the beginning of 1998 (Glaser 1998). But a manual search of back issues showed the first appearance in text to be in the issue of 15 October 1997, in which the "Alliances" column mentioned the Genset-Abbott alliance: "for the use of pharmacogenomics to pinpoint the genes associated with the efficacy and side effects of drugs" (p. 35). The issue of 15 June 1997 mentioned the Monte Carlo conference cited by Jordan (1997) as discussing pharmacogenomics, but although *GEN* did mention the role of human genomics in drug discovery, the term *pharmacogenomics* was not used. Even more significantly, an item (published on 1 March 1997) about the commercial value of the HGP listed technologies due to arise from the HGP: "therapeutic proteins, medical diagnostics gene therapy, targeted molecules, small molecule therapeutics, DNA sequencing, Bioinformatics, functional genomics" (McKowen and Sarin 1997, 30).

Although one could include pharmacogenetics and pharmacogenomics under the heading of medical diagnostics, it seems odd that one of the approaches that is now touted as being the first to bring the results of the HGP into clinics was not worth a mention by name in early 1997. It seems as if the Genset-Abbott agreement focused attention not just on the field of pharmacogenomics but on the term itself.¹⁰

If we accept that 1997 was effectively "year zero" for the term *pharmacogenomics* and that the Genset-Abbott alliance introduced the word into the literature, there is still the question of why it occurred at that point. Why was it that industry felt the need to form these alliances and consortia in 1997? Antonio Regalado (1999, 42) suggested a number of technical reasons for the sudden growth in commercial interest in pharmacogenomics: the viability of gene chip technology, the expansion of DNA databases collected by companies, and the maturation of bioinformatic technologies required to make comparisons between SNP maps. These three explanations are all intimately connected; only with clear evidence of cheap parallel sequencing could pharmaceutical firms see a way of using the vast amounts of data produced by SNP databases. Having all that information in a database is not much use without a way to link it to a patient's genome through cheap testing. The DNA chip bridges the gap between patient and database. The

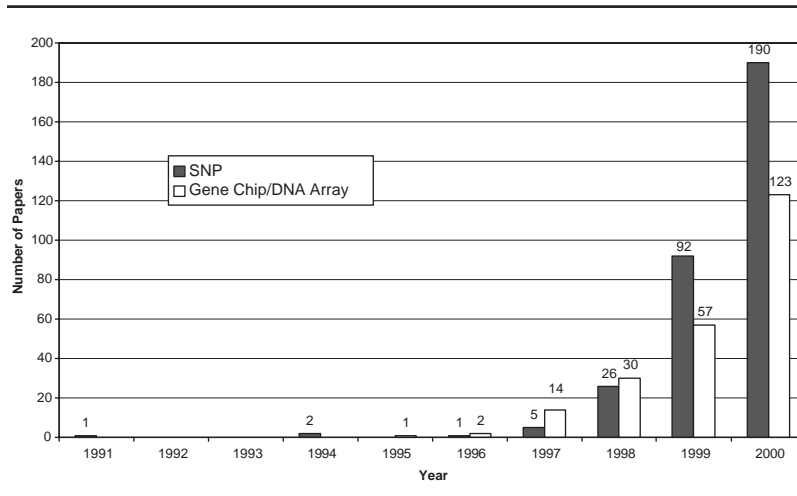


Figure 2. Pharmacogenetic and pharmacogenomic technologies.
NOTE: SNP = single-nucleotide polymorphism.

relationship between DNA chips and SNP databases can be seen in Figure 2, which shows mentions of the terms *SNP* and *gene chip* or *DNA array*. Both graphs follow the now familiar pattern of low citations until 1997, when there was a steep increase in mentions mirroring that of *pharmacogenomics*.

But Regalado (1999) also suggested that pharmaceutical industry psychology plays a large part in the rapid ascent of pharmacogenomics: the high cost of drug development means that industry executives are keen to adopt any technology that will reduce their research and development expenditures. The pressure to adopt is even greater if they see other companies already using that technology (e.g., emphasized by a high-profile alliance). As a result, a “follow-the-leader” effect is produced in the large pharmaceutical companies, fueled by the smaller genomics firms, which have high overheads and research costs and thus a pressing need to sell some sort of product (p. 42-43). Also, those in second place keep their costs down by learning from the leader’s mistakes, gaining latecomer advantage (Freeman and Soefe 1997). Added to this is the growth of managed care organizations (MCOs) in the U.S. health care sector (Housman and Ledley 1998). MCOs not only fund but also provide health care (e.g., hospitals and medical practices) (Brown 1998). Their defining feature is the drive to reduce health care costs and increase efficiency, and thus, they are usually seen in opposition to the pharmaceutical industry (Murray and Deardorff 1998). This tension produces an

environment in which a technology such as pharmacogenomics, which promises to reduce drug expenditures (through targeted prescription and the reduction of ADRs) while reducing drug development costs, will be looked on favorably.

Convincing as this analysis is, there is a blind spot in that it does not explain why the pharmaceutical industry is excited about pharmacogenomics: how does renaming this discipline make it more attractive to funders and researchers? The rest of this article examines the role the term *pharmacogenomics* plays in scientific trend setting.

Negotiating Terms: Pharmacogenetics or Pharmacogenomics

The claim that structural developments in the pharmaceutical industry have had an impact on terms used in published research is hardly surprising. Alliances between firms will create research interest in the areas concerned, funding will become available, and articles will be written. My interest is not in that fact that a commercial alliance stimulated research in a specific area; I am intrigued by the fact that this area is called pharmacogenomics rather than pharmacogenetics. What the differences are between these two terms depends on whom you are asking. A report of the recent Pharmacogenetics and Pharmacogenomics Euroconference, organized by the Pasteur Institute in Paris, admitted that “it was apparent that the difference between pharmacogenetics and pharmacogenomics was not obvious to most delegates” (Grant 2001, 3).

Reading through the literature, it is clear that differing perspectives on what the words *pharmacogenomics* and *pharmacogenetics* mean jostle for position—they are terms under negotiation. In the current discursive space of modern biotechnology, the meaning of *pharmacogenomics* is contested, as shown by the debate within the pharmaceutical industry’s own committee on pharmacogenetic nomenclature. This international committee is made up of representatives of the major pharmaceutical companies. Its remit is to draw up accepted meanings for *anonymized*, *encoded*, and other terms used in clinical trials. This provides a consensus on these terms to allow ethics committees and regulators to process clinical trial applications more speedily, without the worry of having to check what the companies mean by these terms, and decide whether different companies use them in the same way. The industry committee has reached consensus on the meaning of all these terms (including *pharmacogenetics*) bar one: *pharmacogenomics*, on which no agreement can be reached.¹¹

The following sections present broad definitions of *pharmacogenetics* and *pharmacogenomics*, with the aim of showing the wide degree of overlap in meaning between the two terms. There are a number of different definitions of these two terms in the literature, ranging from the idea that they are interchangeable (Snedden 1999; Wieczorek and Tsongalis 2001) to those that define *pharmacogenomics* in terms of the effects of small molecules on the patterns of gene expression displayed by individual cells (Bailey, Bondar, and Furness 1998). Moyses (1999) noted that this variation ranges from “a mass approach to pharmacogenetics” through “both genotypic prediction of response and wider applications of genomics” to the broadest position, at which “pharmacogenomics may be taken to encompass all the pharmaceutical applications of genomics” (p. 199). Within these sweeping definitions, there are narrower, more specific visions of how these technologies will develop. The final sections of this article focus in detail on the visions of pharmacogenomics being constructed in a number of influential review articles and editorials.

Pharmacogenomics as the Successor to Pharmacogenetics

In this broad definition, “pharmacogenomics refers to the entire spectrum of genes that determine drug behaviour and sensitivity, whereas pharmacogenetics is often used to define the more narrow spectrum of inherited differences in drug metabolism and disposition” (Evans and Relling 1999, 488). The range and depth of the power of pharmacogenomics stems from the new technologies such as SNPs and the use of large quantities of genetic data. Although traditional pharmacogenetics relies on the “candidate gene” approach,¹² pharmacogenomics searches large numbers of different genetic polymorphisms: “Pharmacogenomics represents a natural development or evolution of successful pharmacogenetic research by applying genomic techniques to hasten identification of new drug response markers” (Vessell 2000, 119). Thus, the distinction between pharmacogenomics and its predecessor is in part a methodological one:

Pharmacogenetics is the study of genetic variation underlying differential response to drugs . . . [whereby] . . . pharmacogenetic markers . . . [were] . . . discovered through a hypothesis-driven approach in which each polymorphism was identified in a plausible candidate gene. Pharmacogenomics applies large-scale systematic approaches of genomics to speed the discovery of drug response markers. (Kleyn and Vessel 1998, 1820; see also Norton 2001 and Omenn 2001)

These authors presented pharmacogenomics as the successor to pharmacogenetics, the result of a technological revolution (Kurth 2000, 223), with technologies such as DNA chips and SNPs being regularly cited as the driving force behind the development of pharmacogenomics (e.g., Sadée 1999; Anderson, Fitzgerald, and Manasco 1999; Cockett, Dracopoli, and Sigal 2000; Persing and Cheek 2000; Cronin et al. 2001).

The New Pharmacogenetics

Yet it is perfectly possible to discuss novel technologies, such as DNA chips, within the context of traditional pharmacogenetics, defined as “genetically determined variability in drug response” (Wolf, Smith, and Smith 2000, 987). These authors discussed SNP maps and other polymorphisms as a form of pharmacogenetics and their use in the identification of new sites for novel drugs. Pharmacogenetics is explicitly defined in terms of SNPs and other “genomic” technologies, and this position reaffirms the continuity of research between historical pharmacogenetics and more modern developments. As one set of authors noted, “contrary to popular belief in certain quarters of the biotechnology sector, the recognition that much . . . [drug reaction] . . . variation is genetically based . . . is not new” (Pfof, Boyce-Jacino, and Grant 2000, 334). These same authors referred to the “new pharmacogenetics,” which

uses powerful experimental and data-handling techniques in DNA analysis to discover and assemble a comprehensive list of the variations within the human genome—specifically, SNPs—and then defines complex genetic profiles of these SNPs that predict the use of new or existing therapeutic agents with maximal efficacy and minimal toxicity. (P. 335)

As a prime exponent of this position, Allen Roses (2000b)¹³ described how there are two methodological approaches to pharmacogenetics: discovery genetics (which uses disease populations to identify potential targets) and discovery genomics (in which genetic databases are used to identify DNA sequences that may be of relevance) (see also Lau and Sakul 2000¹⁴). Both of these methods use some of the same technologies (e.g., functional genomics), and Roses classified both under the term *pharmacogenetics*. He included a detailed description of the role SNP profiles might play in identifying varying drug responses (pp. 862-63) and discusses the way in which pharmacogenetics may affect health care delivery (p. 863). The adoption and application of new genetic technologies does not require a new term. These technologies “make sense” within the structure of pharmacogenetics (see

also Sykes 1999; Meyer 2000; Chamberlain and Joubert 2001; Jazwinska 2001; Liggett 2001; Shi, Bleavins, and de la Iglesia 2001; Spear, Heath-Chiozzi, and Huff 2001).

The Pharmacogenomics Vision

The Appeal of Genomics

The previous section suggests that there is no technical, internal reason for preferring *pharmacogenomics* to *pharmacogenetics*. Both terms adequately describe the methods, technologies, and approaches required for this kind of research. Both terms are used by participants in the debates surrounding this area, both academic and industrial. The reasons for using one term rather than another lie in social explanation. There are a number of answers to the question, Why *pharmacogenomics*?

- *Genomics* is a modern term coined in 1986 “to describe the scientific discipline of mapping, sequencing, and analysing genomes” (Hieter and Boguski 1997, 601), itself emerging from what was previously seen as a backwater of genetics into the self-fulfilling prophecy of the HGP (Balmer 1996). As such, it is defined in opposition to genetics, which is concerned with the role of individual genes. Clearly, its definition has now spread so broadly that almost any genetic technology, however basic, can be described as genomic (Harris and Buckler 1997). But at its core, the term *pharmacogenomics* implies being up to date and separated from what has gone before.
- *Genomics* is an implicitly commercial term, and the genomics industry is so intertwined with academia that unlike with genetics, associating a topic with genomics implies commercial involvement (Cohen 1997; Brown and Rappert 2000). This is indicated by the higher proportion of articles mentioning pharmacogenomics that have industry-based authors or coauthors, as opposed to pharmacogenetics (see Table 1). Searches on commercial databases support this idea. For example, the biovista.com Web site¹⁵ lists (as of 3 August 2002) 25 news stories mentioning pharmacogenetics and 144 using *pharmacogenomics*, as well as six companies classed as pharmacogenomic and only one as pharmacogenetic. The genomeweb.com Web site¹⁶ had 6 news items listed for pharmacogenetics and 67 for pharmacogenomics.

As an amalgam of genetics and informatics, genomics (both the term and the discipline) implies the use of computers and other advanced technologies in genetic research (Wiley 1998). It implies certain techniques and methods of investigation, and its symbiotic relationship with bioinformatics further heightens the ties between genomics and commercial concerns (Gershon 1997).

Genres in the Construction of Pharmacogenomics

Rather than representing a distinct research discipline, I suggest that the term *pharmacogenomics* is a rhetorical strategy used to enlist support through association with the word *genomics*. In addition to this rhetorical role, it is worth considering the way in which discussions around pharmacogenomics are published. Figure 3 shows publications including *pharmacogenetic* or *pharmaogenetics* divided into articles and commentaries. Articles cover not just research publications that announce original research but any publication that includes new information, such as methodologies. Commentaries include publications covered by the ISI's categories: reviews, editorials, and discussions. These kinds of publications all comment on previously published research rather than introducing novel results. As one would expect from a mature discipline of forty years, Figure 3 shows that in pharmacogenetics, articles significantly outnumber commentaries, in all years. Turning to Figure 4, which displays the same comparison with regard to *pharmacogenomic* and *pharmacogenomics*, a very different pattern can be seen. Here, the numbers are much closer between the kinds of publications; in a couple of years, commentaries outnumber articles. Too little original research has been published using pharmacogenomic techniques to justify this number of reviews if all they were doing was outlining the state of current research.

This pattern makes sense in the context of ideas proposed by Greg Myers (1991) concerning the role of review articles in the construction of scientific disciplines, whereby a review "shapes the literature of a field into a story to enlist the support of readers to continue that story" (p. 45). It is the construction of knowledge in reviews that allows certain experimental reports to be seen as "key" articles, and even the idea of a specific event as the "discovery" of a particular fact depends on review articles to organize the claims and techniques in a particular direction (Myers 1990a; Sinding 1996). It is not just the interpretation of events that is constructed by reviews but epistemological statements themselves, such as new claims about, say, causation (Hedgecoe 2001). In the case of pharmacogenomics, review articles and other commentaries also act to construct the future. As well as reconstructing the past (usually by presenting pharmacogenetics as an old-fashioned approach that provides only sporadic results), these commentaries construct a future vision of pharmacogenomics involving specific technologies (SNP databases, gene chips), certain changes to clinical practice (revealing the genetic bases of diseases, changing clinical specialties), and restructuring the pharmaceutical industry and its practice (changing clinical trials, reducing research costs).

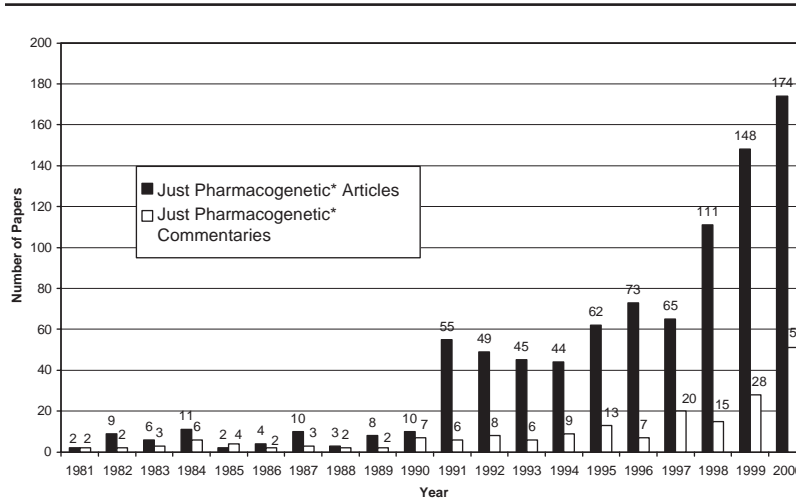


Figure 3. Comparison of pharmacogenetics publications by type.

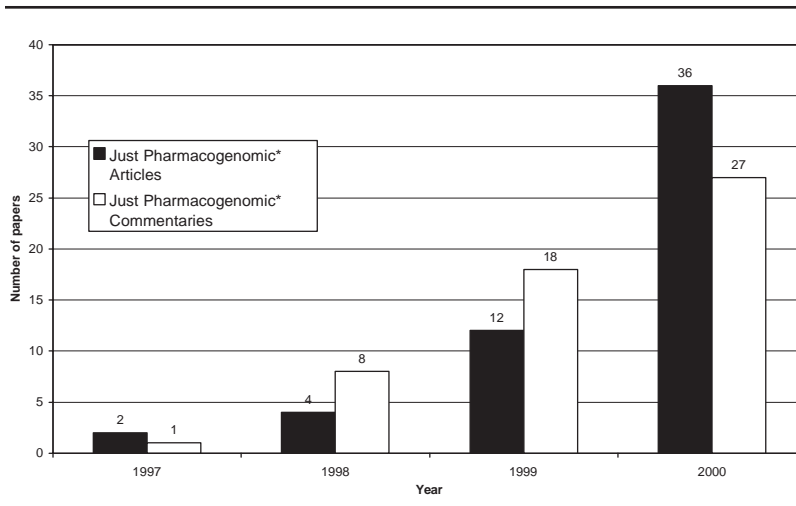


Figure 4. Comparison of pharmacogenetics publications by type.

Clearly, the vision being constructed by the review articles and other commentaries has much in common with some views of modern pharmacogenetics (e.g., Roses 2000a, 2000b), but the construction of pharmacogen-

omics is assisted by both the actual term *pharmacogenomics* itself and the overrepresentation of commentary publications that contribute to the construction of a new discipline and define it as separate from pharmacogenetics.

Consensus?

Developments in this area are fast moving; my tentative conclusions may already have been left behind by recent developments in terminology. The European Agency for the Evaluation of Medicinal Products (2001) is circulating a position paper on terminology in pharmacogenetics in which definitions are proposed of a variety of terms used in research, which, following consultation, “would be consolidated, translated in all EU [European Union] official languages . . . [constituting] . . . a useful technical asset for regulatory authorities, ethics committees, health professional and subjects when confronted with genetic testing protocols in medicinal product clinical trials” (p. 2). This paper defines pharmacogenetics as “the study of variability in drug response due to genetic factors in individuals or populations,” whereas pharmacogenomics is “the determination of the genome (DNA) or its products (RNAs, proteins) . . . [and the application of] . . . this information to drug design, discovery, and clinical development, reflecting the state or response at cellular, tissue, individual or population levels” (p. 3). A similar definition was proposed in the recent pharmacogenetics special issue of the *International Journal of Pharmaceutical Medicine* (Dayan 2001).

This institutionalization of terminology is of course an interesting site for sociological investigation. Elsewhere in medicine, formal terminologies have struggled to impose their wills on everyday usage (see Hedgecoe 2002 for an example from diabetes terminology), and it will be interesting to see whether a broader consensus is forming around these or other formal definitions, as at least some authors have claimed (Lindpaintner et al. 2001).

Conclusion: Pharmacogenomics as a Vision Thing

To construct a research trend, attract funding, and gain support for a particular area of research, authors have to bring to life a future that incorporates the technology concerned. This prophecy, which is hopefully self-fulfilling, is the first step in the production of new technologies and other developments (such as regulatory changes and social attitudes). This particular vision of pharmacogenomics is constructed using a number of rhetorical devices. The central claim of this article is that the term *pharmacogenomics* itself plays an

important rhetorical role; it links to certain technologies and commercial concerns in a way that *pharmacogenetics* does not.

On the basis of the material presented in this article, my conclusions about the rhetorical role of the term *pharmacogenomics* must remain tentative, but there are obvious research directions building on this article. One way to counter the drawbacks of the *SCI* database is to interview participants (industrial and academic) about their uses of the terms *pharmacogenetics* and *pharmacogenomics*. This might also be the way to track down the initial appearance of the term *pharmacogenomics* in discussions in 1996 or 1997. How the possible institutionalization of these definitions affects usage also needs to be examined; will *pharmacogenomics* become “black-boxed,” or will it remain a term open to negotiation, with a meaning flexible according to context?

There are obvious weaknesses of this article. Although the literature lacks widespread criticism of this use of the *SCI* database (as opposed to citation studies), this does not mean that such analysis is unproblematic. I have tried to preempt possible objections but accept that I may have overstated the link between research and publications. The link between the use of the term *pharmacogenomics* and commercial interest can also be overstated. Although many of those writing about pharmacogenomics come from within the pharmaceutical and biotechnology industries, and many articles written from an industry perspective tend to avoid the term *pharmacogenetics* (e.g., Persidis 1998a, 1998b), there are a number of authors from commercial backgrounds who use that term exclusively (e.g., Chamberlain and Joubert 2001; Spear, Heath-Chiozzi, and Huff 2001). There may be institutional reasons for this (see note 14) or some other explanation. Clearly, it would be wrong to claim that the use of *pharmacogenomics* is related solely to commercial interest.

What this article does provide is a possible explanation for the pattern of terminology present in the ISI's databases and a starting point for the empirical investigation of these new genomic technologies and their effect on medicine, industry, and society.

Notes

1. To some extent, this fits in with Fujimura's (1996) concept of a research “bandwagon” that is constructed on more than just internal grounds.

2. For other accounts of such visions and prophecies, see Callon (1986) and Brown, Rappert, and Webster (2000).

3. There was no double counting (i.e., each article was counted only once), and all figures were adjusted by hand to ensure that articles published late in one year were not counted in the following one. The last year searched for was 2000, because articles come into the database on a

piecemeal basis, which means that 2001 articles would “arrive” in the database (classed as 2002 articles) throughout 2002. Therefore, 2000 was the last “complete” year available for searching. Any search for 2001 articles would be unreliable.

4. For example, an article by Kuivenhoven et al. (1998), which suggests a pharmacogenetic link between certain genes and prestatin (a drug for heart disease), is often mentioned by commentators discussing the future of pharmacogenetics and pharmacogenomics (e.g., Kleyn and Vessel 1998; Anderson, Fitzgerald, and Manasco 1999; Evans and Relling 1999; Moyses 1999; Lau and Sakul 2000). But this article does not mention pharmacogenetics or pharmacogenomics. It therefore did not appear in the database search.

5. But see Rabinow (1996) for an example of commercial researchers who used academic publication rather than trade secrecy as a business strategy.

6. The database contains no articles published prior to December 1996 explicitly linking pharmacogenetics and the HGP (using the search terms *pharmacogenetic** AND [*human* AND *genome* AND *project*]).

7. For example, Philipson and Tooze (1987), Palca (1987), Delsi (1988), Dulbecco (1988), Martin (1989), Anderson (1989), and Alwen (1990).

8. An alternative to this explanation is that the journal *Pharmacogenetics* began publishing in 1991, thus providing a whole new specialized outlet for articles focusing on this area. Unfortunately for this argument, the ISI did not add *Pharmacogenetics* to its list of cited journals until 1993 (when fourteen papers were published). If all articles published in the journal *Pharmacogenetics* are removed, the general shape of Figure 1 does not change a great deal; the differences across the watershed from 1997 to 1998 are smoothed out, but the shape of the beginning of the section from 1991 to 1997 remains the same.

9. Brower’s article, published in June, mentions a number of commercial alliances that Marshall in the same journal three months later described as being involved in pharmacogenomics. Brower mentioned only pharmacogenetics. Jordan’s article discusses the use of the term *pharmacogenomics* in May 1997, but only at a conference; because his article was not published until October, it seems as if the term *pharmacogenomics* came to prominence in September 1997, following the late July deal between Genset and Abbott.

10. It was in the title of their press release of 28 July 1997 and cited as the main reason behind their alliance.

11. The committee appears to have agreed to disagree over the definition of *pharmacogenomics*. Information on this committee can be found at <http://www3.diahome.org>.

12. This involves focusing on a gene already suspected of involvement in drug metabolism.

13. Roses works for GlaxoSmithKline (then GlaxoWellcome), and it is this company’s policy to use the term *pharmacogenetics* rather than *pharmacogenomics* because of the confusion surrounding this latter term. This strengthens my claim that genomic technologies can be used within a genetic framework.

14. The title of these authors’ chapter is “Pharmacogenomics,” yet in the text they refer only to pharmacogenetics. In addition, the chapter heading at the top of each alternate page is “Pharmacogenetics.”

15. “The web site of biotechnology corporate intelligence products and services . . . Biovista publishes printed and electronic information resources in the field of biotechnology . . . All Biovista products are compiled by an independent and experienced group of industry participants offering significant benefits to users.”

16. “GenomeWeb.com offers breaking news coverage, original reporting, in-depth interviews, and commentary from celebrated researchers and industry leaders. Readers of GenomeWeb include research enterprises in the pharmaceutical, agriscience, biotechnology,

academic, and government sectors, as well as suppliers of information, software, IT services, and analytical instrumentation.”

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