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The Role of Incumbent Firms and Universities as Drivers of Innovation: Evidence from the Comparison of the Markets for Anti-cancer and AIDS-treatment Drugs

By

M. Lourdes Sosa
London Business School
London NW1 4SA, UK
lsosa@london.edu

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The Role of Incumbent Firms and Universities as Drivers of Innovation:
Evidence from the Comparison of the Markets for Anti-Cancer and AIDS-Treatment Drugs

M. Lourdes Sosa
Strategic and International Management, London Business School, London NW1 4SA, UK, lsosa@london.edu

In this paper, I compare the dynamics of two different markets within the pharmaceutical industry: anti-cancer and AIDS-treatment drugs. The anti-cancer drug market was born in 1949 and had been in operation for decades prior to 1983, when the biotechnology revolution first disrupted it. In contrast, the market for AIDS-treatment drugs was born around 1985, *during* the biotechnology revolution. This implies that incumbents with respect to the biotechnology revolution can only be found in the former market. Based on field interviews, data on patented molecules from the *Derwent World Patent Index* collection 1994-2004, and data on drugs entering clinical trials from the *Pharmaprojects* database 1989-2004, I examine the differences in innovative output (measured in drug molecules per firm) among firms competing in each market. Preliminary results indicate that average productivity is higher in the anti-cancer drug market than in the market for AIDS-treatment drugs, but only for the early stages of R&D. At the point of approval, the markets exhibit equal rates. The reverse is true for differences across technological regimes: the differences are not significant in early stages but are significant later on. Lastly, differences in per-firm productivity are always significant across firm profiles (with incumbents always sustaining the highest rate) whereas total proportion of production of innovations is always led by the group of de novo firms. Universities do not lead in total proportion of innovations generated, nor do they play a significant role as co-assignees of other organizations in the generation of patented molecules. Although this paper offers only tentative initial analyses, with further work necessary to implement feedback from participants of the Sloan Industry Studies meeting, it has clear potential to contribute to understanding the role that large incumbents and universities play in shaping the dynamics of innovation.

Key words: university-industry collaboration; technological change; biotechnology; pharmaceuticals

1. Introduction

At least as far back as Schumpeter (1934, 1950), scholars have been interested in the transition of markets through technological discontinuities. Attention has been focused on the fate of incumbent firms, as different factors determine whether their innovation ability decreases when faced with a new technological regime, and whether in spite of that loss of innovation ability, these firms retain significant market share as the disruption subsides (see Chesbrough, 2001, for a review). In contrast, recent research has centered on the dynamics surrounding the birth of markets, settings that therefore have no incumbents. Such research has been particularly fruitful in furthering our understanding of the differences in innovative ability between entrants to a market that have a pre-history (i.e., diversifying entrants also referred to as *de alio* firms) and those that do not (i.e., de novo firms). Studies in this recent tradition have spanned medical devices (Mitchell, 1994), automobiles (Carroll et al., 1996), and television sets (Klepper and Simons, 2000).

In light of the studies in both traditions mentioned above, contrasting inferences have been made about the impact of established firms, either incumbents or diversifying firms (i.e., entrants with a pre-history), on total market-level innovative output. On the one hand, in creative destruction incumbents have been found to lose productivity in the research and development (R&D) of products under the new technological regime (Henderson, 1993), even if they do not ultimately lose the market (Tripsas, 1997). Therefore, the suspicion is that these firms do not easily cope with technological discontinuities, and in the presence of barriers to entry and exit, they slow down the innovative progress of the market as it transitions through the discontinuity. On the other hand, in studies where the technological discontinuity marks the birth of the market, diversifying firms have been found to outperform de novo firms (i.e., newly born firms) in several dimensions, including survival (e.g., Mitchell, 1994; Carroll et al., 1996) and new product introductions (e.g., Methe, Swaminathan, and Mitchell, 1996). Therefore, it seems natural to infer that these firms indeed stimulate the innovative progress of the market.

Nonetheless, it remains an open question whether the contrasting roles that established firms can have in the innovative progress of a market are a result of the research design employed and the unavailability of fine-grained datasets. Indeed, recent creative destruction research has found that once entrants are separated into diversifying and de novo firms as well, the difference between the innovative performance of the two firm categories with a pre-history, namely incumbents and diversifying entrants, is not significant, and that the main gap exists between established and de novo firms (Sosa, 2005, 2006). Therefore, the explanatory variable for the different findings of incumbents and diversifying entrants in transitioning vs. emerging markets could be attributed to differences in market characteristics.

In this study, I set out to compare two markets that constitute an ideal matched pair due precisely to their differences and similarities. On the one hand, these markets differ in the point in their life cycles at which the technological discontinuity is impacting them (a transition after decades of a previous technological regime for one and the birth of the other). This characteristic allows me to contrast a market with incumbent firms in transition (the former case) versus a market without incumbents (the latter case). On the other hand, these markets are similar in a number of key dimensions: both include diversifying and de novo entrants; both are among the most science-intensive markets within the pharmaceutical industry; both are facing the same technological discontinuity, that is, the biotechnology revolution; both have low price sensitivity and are far from satiation in the areas of efficacy and safety that consumers value; and both have involved a significant amount of university research in the history of their progress.

Beyond the matched pair that these particular empirical settings represent, I incorporate in this study a uniquely fine-grained level of measurement of innovation. In order to further understand the innovative output of these firm categories under contrasting market structures, I measure innovative output at three different points of the R&D process of a firm in this industry: the generation of patented drug molecules; the entry of some of those molecules into clinical trials; and the approval of some of those molecules after successful completion of clinical trials.

In preliminary results, I find that the average innovative output per firm is higher in the anti-cancer drug market than in the market for AIDS-treatment drugs only for early-stage research. At the point of approval, both markets sustain the same average rate per firm. Furthermore, when I distinguish within the anti-cancer drug market (the only one in transition) between the old (cytotoxic) technology for drug discovery and the new (targeted), I find no differences in the average rate of production across the technologies in the early stages of R&D (prior to clinical trials), but significant differences in the later stages (entering clinical trials). This is true for all firm profiles. Nonetheless, the difference in rate of production of innovations is significant across firm profiles at all stages, with incumbents leading with the highest per-firm average. Lastly, I look at the co-assignment of patents for drug molecules and find that public organizations (universities and governmental laboratories) do not, in absolute numbers, account for the largest proportion of activity. De novo firms as a group account for the largest proportion of innovations in the earliest stage, even if per firm their rate of production is the lowest. Beyond their role as producers of early-stage innovations, universities do not seem to play a formal role as co-assignees with other firms, with their proportion of formal collaboration with incumbents and diversifying firms being negligible in both markets. It must be the case then that universities are either fully transferring all property rights to these established firms when they collaborate, or contributing to their R&D efforts through a less formal mechanism.

Although the research exercise presented is a work in progress and as such has significant limitations, if corroborated by further work, it should represent significant implications for our understanding of the role that incumbents and universities play in shaping the dynamics of innovation.

2. Empirical Setting

In order to analyze the contribution that incumbent firms make to market dynamics, I present in this paper a comparison of two contrasting market structures. The first is the market for anti-cancer drugs, a market that was in place long before the biotechnology revolution first disrupted it in 1983 and that therefore has had a set of market incumbents transitioning into biotechnology. In contrast, the second market is the

market for AIDS-treatment drugs, a market that was born during the biotechnology revolution and that therefore has no market incumbents. These two markets offer a reasonable match for a paired design because they coincide in several of their primary characteristics, two of which are of particular interest in this paper. These two markets are science-intensive, which means that the research of the application itself (i.e., the therapeutic category) is as complex and value-adding as any of the technological platforms used in drug discovery and development (see also Weinberg, 1996, for the case of the anti-cancer drug market, and Kanki and Essex, 2005, for the case of the AIDS-treatment drug market). Since prior research (Sosa, 2008) has identified the complexity of the application-specific knowledge as a key driver in the dynamics of innovation in the transition of drug development into the biotechnology revolution, avoiding variance in this characteristic was of utmost importance. Furthermore, both markets have low price sensitivity, and are far from satiation on the part of consumers in terms of efficacy and safety, the two main aspects of merit in most pharmaceuticals.[1]

I offer next further detail on these markets, their timelines and their measures.

4.1. The Anti-Cancer Drug Market

Although this market has long been in existence, the technological regime preceding the biotechnology revolution, namely cytotoxic drug development (commonly referred to as "chemotherapy"), started in 1949 (Chabner and Roberts, 2005). I took the approval of the first anti-cancer drug influenced by biotechnology, *Intron-A®*, introduced in 1983, as the start of the biotechnology discontinuity. In 1983, the anti-cancer drug market began its transition from cytotoxic agents (e.g., alkylating agents, etc.) to the radically new category termed targeted drugs (e.g., tyrosine kinase inhibitors, etc.). In order to analyze the dynamics of innovation in this market, it is important to characterize the transition in terms of the comparison of the technological regimes used in cytotoxic vs. targeted drug R&D. The first question is whether the difference between the technological paradigms is incremental or radical (Henderson and

[1] For an example of an exception to this feature within pharmaceuticals, see Christensen (1996).

Clark, 1990).[2] A second though related question is whether the difference is competence-destroying to the resources and capabilities that market incumbents have mastered in the R&D operations within their standing value chains (Tushman and Anderson, 1986).[3] Studies have shown that the transition from cytotoxic to targeted R&D in anti-cancer drugs has been a radical and competence-destroying change to this market (Rang, 2006: 49),[4] albeit only to the preclinical (i.e., drug discovery) phase of R&D. A description of a representative value chain in this market is shown in Figure 1, where drug discovery can be identified. The description of this technological change as radical and competence-destroying is consistent with the responses of interviewees in this study and with the description offered in prior literature about biotechnology's impact on the pharmaceutical industry (e.g., Henderson, Orsenigo, and Pisano, 1999; Rothaermel, 2001).

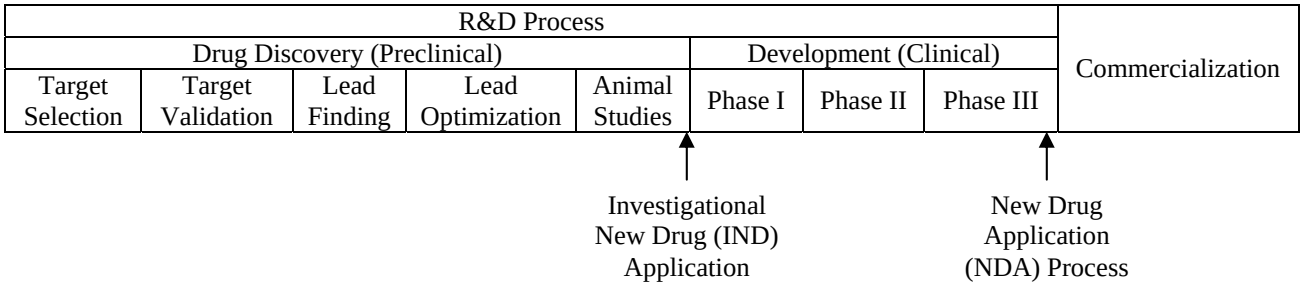

Figure 1: Representative Value Chain in the Pharmaceutical Industry.
Adapted from Rang (2006: 44).

As mentioned above, it was important to select a pair of markets where consumers were far from satiation in the main dimensions of product merit. In the case of the anti-cancer drug market, that implied that the change, although a radical shift in technologies and competence-destroying to incumbents' value

[2] In the case of assembled products, a further characterization would be needed to identify whether only the components are changing (modular change) or only the architecture is changing (architectural change).

[3] I refer to the contrast between incremental vs. radical and competence-destroying vs. competence-enhancing as related because some of their categories could be superimposed: incremental changes are competence-enhancing, whereas it could be argued that modular, architectural, and radical are all competence-destroying to varying degrees.

[4] Accounts of the development of targeted anti-cancer drugs also illustrate this point (e.g., Capdeville et al., 2002).

chain, should be "sustaining" in customer preferences (Christensen, 1997). According to data by the American Cancer Society (2000), at the start of the discontinuity (and indeed for the full period of observation in this study) the market was far from satiation in levels of efficacy and safety, the main dimensions of merit considered in an anti-cancer drug. Indeed, the 5-year survival rate had changed from 50% in the years 1974-1976, to 51% in the years 1980-1982, to 59% in the years 1989-1995, a trend that proves the market in general was far from satiation (even though the difference in rates between 1974-1976 and 1989-1995 is statistically significant at $p<0.05$). Customer preferences were clearly the maximization of efficacy and safety, with ample room for improvement in those dimensions by any firm in competition.

Market-Specific Explanatory Variables in the Anti-Cancer Drug Market

Anti-Cancer Drug Market Incumbents These firms must have been present in the market for cytotoxic anti-cancer drugs before the era of biotechnology, and they must have been venturing into targeted anti-cancer drugs in the years under examination.[5] Since the era of chemotherapy (i.e., cytotoxic anti-cancer drugs) in cancer treatment started in the 1940s (Chabner and Roberts, 2005), most records are incomplete.[6] I therefore triangulated three different sources to identify incumbent firms: the records available from the Federal Drug Administration (FDA) on all approved drugs;[7] the records available on anti-cancer

[5] This implied that I would select incumbents contingent on investment in the radically new technology (i.e., a subset of all incumbents). In the end, this restriction made no difference because all incumbents still in the market by 1983 had invested in the new technology. Furthermore, all incumbents invested in the new technology from the start of the revolution.

[6] For example, FDA records for drug approval are incomplete before 1982, mainly because this was prior to the approval of the Drug Price Competition and Patent Term Restoration Act of 1984 [the Hatch-Waxman Act], which gave rise to today's generics drug industry.

[7] From Drugs@FDA, available electronically at http://www.accessdata.fda.gov/scripts/cder/drugsatfda/.

drugs in particular from the FDA's Center for Drug Evaluation and Research (FDA-CDER);[8] and the printed collection of the *Physicians' Desk Reference* (PDR) drug directories for the years 1947-2005. I took the approval of the first anti-cancer drug influenced by biotechnology, *Intron-A*® (a recombinant-DNA molecule), introduced in 1983, as the start of the era of targeted anti-cancer drugs. An incumbent therefore would be a firm that was present in the market before 1983 and that after 1983 had at least one targeted anti-cancer drug either in clinical trials or already launched. Firms that were in the market but left for a significant period of time and were returning because of the biotechnology revolution were not considered incumbents but diversifying entrants.[9] I therefore further corroborated the presence of the firms around 1983 by requiring that at least one of the cytotoxic anti-cancer drugs for the firm in question still generated revenue after 1983. I estimated this through one of two different proxies: at least one of the cytotoxic anti-cancer drugs for the firm in question must have had revenues listed in the Med Ad News' yearly report of *Top Prescription Drugs* in the period 1991-2002, or must have had a generic introduction after the generics industry took off in 1984.[10]

Anti-Cancer Drug Market Diversifying vs. De Novo Entrants The identification of these two categories was done through access to their corporate histories, culled mainly from their company websites. Firms that had a pre-history prior to their incursion into the anti-cancer drug market were classified as diversifying entrants, regardless of whether they continued their presence in markets other than anti-cancer drugs during their incursion into this market. I defined a "pre-history" strictly as a prior stream of revenue. Therefore, entrants that experimented with different therapeutic categories were still classified as de novo

[8] From FDA-CDER Oncology Tools, available electronically at http://www.fda.gov/cder/cancer/druglistframe.htm.

[9] For example, Merck made two attempts to enter the anti-cancer drug market with Nitrogen Mustards *Mustargen*® and *Cosmegen*® in the years 1949 and 1966, respectively, but was by 1983 long gone from the market. Neither product had significant sales by 1983. Cosmegen is even reported as unprofitable in Merck's Annual Report in 1951. As Merck was attempting to enter the anti-cancer drug market again, it is classified as a diversifying entrant.

[10] I assume that only anti-cancer drugs with positive revenues will incite generic competition.

entrants. In contrast, entrants that derived a revenue stream from any other business (e.g., medical devices or research services) were classified as diversifying entrants, even if the firm itself was rather young and small.

4.2. The Market for AIDS-Treatment Drugs

As mentioned above, in contrast to the anti-cancer drug market, the market for AIDS-treatment drugs was born during the biotechnology revolution. According to the USA Centers for Disease Control and Prevention (CDC, 2007), HIV (Human Immunodeficiency Virus) was first identified in the United States in 1981. Although the deadly disease was first described as a rare pneumonia, by December 1982 publications would refer to the disease as Acquired Immune Deficiency Syndrome (AIDS). Indeed, according to scientific accounts, although the virus responsible for the disease was a genetic relative of a known virus, it had been recently introduced to humans from a primate reservoir (Essex and Kanki, 1988). This particular characteristic makes the market for AIDS-treatment drugs a perfect contrasting market to the anti-cancer drug market: although demand for cancer treatment had existed long before the transition into biotechnology and in fact demand had existed long before supply started to become available, the market for AIDS-treatment drugs had neither supply nor demand prior to 1982. Interest in researching the application-side of R&D in the AIDS-treatment drug market grew rapidly as did the availability of public funding for this research (Kanki and Essex, 2005), and by 1984, HIV was recognized as the etiologic agent that causes AIDS. As the application-side of the R&D of this market evolved, so did specific applications of technological platforms (e.g., polymerase chain reaction [PCR]). By 1985, for example, the first blood test to identify antibodies to the virus and hence diagnose the disease (namely, the ELISA test) was finally available (CDC, 2006).

Market-Specific Explanatory Variables in the AIDS-Treatment Drug Market

As mentioned above, this market itself had no pre-history, that is, the market had not existed in a prior technological regime. Indeed, the consumer need itself did not exist prior to 1981 since this specific disease is a recent genetic mutation transferred to humans from the animal world. This implies that there are

no incumbent firms in this market, and that there are no contrasting technological regimes in the history of the market. The only market-specific explanatory variable, therefore, is the differentiation of diversifying and de novo entrants, and I describe this next.

AIDS-Treatment Drug Market Diversifying vs. De Novo Entrants The identification of these two categories was also done through access to their corporate histories, again culled mainly from their company websites. Firms that had a pre-history prior to their incursion into the AIDS-treatment drug market were classified as diversifying entrants, regardless of whether they continued their presence in other markets. As with the anti-cancer drug market, I defined a "pre-history" strictly as a prior stream of revenue.

4.3. Nonmarket-Specific Quantitative Measures

For the comparison of the two above-mentioned markets, I had to use a series of variables that are firm-specific but not market-specific (i.e., in the above sections, the same firm could be an incumbent with respect to the anti-cancer drug market, but a diversifying entrant with respect to the AIDS-treatment drug market). I describe these nonmarket-specific variables next.

Dependent Variables

Number of Patented Drug Molecules According to the value chain presented in Figure 1 above, a firm in the pharmaceutical industry, whether in anti-cancer or AIDS-treatment drug development, will generate many new drug molecules during the drug discovery stages, and patent them at different points though always prior to starting the transition toward clinical trials, since this transition implies disclosure. In order to measure this step, I used Thomson Scientific's *Derwent World Patent Index* (*DWPI*) database. The DWPI database consists of innovation records identified through the categorization of patents into predetermined classes (identified by a code) by expert librarians. Patents are collected from the 40 largest jurisdictions, and the classification process includes the matching of patents containing the same idea to the same innovation record. Therefore, the unit of analysis is the innovation, and each record can be matched to one or several granted patents. Because the classes are defined by the librarians themselves, anti-cancer and AIDS-treatment drugs are defined, but other therapeutic classes are not. Furthermore, anti-

cancer and AIDS-treatment drugs are defined starting only in 1994, so this measure can only be made in the window of 1994-2004. In the case of anti-cancer drugs, it was important to also differentiate between the two technological regimes. I therefore differentiated between standard chemotherapy (i.e., cytotoxic anti-cancer drugs) and biotech-based drug development (i.e., targeted anti-cancer drugs) through further use of the DWPI codes. In fieldwork, interviewees had described the different subclasses contained within cytotoxic vs. targeted drugs in anti-cancer research (e.g., interleukins and tyrosine kinase inhibitors among targeted drugs). Therefore, I identified all codes pointing to sub-classes of targeted anti-cancer drugs, to then aggregate to the technological regime.

Number of Drug Molecules Introduced in Clinical Trials Continuing along the value chain presented in Figure 1 above, after the generation of new drug molecules during the drug discovery stages, a sub-set of these drug molecules will enter clinical trials. In order to examine this transition, I collected data on all drugs that entered clinical trials for treatment of cancer and AIDS, as reported in the *Pharmaprojects* database. This database starts in 1989 and records all drugs launched into clinical trials worldwide along with their histories, as represented through press releases. In the case of anti-cancer drugs, I further differentiated between the old and new technology, namely cytotoxic and targeted anti-cancer drugs, through the dummy "targeted." I again did this by measuring first two sub-classes of targeted drugs, in this case targeted *small* molecules and targeted *large* molecules, to then assess the full category of targeted drugs. The identification of targeted large-molecule anti-cancer drugs is reliably documented in the *Pharmaprojects* database. To identify targeted small molecules, I selected all small molecule drugs with mechanisms of action described in industry reports (Bear Sterns, 2002; Stephens Inc., 2002; UBS Warburg, 2001) and in interviews as targeted in anti-cancer drug R&D (in the end, mainly comprising angiogenesis and kinase inhibitors).

Number of Drug Molecules Approved for Market Launch At the end of the R&D process depicted in the value chain shown in Figure 1, a sub-set of drugs in clinical trials is granted approval to launch on the market (even though it remains discretionary to the firm how much later and through which channels to

commercialize the innovation). I measured this through the full collection of Thomson Scientific's *Physicians' Desk Reference* (*PDR*) annual directory of approved drugs, 1947-2004. Although a full record of approved drugs can be requested from the FDA, for example, as mentioned in the definition of anti-cancer drug market incumbents, the information is often incomplete prior to 1984, the year when the Hatch-Waxman Act entered into effect. Hence, the use of the *PDR* collection granted further systematic coverage. In order to differentiate between cytotoxic and targeted anti-cancer drugs, I again used the information in the PDR collection to classify drugs into sub-classes of targeted drugs to then aggregate.

Nonmarket-Specific Explanatory Variables

Public Research Organizations In contrast to the firm categories I specified in each market, the classification of nonprofit organizations was not market-specific. I therefore distinguished only between private and public research with the dummy variable "public research," which spanned all nonprofit organizational arrangements, including universities, government laboratories, and nongovernmental organizations.

5. Preliminary Analyses

5.1. Descriptive Statistics

In preliminary analyses, significant differences can be seen in the trends of innovative output both across the different stages of the R&D pipeline, and in each stage across firm categories and technological regimes.

Figure 2 below shows simply the contrast of approved drugs between the two markets in the history of their evolution. Although there is a marked fluctuation in the anti-cancer drug market around 1971, this is mostly due to a change in the accounting of pain medication as a cancer-only adjuvant in the *PDR* collection that served as the information source.

Table 1 presents the total number of drugs at each of the three stages in the R&D pipeline of both markets.

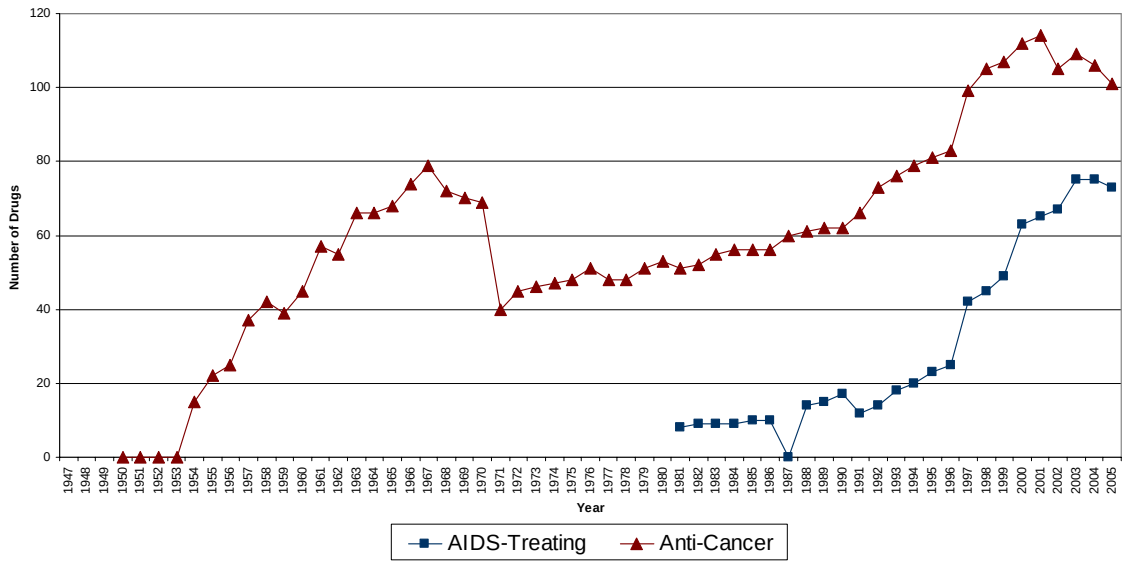

Figure 2: History of Available Drugs per Year for Cancer and AIDS Treatment, according to the *Physician Desk Reference* Collection

Table 1: Total Number of Drugs Generated per R&D Stage across both Markets

	Patented Molecules	**Drugs in Clinical Trials**	**Approved Drugs**	
Anti-Cancer	55,242	6,851	307 (since 1949)	122 (since 1983)
AIDS-Treatment	3,168	1,244	56	

The increase in the number of molecules in earlier stages (i.e., the comparison of the volume of patented molecules versus those entering clinical trials) shown in Table 1 is partly explained by the expanded coverage that the sample of firms based on patented drug molecules generates. Many firms from developing countries (e.g., Mexico, India, Tanzania) appear in this early-stage sample and do not appear in later stages, either because their drugs do not make it into clinical trials (due to regulatory or firm-specific decisions), or because these drugs do not require an official clinical trial (i.e., complementary and alternative medicine).

Figure 3 presents the gap in innovative output between the two markets as it widens over time, as measured at the first stage in this study, namely patented molecules in early-stage R&D.

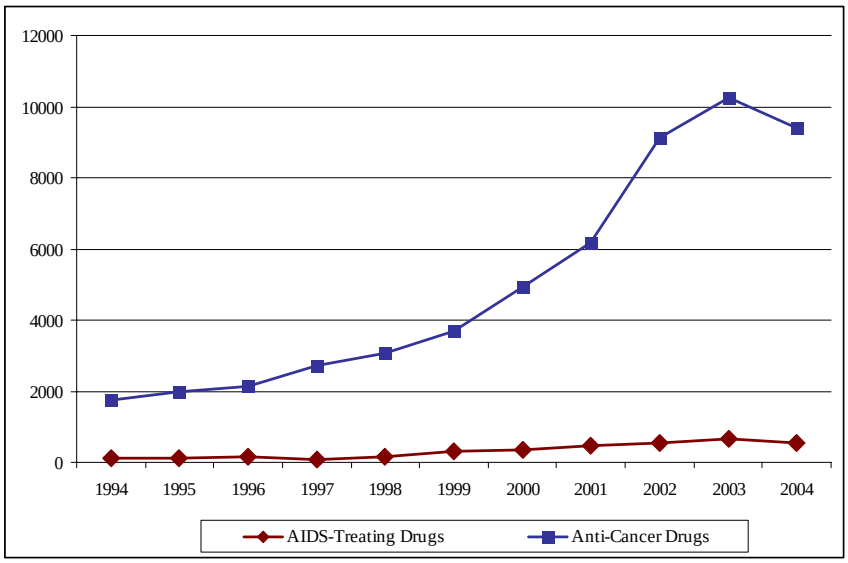

Figure 3: Gap in Innovative Output between the Anti-Cancer and AIDS-Treatment Markets over Time, as Measured in Early-Stage R&D (Generation of Patented Drug Molecules)

Indeed, the gap in innovative output is sustained across the years in the period of observation, not only in terms of absolute volume of drugs but also in terms of per-firm productivity, as seen in Figure 4 below.

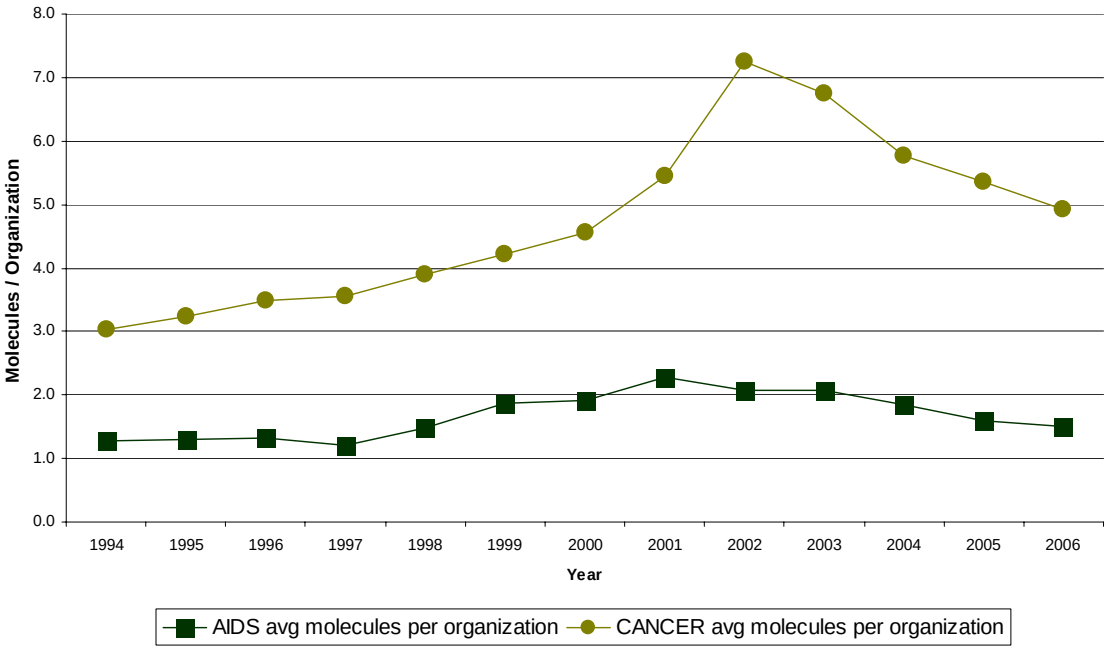

Figure 4: Persistent Gap between the Average Innovative Output of Firms in the Anti-Cancer and AIDS-Treatment Drug Markets, as measured in the Generation of Patented Molecules in Early-Stage R&D

5.2. Initial Analyses

Table 2 below presents the differences in the per-firm rate of production of innovations at each stage of R&D analyzed. As can be seen, the per-firm output for the anti-cancer drug market is higher than that of the AIDS-treatment market only for early-stage research. The difference disappears at the point of approval.

Table 2: Rate of Production of Innovations per Firm per R&D Stage
for the Anti-Cancer and AIDS-Treatment Drug Markets

	Patented Molecules	**Drugs in Clinical Trials**	**Approved Drugs**
Anti-Cancer Drug Market	29.9	5.4	1.5
AIDS-Treatment Drug Market	7.2	3.7	1.5
	between-market diff+	between-market diff**	

+ $p < 0.1$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 3 distinguishes the different firm profiles, emphasizing the fact that the profiles are market-specific. Per-firm average rate of production of innovations is significantly different across firm profiles in both R&D stages measured, as can be seen with two different specifications: a simple OLS, and a Negative Binomial, which accounts for the fact that the dependent variable is a count. In future work, a Cox regression with repeated events per firm will be implemented to account for the possibility of a time-varying rate of production of innovations as done in prior work (Sørensen and Stuart, 2000).

Table 4 then distinguishes within the anti-cancer drug market (the only one in transition) between the old technology (cytotoxic) for drug discovery and the new one (targeted therapies). As can be seen, I find no differences in the per-firm average rate of production across the technologies in the early stages of R&D (prior to clinical trials): the coefficients for "targeted" and for the interactions "anti-cancer incumbent x targeted" and "anti-cancer diversifying x targeted" are all not significantly different from zero. Nonetheless, the differences across technologies are significant in the later stages (entering clinical trials) for all firm profiles.

Table 3: Rate of Production of Innovations per Firm Profile per R&D Stage
(Note: differences in coefficients are all significant; anti-cancer novo firms are the omitted category)

	Patented Molecules		**Drugs in Clinical Trials**	
	OLS	**Neg. Binomial**	**OLS**	**Neg. Binomial**
Constant	21.0* (8.7)	3.0*** (0.4)	3.8*** (0.5)	1.3*** (0.1)
AIDS-Treatment Diversifying	7.9 (10.5)	0.32 (0.5)	4.6** (1.8)	0.8*** (0.2)
AIDS-Treatment Novo	-16.7* (8.74)	-1.59*** (0.5)	-0.5 (0.7)	-0.1 (0.2)
Anti-Cancer Incumbent	638.1*** (109.6)	3.45*** (0.4)	91.8*** (22.5)	3.2*** (0.3)
Anti-Cancer Diversifying	58.5** (18.9)	1.33** (0.5)	8.8*** (1.8)	1.2*** (0.2)

+ p < 0.1, * p < 0.05, ** p < 0.01, *** p < 0.001

Table 4: Rate of Production of Innovations per Firm Profile per Technology per R&D Stage
(Note: differences in coefficients are all significant; anti-cancer cytotoxic novo firms are the omitted category)

	Patented Molecules		**Drugs in Clinical Trials**	
	OLS	**Neg. Binomial**	**OLS**	**Neg. Binomial**
Constant	14.3**	2.6***	3.4***	1.2***
AIDS-Treatment Diversifying	2.4	0.1	5.0**	0.9***
AIDS-Treatment Novo	-10.2*	-1.3***	-0.1	-0.0
Anti-Cancer Incumbent	388.9***	3.3***	84.6***	3.2***
Anti-Cancer Diversifying	28.6**	1.1**	8.2***	1.2***
Targeted	-1.6	-0.1	-0.7	-0.2
Anti-Cancer Incumbent X Targeted	145.7+	-0.4	-79.7***	-2.2***
Anti-Cancer Diversifying X Targeted	3.7	0.1	-6.7***	-0.8**

+ p < 0.1, * p < 0.05, ** p < 0.01, *** p < 0.001

Lastly, Table 5 shows the co-assignment of patents for drug molecules across all firm profiles. Notice that public organizations (universities and governmental laboratories) do not represent the largest proportion of activity in these markets in absolute numbers. De novo firms as a group account for the largest proportion of innovations in the earliest stage, even if per firm their rate of production is the lowest. Furthermore, universities do not seem to play a formal role as co-assignees with other firms, with their proportion of formal collaboration with established firms (both incumbents and diversifying entrants) being

negligible in both markets (a total of 0.4% for the AIDS-treatment drug market, and 0.5% for the anti-cancer drug market).

Table 5: Co-Assignments among Firm Profiles across Markets

	AIDS-Treatment		Anti-Cancer	
	Number of Molecules	**%**	**Number of Molecules**	**%**
Novo	1,778	56.1%	23,467	47.9%
Diversifying	875	27.6%	10,462	21.4%
Public	317	10.0%	6,158	12.6%
Incumbent			5,045	10.3%
Novo-Public	79	2.5%	1,525	3.1%
Diversifying-Novo	87	2.7%	1,077	2.2%
Incumbent-Novo			358	0.7%
Diversifying-Public	12	0.4%	154	0.3%
Diversifying-Incumbent			146	0.3%
Incumbent-Public			77	0.2%
Other	20	0.6%	511	1.0%

6. Concluding Remarks

Although the analyses of the project outlined in this paper, presented at the Sloan Industry Studies Conference 2008, is still in progress, initial analyses provide evidence of the advantages that the uniquely paired market design along with fine-grain measurement of R&D output can offer to studies of the drivers of innovation. In future work, significant feedback collected from Sloan Industry Studies participants will be incorporated to corroborate the findings and clarify the mechanisms behind them.

There are significant potential implications of this study, after further work corroborates its findings. The first implication is connected to the significant differences across the two markets in rates of production of innovations in early-stage R&D but not at time of approval. Such pattern might identify an additional consequence from the presence of an intensification of the use of science (as opposed to trial-and-error experimentation) in recent decades. Prior research (Arora and Gambardella, 1994) has argued that the main consequence of the "scientification" of R&D is a disruption to the standing division of labor in

industrial R&D and thus to the availability of R&D outsourcing. Nonetheless, such "scientification" might also have consequences for R&D productivity that are not linked to outsourcing strategies.

Furthermore, the reverse result when comparing the rates of production of innovations between the two technological regimes across firm profiles, with negligible differences in the productivity rates of different firm groups in early-stage R&D but significant differences later on can also have important implications. This result might shed some light on the differences in the strategies pursued by established firms, for whom the new technology represents a transition, as compared to the strategies of their de novo counterparts, for whom the new technology represents the first stage of their corporate history.

Lastly, documenting the extent and nature of the R&D collaborations of universities with for-profit firms has the potential to extend prior research (Murray, 2002; Edwards, Murray, and Yu, 2003) that has analyzed the similar or different roles that these institutions play in the dynamics of industry and of science.

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