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Decoupling Market Incumbency from Organizational Experience: Locating the Real Sources of Competence in the Research and Development of Radical Innovation

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Decoupling Market Incumbency from Organizational Experience:
Locating the Real Sources of Competence in the Research and Development of Radical Innovation

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ABSTRACT

This paper examines the proposition that, during a radical technological change, incumbents' "incompetence" in researching the new technology results from their organizational inertia. I argue that prior studies have inappropriately assigned the disadvantage of organizational inertia and (implicitly) the advantage of competence re-use (both consequences of previous organizational experience) only to incumbents or to diversifying entrants respectively (both categories of experienced firms), because they failed to decouple market incumbency from organizational experience. I explore this proposition in the context of the anti-cancer drug market as it is disrupted by the biotechnology revolution through a combination of direct observation (based on semi-structured interviews and industry presentations) followed by statistical analysis (based on several sources to understand the market in the period 1949-2004). I find that when destroyed and re-usable competences are considered, the significant firm categories to compare are no longer incumbents vs. entrants, but experienced (i.e., incumbents and diversifying entrants) vs. de novo firms. Moreover, within the area of R&D with the most competence destruction, I find that, counterintuitively, incumbents outperform all other firms, supporting my final proposition to integrate the corporate diversification framework into creative destruction studies.

Beginning with Schumpeter (1934, 1950) and motivated by the impact that technological change has on economic growth (Solow, 1957),[1] a long research tradition has studied the disruptions generated in the economy by radical technological change. Although the technological disruption takes place at the industry level (e.g., the automotive industry) and therefore affects the entire supply chain to different extents (e.g., automobile as well as tire producers), the firm-level analysis of strategic action is always centered on a relevant market[2] (either the market for automobiles [Abernathy, 1978] or the market for tires [Sull, Tedlow and Rosenbloom, 1997]). Characteristically, a market disrupted by radical technological change undergoes a period of transition during which both old and new technologies coexist in the market. These periods can last up to twenty years or even longer depending on the market (Cooper and Schendel, 1976). Once the transition ends, the market stabilizes and enters a "regime" in which only the new technology is available (Abernathy and Utterback, 1978).

It is after this transition has taken place that, retrospectively, an empirical regularity is observed: firms that were present in the market prior to the disruption (*incumbent* firms) frequently lose their market leadership to firms that enter the market during the transition to the new technology (*entrant* firms). This empirical regularity of firm substitution in a market is a source of considerable socioeconomic advantages, such as the destruction of monopoly power, and disadvantages, such as the inefficient re-absorption of incumbents' employees into the labor market or into the rest of the

[1] See Griliches (1996) for a historical review of the debate on the measurement of the impact of technological change on economic growth.
[2] The basic definition of a market in economic theory is a set of products that are substitutes for one another.

corporation.[3] Despite the importance of such implications, scholars have reached little consensus on the determinants of incumbents' lower market performance during these technological discontinuities (e.g., Tushman and Anderson, 1986; Henderson and Clark, 1990; Christensen and Bower, 1996; Tripsas and Gavetti, 2000).

However, scholars of creative destruction agree that, within research-intensive industries, the demise of market incumbents is significantly determined by their lower productivity in researching the radically new technology (Henderson, 1993). Such differences in the research productivity, or research *competence,* of incumbent vs. entrant firms are explained through theories about established vs. new firms (e.g., Nelson and Winter, 1982). Prior experience is then argued to be the source of incumbents' "incompetence" in researching the new technology. A disconnect arises because, more often than not, the most innovative and successful entrants are established (experienced) firms themselves (*diversifying* entrants).

In fact, when the same phenomenon is viewed within the framework of the corporate diversification literature (e.g., Roberts and Berry, 1985), market incumbents and diversifying entrants are simply comparable experienced firms deciding whether and how to diversify across technologies and/or markets. Moreover, strategy studies in which diversifying and de novo entrants are compared do not include incumbent firms by design, but find in diversifying entrants the same mechanisms that the creative destruction literature argues take place in incumbent firms (e.g., Mitchell and Singh, 1993; Carroll et al., 1996).

[3] The empirical regularity is that firms fail in a specific market. This does not imply the firm itself dies unless this was the only market in which the firm was present.

Taken together, the differing approaches of the creative destruction, the corporate diversification, and the strategy literatures evoke an important question: Would decoupling market incumbency from organizational experience in studies of creative destruction alter our conclusions about the differences in research competence across firm categories?

With this question in mind, I present in this paper a study that decouples market incumbency from organizational experience by distinguishing not only between incumbents and entrants, but also between experienced and inexperienced entrants (i.e., diversifying and de novo firms) to examine differences in research competence in a technological discontinuity.

Differentiating incumbents, diversifying and de novo entrants in order to decouple market incumbency from organizational experience as mentioned above introduces a further factor to consider for research design. Strategy studies comparing diversifying and de novo entrants intentionally exclude incumbents but show that the experience of diversifying entrants gives them the advantage of accrued competence re-use (e.g., Carroll et al., 1996). If incumbents are also experienced firms, they might also be advantaged by the re-use of some of their competences. Under a classic binary characterization of technological disruption as competence-destroying or competence-enhancing to the entire R&D process (Tushman and Anderson, 1986), only diversifying entrants or incumbents, respectively, have access to competence re-use. The actual mix of competence destruction and re-use that both experienced firms enjoy in every disruption is masked. I therefore unpack the R&D process into finer categories that vary in the level of competence destruction (and therefore "enhancement") in the spirit of the

most recent research in the characterization of technological disruptions (Gatignon, Tushman, Smith and Anderson, 2002). By further breaking down the R&D process into sub-categories, I allow incumbents to also be at risk of competence re-use, precisely in the sub-categories of R&D with lower levels of competence destruction.

In order to gain depth into the research and development (R&D) process, I sacrifice breadth over other steps that lead to innovation (e.g., the investment decision-making process). I therefore select firms *contingent on investment* in the radically new technology and take R&D competence as the main *dependent* variable (see Figure 1 for the place of this study in the larger literature on creative destruction).

Insert Figure 1 about here

I minimize the consequences of the loss of breadth by my choice of setting: the anti-cancer drug market, the market with the most research activity within the most R&D-intensive industry, as it undergoes the disruption of the biotechnology revolution. I develop this study through a combination of direct observation followed by statistical analysis. Specifically, I combine 40 semi-structured interviews (from which 4 interviewees became recurrent informants) and numerous industry presentations as sources for qualitative data, with several sources in the period 1949-2004 as sources of quantitative data, to present the case of this market under disruption.

THEORETICAL BACKGROUND

The Literature on Creative Destruction

Amidst the debate within the creative destruction literature on the determinants of incumbents' market failure (see Figure 1), scholars do agree that within research-intensive industries, one of the most significant determinants is these firms' lower productivity in researching the radically new technology (Henderson, 1993). Such differences in the research competence of incumbent vs. entrant firms are explained in the literature through theories about established vs. new firms (e.g., Nelson and Winter, 1982; Galbraith, 1973).[4] A disconnect arises because, more often than not, the most innovative and successful entrants are established (experienced) firms themselves (diversifying entrants).

For example, in one of the earliest classics in creative destruction, Abernathy (1978) introduced to the literature the concept of a "productivity dilemma" faced by market incumbents. He explains how, over the life cycle of a market, incumbents are faced with a dilemma: as a dominant design settles in the market, incumbents necessarily invest in productivity increases, yet the same process that gives rise to productivity in the short-run marks the end of these firms' ability to innovate in the long-run. The author exemplifies the dynamics of this dilemma in a detailed study of the history of the Ford Motor Company and its presence in the US market for automobiles until 1978.

[4] The dynamics of organizational experience are rather complex and have therefore been explained through many classics from Organizational Theory. Specifically, the dynamics in Galbraith (1973) explain how as organizations accrue experience they *also* grow in number of employees and engage in a dilemma of differentiation vs. integration (Lawrence and Lorsch, 1967). It is in the attempt to resolve such dilemma that organizations engage in departmentalization and general organizational design concerns (Galbraith, 1973).

In another classic study in creative destruction, Tushman and Anderson (1986) introduced to the literature the idea that technological discontinuities can be understood as either competence-enhancing or competence-destroying for market incumbents, offering evidence for this typology based on 32 technological disruptions. Furthermore, based on data on the minicomputer, Portland cement and scheduled passenger airline transport markets from their births through 1980, the authors show that, retrospectively, products that represent drastic changes in performance in these settings are competence-destroying to incumbents and only reach the market through entrant firms. Incumbent firms are mainly able to launch innovations that are competence-enhancing for them.

Lastly, in a later landmark study in the creative destruction literature, Henderson and Clark (1990) offered in-depth qualitative evidence of four waves of architectural innovation in the market for photolithographic alignment equipment. As the authors explain, in each wave of disruption incumbents consistently underperformed entrants in the research and development of the new technology. A representative example of the dynamics of incumbents' underperformance is Kasper Instruments' failure in the face of Canon's entry into this market. When Canon, the entrant firm, introduced its innovative proximity aligner in 1973, Kasper Instruments, the incumbent, asked its own engineers to evaluate the competitor's piece of equipment. The team of engineers "overlooked" the new features in Canon's proximity aligner because they were "blinded" to them by the inertia of their former organizational experience.

During the years prior to the disruption, the incumbent firm built a set of communication channels and information filters to become efficient in the research and development of its old contact aligners (March and Simon, 1958; Galbraith, 1973; Arrow,

1974). This efficiency then marked the firm's market demise when a significant change in the organizational structure became necessary in order to innovate. In the face of radical technological change, incumbents' attempts to use available resources for a new endeavor become a larger disadvantage than starting from scratch. The organizational inertia that obstructs incumbents' ability to innovate is representative of these firms' disadvantage in the face of technological innovation that is "radical in the organizational sense" (Henderson, 1993, p. 249).[5]

The creative destruction literature has clearly paid in-depth attention to incumbent firms, but this focus has taken little into account regarding the characteristics of entrants. The progress of the literature has left entrants as a homogeneous category to be studied in aggregation. This assumption leads logically to an additional implication: if organizational inertia is present among incumbents only and explains their underperformance, then entrants must be a homogeneous category of de novo firms (see Figures 2a and 2b). This, however, contradicts empirical evidence.[6]

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[5] As Henderson and Clark (1990) explain, innovations in the photolithographic alignment equipment market were architectural in terms of the product. Architectural innovations require less competence acquisition and represent a greater challenge in terms of organizational inertia for a firm than do radical and modular innovations. Henderson's (1993) later analysis applies to the general phenomenon of innovations that have an impact that is "radical in the organizational sense" on incumbent firms (i.e., where these firms' organizational inertia inhibits their ability to innovate). The analysis therefore applies to all "non-incremental" (i.e., radical, architectural and modular) innovations. Because among non-incremental innovations, architectural innovations represent the most extreme form of innovation that is radical in the organizational sense, it is architectural innovations that are used in the classic quantitative analysis in Henderson (1993).

[6] Although underexplored, within the creative destruction literature there is evidence of both the presence and innovative capacity of these experienced firms among entrants. Tripsas (1996) reports four waves of technological disruption in the market for typesetters. According to her data, in each and every wave more than 50% of entrants (successful or not) were diversifying entrants. The same can be found, for example, in Tushman and Anderson (1986), Cooper and Schendel (1976), Peck (1961) and Enos (1962). Furthermore, my analysis of Tilton's (1971) account of the transistor revolution of 1952-1968 (i.e., the transition from receiving tubes to transistors) offers evidence that diversifying entrants are not only significantly present among entrants, but they are also some of the most active innovators among these firms. Tilton (1971) reports (Table 4-2 in the original) the patenting activity per firm of all firms in this market during the transition. Although the author classifies firms in the classic incumbent and entrant categories, I traced the corporate history of each entrant firm in historical sources such as the *Moody's*

This literature always traces incumbents' lower research competence in the face of radical innovation to broad-range theories about experienced organizations in general. Organizations generally build communication channels and information filters to increase their efficiency (Galbraith, 1973; March and Simon, 1958; Arrow, 1974); they develop routines to better perform the tasks at hand (Nelson and Winter, 1982); and they give rise to internal groups whose power and status become ingrained in the status quo (Burns and Stalker, 1966). When faced with the challenge of gearing toward a "new endeavor," these same routines, communication channels, information filters, and power and status structures give rise to the organizational inertia that inhibits the organization's ability to innovate. However, as some of the entrants to a disrupted market have, like incumbents, accrued organizational experience, they should then, like incumbents, be prone to the disadvantage of organizational inertia.

It could, nonetheless, be argued that, although incumbents and diversifying entrants are both experienced firms, incumbents' inertia is inherently a larger disadvantage due to these firms' current presence in the disrupted market. That is, they are both experienced firms and should be disadvantaged by inertia, but diversifying entrants *choose* to enter the disrupted market and incumbents have *no choice*, or do they?

Experienced Firms and Diversification

The corporate diversification literature (e.g., Berry, 1974; Haveman, 1992) has long been interested in the study of diversifying corporations. In particular, Roberts and

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Industrial Manual collection. I found approximately 89% of all patents generated by entrants in that period come from diversifying entrants. When doing the same analysis with the report of yearly market share (Table 4-5 in the original), I found as well that 2 out of the 3 top sellers in those years were diversifying entrants.

Berry (1985) explain how, for research-intensive industries, the choice a firm makes to incur diversification can be understood as a "map" where the firm is in the origin facing a radical change in technologies in the horizontal axis, a radical change in markets in the vertical axis, and combinations of both in the rest of the map. The firm confronts the decision to diversify across technologies and/or markets, and different strategies seem better fits depending on what the move within this map represents for the firm. In that framework, we can identify market incumbents facing a radical technological change as a straight move on the horizontal axis. Diversifying entrants, on the other hand, can be identified in the *rest* of the map, that is, anywhere except for the horizontal axis (see Figure 3). The extreme challenge for an experienced firm is found not in the horizontal axis (i.e., incumbents) but in the diagonal, when a diversifying entrant is unfamiliar with the new technology and the incumbent's market, but nonetheless decides to venture into both (the diagonal case is also illustrated in Figure 3).[7] In this framework, incumbents, like diversifying entrants, decide whether to engage in a corporate venturing attempt, and they can also choose to exit. Incumbents and diversifying entrants are simply comparable experienced firms deciding whether and how to diversify across technologies and/or markets. In fact, when we compare only those firms undergoing a straight diversification in either axis, the different strategies for the firms to consider are almost identical.[8]

Beyond the corporate diversification literature, the mainstream strategy literature provides evidence that, like incumbents, diversifying entrants exhibit the disadvantage of organizational inertia resulting from their organizational experience. In particular,

[7] Although this option sounds extremely disadvantaged, Roberts and Berry (1985) offer empirical evidence that experienced firms do venture into this option.

[8] The only difference is that licensing becomes an additional viable option for market incumbents moving from an old to a new technology.

Mitchell and Singh (1993) describe how diversifying firms also face their own "productivity dilemma." The authors explain that expansion may "disrupt successful routines in [the diversifying entrants'] existing business [Nelson and Winter, 1982]" (p. 152). It is then that the authors argue the dynamics of expansion (i.e., the dynamics of diversifying entrants) also include some degree of "competence destroying activity" (p. 157). In this study, Mitchell and Singh (1993) examine how *industry* incumbents[9] decide to diversify into new markets whose birth is the result of specific technological innovations[10] in a study that comprises 35 years of history of the diagnostic equipment industry. The authors find that diversifying entrants that successfully expand enjoy an additional premium in their performance in their base business. Those with failed expansion attempts, however, experience an erosion of their base business as well.

Definitions: Market Incumbency, Organizational Experience, and the Firm Categories in Competition

The first steps in designing the analysis put forth in this paper are to delineate two key definitions, organizational experience and market incumbency, to then define all firm profiles (in respect to the identified focal market).

I use *organizational experience* to refer to all processes described in the literature by which a firm gains efficiency and expertise at its current "business." Organizational experience is intended to include all kinds of processes taking place as a firm is in

[9] The incumbents in the creative destruction literature are always *market* incumbents, so their products are substitutes for one another, and hence as entrants gain market share, market incumbents lose it. In strategy studies such as this one, firms are incumbents to the industry at large, where industry represents the next level of aggregation containing several markets (such as the pharmaceutical industry containing the market for anti-cancer drugs as well as the market for anti-infective drugs; or the automotive industry containing the market for automobiles as well as the market for tires).

[10] For example, as Nuclear Magnetic Resonance was invented, the market for Magnetic Resonance Imaging (MRI) equipment was born.

operation for a particular business. It includes then processes of emerging routines (Nelson and Winter, 1982) and organizational structure (March and Simon, 1958; Galbraith, 1973), but also processes of emerging power and status hierarchies within the organization (Burns and Stalker, 1966).

It is not until the firm is faced with the need to innovate in order to succeed in a diversification attempt (whether across technologies and/or markets) that its organizational experience gives rise to *organizational inertia*, an obstacle to innovation.

It becomes important to differentiate organizational experience from its resulting disadvantage, organizational inertia, because organizational experience can provide advantages as well, as will be discussed later in this paper.

I use *market incumbency* to refer to the presence of a firm in the focal market at the time this market is disrupted by a radical technological change. By definition, when a firm is a market incumbent, the firm is an experienced organization, since the firm must have accumulated experience in at least one market (precisely the focal market) prior to the start of the disruption under study.

Decoupling market incumbency from organizational experience allows us to see that the first is a characteristic that refers to a firm's position in a market, whereas the latter is a characteristic ascribed to the firm itself (once a firm is organizationally experienced, it carries the consequences of its experience to every market it attempts). To the extent that the empirical regularity of failure in comparative studies is linked only to market incumbency (a market position) and not to organizational experience itself (a firm characteristic), we may have been blaming experienced firms in general for a failure

rate we have not yet proven they exhibit other than in the specific cases when they happen to also be market incumbents.

As result of failing to decouple market incumbency from organizational experience, studies of creative destruction have systematically confounded the definitions of new (de novo) with that of new to a market (entrant), and the definitions of established (experienced) with that of established in a market (incumbent). The implementation of this decoupling requires the clear definition of three specific firm profiles.

Incumbent firms are experienced firms established in one or more markets, including the focal market at the moment this market is disrupted by the radical technological change. That is, they exhibit both market incumbency and organizational experience.

Entrants are firms that were not in the focal market prior to the period of radical technological change and that enter it now during the transition to the new technology.

Diversifying entrants are those entrants that were established in other market(s) prior to the start of the disruption in the focal market and that enter it by diversification. They therefore have prior organizational experience with the advantages and disadvantages this implies.

De novo entrants are those entrants born in the focal market during the period of ferment and therefore have no prior organizational experience.

It is then that *incumbents* and *diversifying* entrants are both *experienced* firms, that is, firms established in one or more markets prior to the period of radical technological change, regardless of whether that market(s) includes the focal market.

The implications of these definitions for the creative destruction literature are illustrated in the comparison of Figures 4a and 4b.

Insert Figure 4 about here

Intel's detailed history of movements across technologies and markets as reported in Burgelman (1994) allows me to illustrate an example of the difference between market incumbency and organizational experience. Created in 1968 to commercialize DRAM memories and replace "magnetic cores as the standard technology used" (p. 32), the company was then a de novo entrant into the memory products market. The company stayed in that market "for four successive product generations" (p. 35) through which it remained always a market incumbent. While still in the market for memory products, engineers at Intel invented microprocessors in response to customer firm Busicom's request. As Intel gradually started its R&D and manufacturing of microprocessors during the early 1980s, it was a diversifying entrant into the microprocessors market, although it remained a market incumbent in the market for memory products until its exit in 1985. Observe that Intel was a market incumbent or diversifying entrant in different markets. However, after its entry into the memory products market, its first entry into any market (hence the only time when the firm qualifies as a de novo firm), it continuously accumulated organizational experience for the rest of its corporate history. That is, in both the market for microprocessors and the subsequent product generations in the market for memory products, Intel was an experienced firm in competition.

The Case for Competence Re-Use

Designing a study that decouples market incumbency from organizational experience by distinguishing three firm categories introduces an additional factor for research design. A set of recent mainstream strategy studies examines diversifying entrants and de novo firms in competition in settings in which the radical technological innovation marks the birth of the market (settings that therefore include no incumbents).[11] In these studies, however, prior organizational experience confers diversifying entrants the advantage of being able to re-use their previously acquired competences.

Mitchell (1994), for example, finds diversifying entrants outperform de novo firms as measured by divestiture and dissolution rates in a study of the birth of each of seven new markets within the diagnostic equipment industry. In another study comprising a series of markets within the telecommunications and medical sectors, Methe, Swaminathan and Mitchell (1996) find diversifying entrants[12] outperform de novo

[11] There are, though, studies outside of creative destruction that investigate the behavior of firms during a technological disruption that does not coincide with the birth of the market and that will therefore have incumbent firms present. However, uninterested in incumbents' dynamics, these studies do not sample them. A perfect example is Holbrook et al., (2000) where the authors present a rich historical account of four firms competing during the transistor revolution: Sprague Electric, Motorola, Shockley Semiconductor Laboratories and Fairchild Semiconductor. My further inquiry into the corporate histories of these firms reveals they are all diversifying and de novo entrants to the market that transitioned from receiving tubes to transistors. Tilton (1971) defines the transistor revolution as starting in 1952. Based on information from Tilton (1971), corporate histories available through the *Moody's Industrial Manuals* collection and existing firms' corporate websites, I distinguished each firm's profile. Fairchild, born in this market in 1957, is a de novo entrant. Motorola was founded in 1928 as Galvin Manufacturing Corp. Sprague Electric was founded in 1926 and first appeared in *Moody's Industrial Manuals* in 1945 as selling capacitors, resistors and ceramic-coated copper wire. Shockley Transistors Corp. was created by Beckman Instruments as a wholly owned subsidiary in 1958. Beckman Instruments itself was founded in 1934 as National Technical Laboratories. These latter three firms were never present in the market for receiving tubes prior to their incursion into transistors and were therefore diversifying entrants. Because the study is not in the creative destruction literature, by design the authors did not sample incumbent firms (e.g., General Electric, Raytheon, Western Electric).

[12] In Methe et al. (1996), it is impossible to discern which of these industry incumbents are market incumbents as well (and which are just diversifying entrants) based on the information in the paper. The list of innovations presented in Table 1 (p. 1189) is described by the authors as newly born markets and should therefore have no market incumbents by definition. For Table 2 (p. 1190), however, the authors

firms in the number of innovations introduced in each market. These authors further distinguish between diversifying entrants that come from other markets within the industry (*industry* incumbents) and those that come from outside the industry, and find the latter additionally advantaged. Even more importantly, scholars interested in differences in firm survival find that diversifying entrants (*de alio* firms) outlive de novo firms, and assert that this advantage stems from the former's ability to re-use previously acquired competences (Carroll et al, 1996; Klepper and Simons, 2000; Khessina and Carroll, 2002).

Connecting the Literatures: Mechanisms at Play

The creative destruction and strategy literatures exhibit important commonalities that allow for the identification of the three main mechanisms at play.

The first mechanism is the *competence re-use* always present in experienced firms to different extents. It has been described for market incumbents (as competence enhancement [Tushman and Anderson, 1986; Gatignon et al., 2002]), and for diversifying entrants (Carroll et al., 1996), and it involves the advantage of having competences accrued through prior organizational experience that can now be re-utilized.

The competence destruction generated by a disruption to the status quo can be understood as two-fold.

On the one hand, it gives rise to *organizational inertia*, the second mechanism, which implies a "loss in efficiency," because experienced firms are unable to identify some of the competences destroyed and hence keep attempting to use them when they are

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only offer details about experienced firms at the industry level. Unable to identify if there are market incumbents in the sample of Table 2, I refer to them as diversifying entrants in general.

no longer appropriate. This inefficiency stemming from *organizational inertia* has been described for incumbents (Henderson and Clark, 1990), and for diversifying entrants (Mitchell and Singh, 1993).

On the other hand, experienced firms are able to correctly identify other competences destroyed, and in those cases, they stop attempting to use them and instead start from scratch to build new competences. This then is the third mechanism, *competence development*, which might be pursued in-house or acquired from other firms in a spot (acquisition) or relational (research alliance) transaction, but is nevertheless also always present. It has been described for incumbents (as competence acquisition[13] [Gatignon, et al., 2002]) and for diversifying entrants (Roberts and Berry, 1985).

In fact, devoid of *organizational* experience and its disadvantage, and of re-usable *firm-level* competences and their advantage,[14] de novo entrants are the only firm category dedicated entirely to competence development.

In a classic conceptualization where a radical technological shock is either fully competence-destroying or fully competence-enhancing (Tushman and Anderson, 1986), only diversifying entrants or incumbents, respectively, have access to competence re-use. The actual mix of competence destruction and re-use that both experienced firms enjoy in every disruption is masked. Therefore, decoupling market incumbency from

[13] I refrain from using the term "competence acquisition" because it could give a sense of external acquisition, and the central part of the mechanism is that new competences should be developed. Whether the firm decides to outsource the development is a different matter (a matter of vertical integration).

[14] Note that the individuals working for de novo entrants (and for all firm categories in general) do have individual-level inertia and do have individual-level competences to re-use. The first effect was shown in a study of engineers by Allen and Marquis (1964), and is well known in experimental psychology settings (see, for example, anchoring effects in Tversky and Kahneman, 1982). The second effect has begun to receive attention in recent studies, such as the comparison between spinoffs and startups offered in Klepper and Sleeper (2005). There is no evidence, however, that these effects are disproportionately present in the personnel employed either in incumbent, diversifying or de novo firms. To the present state of our evidence, these effects require no control variables in a comparative analysis at the firm-category level.

organizational experience in creative destruction studies requires the measurement of the disruption to the R&D process in finer categories that capture different levels of competence destruction and re-use, taking the direction suggested on the most recent research in the characterization of technological disruptions (Gatignon, et al., 2002). In doing this, I propose to not only decouple market incumbency from organizational experience in order to appropriately assign the disadvantage of organizational inertia, but also to measure in finer categories the levels of competence destruction within the R&D process in order to appropriately assign the advantage of competence re-use.

RESEARCH DESIGN

To summarize, in the present study I decouple market incumbency from organizational experience by distinguishing the three firm categories in competition: market incumbents (experienced, incumbent firms), diversifying entrants (experienced, entrant firms), and de novo firms (inexperienced, entrant firms). I then unpack the R&D process into categories that vary in their level of competence destruction. This design allows for the appropriate assignment of the disadvantage of organizational inertia (not only to incumbents but also to diversifying entrants) and the appropriate assignment of the advantage of competence re-use (not only to diversifying entrants but also to incumbents). The only mechanism present in all three categories of firms is then competence development, which is then "controlled for" in the category of de novo firms, the only category devoid of organizational experience and its advantages and disadvantages.

Existing theories do not allow for clear predictions of the differences in research competence when this research design approach is used. Incumbents underperform all entrants aggregated when all incumbents' competences are destroyed (e.g., Tushman and Anderson, 1986). De novo firms underperform diversifying entrants when no incumbents are present and competences are, to a large extent, re-usable from other markets (e.g., Carroll et al., 1996). But only partial hypotheses can be derived when the three firm categories and a mix of competence destruction and re-use are taken into account. It can be hypothesized, for example, that if incumbents underperform all entrants when competences are fully destroyed, then at least one sub-category of entrants should outperform incumbents in fully disrupted areas of R&D.

Unable to build full predictions, I restrain from building hypotheses and simply set out to answer a series of open questions: What are the differences in research competence in the radically new technology among these three firm categories for the case of the *most* disrupted area of R&D?; for the *second*-most disrupted area?; for the *third*-most disrupted?; and so on.

Figure 4b presented previously shows the research design used for *each level* of disruption (i.e., competence destruction) within the R&D process considered.

EMPIRICAL SETTING

I implement this study using the market for anti-cancer drugs[15] and its transition from cytotoxic agents (i.e., antineoplastic antibiotics, alkylating agents, taxanes, etc.) to the radically new category termed targeted drugs (i.e., tyrosine kinase inhibitors, monoclonal antibodies, etc.), a transition brought about by the biotechnology revolution. As will be explained below, I operationalize this study through the selective use of data sources. Throughout the course of this project I interviewed 40 individuals, 4 of them repeatedly, with an evolving semi-structured interview guide, in order to clarify the market dynamics, verify the veracity of the statistical analysis and its interpretation, and document examples of specific cases. Concurrently, I collected data from the archival sources explained below to test statistically for the dynamics proposed.

This setting has many advantages. It centers on a specific market (i.e., the products under study are substitutes for one another) in contrast to groundbreaking studies of the biotechnology revolution done at the industry level (e.g., Zucker, Darby, and Brewer, 1998). Additionally, the radical technological change in this study is a shock to the market but does not represent its birth, hence the presence of both incumbents and entrants, in contrast to studies where all firms are entrants since the shock marks the birth of the market (e.g., Carroll et al., 1996). The study focuses on

[15] Note that economic theory defines products as being in the same market if they are substitutes for one another. Although confusion arises because cancer is a therapeutic category with several indications (e.g., breast cancer, lung cancer, etc.), where each indication has a separate line of treatment (i.e., a separate combination of surgery, radiotherapy and/or chemotherapy), each specific cancer indication does not constitute an independent market. Because an anti-cancer drug might treat several indications (e.g., Xeloda© is indicated for breast and colorectal cancer), even though it cannot treat them all (e.g., Xeloda© is not indicated in any of the leukemias), indications constitute "sub-markets" (Sutton, 1998) of the anti-cancer drug market. Many high-tech products constitute markets with sub-market fragmentation as reported for flowmeters (Sutton, 1998) or the case of transistors (Tilton, 1971). According to Sutton (1998), this market fragmentation explains, for example, the fact that these markets exhibit an economic irregularity: although they are highly intensive in R&D expenditure, they exhibit low levels of market concentration.

research competence, and pharmaceuticals is the most research-intensive industry in the U.S. (PhRMA, 2003a) where research competence and resulting drug quality is a major determinant of profitability (Lu and Comanor, 1998). Finally, among therapeutic areas within pharmaceuticals, cancer research has the most new drugs in development (PhRMA, 2002) and an extreme boom in commercial activity (PhRMA, 2003b).

It is worth emphasizing that the choice of setting makes this a *prospective* study, that is, a study in which the main end-point to measure, namely the final state of the market, has not yet taken place (Rothman, 2002). In contrast, the literature comprises only *retrospective* studies, that is, studies in which the final state of the market has been achieved. This difference carries several advantages in the execution of the current project, among which are firm survival bias minimization and richer data collection. It also carries two limitations: the absence of the final distribution of market share after the period of radical technological change, and the differential evolution of research competence across firm categories. The first limitation has minimal impact due to my choice of R&D competence instead of market performance as the dependent variable. The second has a significant impact. It limits my ability to speak about the research competence of firms over the entire transition to biotechnology. I can only conclude what the differences in research competence are *at this point* in the revolution.

The prospective nature of the present project also has an impact on the process of identifying a radical technological change for analysis. According to the literature, radical technological changes can be identified in two different ways. One is to *retrospectively* look for a discontinuity in final product performance and trace it back to a radical change in the underlying science or technological competence (Tushman and

Anderson, 1986). The other is to *prospectively* identify a discontinuity or shift in the underlying science or technological competence used for research and development.[16] In the present prospective paper, I identify the radical disruption for study (biotechnology) based on the requirement that the market undergoes a shift in the underlying science or technological paradigm used for research and development.[17] It is also important to emphasize the fact that, prospectively, all definitions of radical innovation concur in describing it as requiring a new science, knowledge or technological paradigm (Dosi, 1982; Tushman and Anderson, 1986; Henderson and Clark, 1990).

Next, I describe my empirical strategy for identifying firms and firm categories. I then proceed to the characterization of the disruption to the R&D process and the identification of sub-categories with differential levels of competence destruction. I then define the measurement of dependent and independent variables per sub-category of R&D, and finish the Empirical Setting section with a test of the reliability of the drug ownership assignment to firms.

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[16] Tushman and Anderson (1986) explain that "… technological discontinuities [in terms of products that represent drastic changes in performance and that are finally adopted in the market]… are only known in retrospect…" (p. 443). In retrospective measurement, such discontinuities in performance can be traced back to competence-destroying technological changes for many markets. However, the authors' discussion implies that *prospectively*, a technological change that is competence-destroying for incumbent firms would have to be identified by its nature: "… [the fact that the new products] require new skills, abilities, and knowledge in both the development and production of the product" (p. 442).

[17] Furthermore, notice that what I require empirically is the assurance that the discontinuity is a shock to the R&D process (the focus of this paper). The shift of technological paradigm that biotechnology represents for the market for anti-cancer drugs is already resulting in significant increases in final product performance (see, for example, the case of Gleevec's Phase III clinical trial results as reported by the National Cancer Institute at http://www.nci.nih.gov/clinicaltrials/developments/newly-approved-treatments/page16, visited on July 18, 2005). However, it is still possible for the radical shift in technological paradigm that biotechnology represents not to result in drastic improvements in the average performance of products finally adopted in the market. This possible future divergence between the radical shift in technological paradigm and the final product performance at the end of the disruption does not affect the internal validity of my present study as long as I can control for the presence of investment (i.e., as long as I can see if over the timeframe of my study, firms stopped investing in biotechnology as they realized this shift in technological paradigm would not bring about increases in final product performance).

Identification of Firms and Firm Categories

I started by identifying the appropriate universe of firms. When selecting an incumbent firm for this study, I look for a market incumbent that has decided to venture into the radically new category of targeted drug development.[18] By applying this restriction, I selected incumbents contingent on investment in the radically new technology, as set forth in the introduction of this paper (Figure 1). Therefore, the universe of firms under study is composed of diversifying and de novo entrants and incumbents venturing into anti-cancer targeted drugs (a subset of all incumbents, termed simply incumbents hereafter for convenience).

To map this universe of firms, I used PJB Publications' database *Pharmaprojects*. I identified all anti-cancer drugs in clinical trials in the period 1989-2004 and then focused on the firms responsible for them. The search generated a list of 1,257 firms (responsible for a total of 6,177 different anti-cancer drugs) after excluding the National Institutes of Health (NIH) and a category for Non-Industrial Sources (that account for 205 and 469 additional anti-cancer drugs, respectively). In order to generate a sample from the population that included firms with a clear intention to compete in the anti-cancer drug market,[19] I matched the 1,257 firms from *Pharmaprojects* to the firms reported in all available PhRMA Surveys *New Medicines in Development for Cancer* (administered in 1988, and every two years from 1989 to 2003). This match generated a sample of 181 firms (14% of the total firms) responsible for 2,972 clinical trials (44% of

[18] Note that it is possible that with the advent of the new technology, an incumbent will opt for just "milking" the old-technology for as long as possible and then exit the market.
[19] I avoid selecting firms that self-reported as working in cancer research but were rather committed only to a nearby area, such as AIDS or immunology in general.

the total anti-cancer drugs clinical trials in *Pharmaprojects*).[20] After I matched firms to their parent company to count only the latter, identified recent mergers and acquisitions up to the end of 2004, and discarded drugs with missing data, I identified the final sample, which comprises 165 firms (responsible for 2,281 anti-cancer drugs in clinical trials).

Next, I categorized firms as incumbents, diversifying or de novo entrants. Identifying the latter two categories was done through access to their corporate histories, culled mainly from their company websites. The major challenge was the identification of the relevant incumbent firms. These firms must have been present in the market for cytotoxic anti-cancer drugs before the era of biotechnology, and they must be venturing into targeted anti-cancer drugs now. 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.[21] I therefore triangulated three different sources to identify incumbent firms: the records available from the Federal Drug Administration (FDA) on all approved drugs;[22] the records available on anti-cancer drugs in particular from the FDA's Center for Drug Evaluation and Research (FDA-CDER);[23] and the printed

[20] The fact that the remainder outside of the selected sample has 1,076 firms with 3,205 drugs reflects an average of 3 drugs per firm. Such small portfolios are typical of de novo entrants, firms particularly prone to declaring more therapeutic areas than they end up focusing on. This supports the idea that my sampling strategy is working in the intended direction.
[21] For example, FDA records for drug approval become partially incomplete before 1982, mainly because they are 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.
[22] From Drugs@FDA available electronically at http://www.accessdata.fda.gov/scripts/cder/drugsatfda/
[23] From FDA-CDER Oncology Tools available electronically at http://www.fda.gov/cder/cancer/druglistframe.htm

collection of the *Physician Desk Reference* (PDR) drug directories for the years 1947-2005.[24]

I took the approval of the first anti-cancer drug with influence from biotechnology, *Intron-A*® (a recombinant-DNA molecule) introduced by Schering-Plough in 1983, as the start of the era of targeted anti-cancer drugs.[25] An incumbent therefore would be a firm that was present in the market before 1983 and that after 1983 has 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 are now returning because of the biotechnology revolution are not incumbents but diversifying entrants.[26] 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

[24] The PDR collection generated the richest list of drugs related to cancer (406 drugs). After discarding targeted anti-cancer drugs and drugs with low cross-elasticity of demand to cancer treatment (e.g., pain killers such as codeine listed in the PDR as indicated for a long list of uses beyond cancer treatment), I documented 146 cytotoxic drugs corresponding to 36 different parent firms, which I then cross-referenced with the FDA and FDA-CDER sources. Many of these firms have either left the anti-cancer drugs market and to date have not re-entered (e.g., Hynson, Westcott & Dunning), or have consolidated through later mergers and acquisitions (e.g., Sterling Winthrop, acquired by Kodak, and later by the firm today known as Sanofi-Aventis).

[25] Although *Intron-A*® is approved for indications other than cancer and is reported in the FDA-CDER Oncology Tools only after 1997, it is listed as an Antineoplastic (i.e., anti-cancer drug) in the PDR manual (of wider use among the medical community than FDA-CDER Oncology Tools) starting in 1987. For all other drugs in this study, the PDR manual reported a lag of 2 years from start of use, and therefore, the starting point for the biotechnology revolution in the anti-cancer drug market can be reliably estimated as sometime between 1983-1985. Use of any year in that window does not alter the definition of incumbent firms for the present analysis. Furthermore, expert interviewees supported the reliability of this choice.

[26] For example, Merck made two attempts to enter the anti-cancer drugs 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 after 1983 (as shown by their absence from the *Med Ad News Top 500 Prescription Drugs* Reports 1991-2002 and their lack of generic introduction after 1984). Cosmegen is even reported as unprofitable in Merck's Annual Report in 1951. Now that Merck is attempting to enter the anti-cancer drugs market again, it is classified as a diversifying entrant.

period 1991-2002, or must have had a generic introduction after the generics industry took off in 1984.[27]

The decision tree followed for the categorization of firms as incumbents, diversifying entrants or de novo entrants, including data sources accessed, is depicted in Figure 5.

Insert Figure 5 about here

The sample of 165 firms therefore comprises the following: 8 incumbents, a list that is exhaustive; 44 diversifying entrants; and 113 de novo entrants. The latter two firm categories are not exhaustive but rather representative samples.[28] It is important to clarify that the category of incumbents does not coincide with the firms popularly known in this industry as "big pharma." Incumbents in this study are *market-level* incumbents. "Big pharma" are a subset of *industry-level* incumbents. They appear in this study only if they were present in the anti-cancer drug market before biotechnology (in which case they appear as incumbents) or if they are now entering the anti-cancer drug market in the transition to biotechnology (in which case they appear as diversifying entrants).

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

[28] The unbalanced nature of this panel, especially the small number of incumbents, is a key characteristic of the phenomenon of creative destruction. Since, by definition, incumbents have been in the market for a long period (prior to the transition to the new technology), they underwent a period of market consolidation and exit typical of any path of maturation for a given technology in a given market (regardless of the explanatory mechanism proposed, scholars consistently report the empirical regularity that markets consolidate as they mature, see Klepper and Graddy, 1990; Utterback, 1994; Jovanovic and MacDonald, 1994).

Characterization of the Disruption to the R&D Process

In order to analyze the technological disruption in multiple categories rather than a binary of full competence-destruction or full competence-enhancement, I first offer a more elaborate picture of the impact of the biotechnology revolution on anti-cancer drug development. The idea is to follow the measurement of firm competences in the *smallest number* of relevant categories that capture the gist of the variance in competence destruction (Gatignon et al., 2002).[29] Based on interview material with scientists and clinical oncologists, I document the biotechnology disruption to anti-cancer drug development as taking place in two directions: the mechanism of action of the drug, and the molecule size (see Figure 6).

Insert Figure 6 about here

Considering these directions, I classify the level of competence disruption (i.e., the mix of competence destruction and enhancement) in three relevant sub-categories: preclinical drug design, manufacturing process design, and the execution of clinical trials (see Figure 7).[30] Notice that at this point of the biotechnology revolution interviewees

[29] The proposition in Gatignon et al. (2002) is to use survey data and find a more detailed measurement for key characteristics of the disruption dynamics. However, I departed from that specific design due to my decision to make R&D competence the dependent variable (instead of the independent variable as is common). I therefore identified instead the minimum number of categories in the R&D process that can be used to capture the gist of the variance in levels of competence destruction. This is closer to the methodology used in Burgelman's (1994) study of innovation at Intel, notwithstanding the fact that this classic study implemented categories for the entire innovation process, not only R&D.

[30] Two crucial questions are raised once the process for anti-cancer drug development (anti-cancer drug R&D process) is broken down into these three categories: (1) are manufacturing process design and clinical trials execution part of the R&D process or of the commercialization process (mainly, as a complementary asset for commercialization)?; and (2) is anti-cancer drug clinical trials execution a firm-specific competence even though clinical trial execution is frequently outsourced in the pharmaceutical industry?

describe clinical trial execution as largely undisrupted although they do report that significant changes are starting to take place (e.g., the use of biomarkers in clinical trial design [Arteaga and Baselga, 2004]).

Insert Figure 7 about here

Based on this operationalization, my proposition implies moving away from the usual 1X2 design[31] in creative destruction studies on R&D, and into a 3X3 design[32] (see Figures 8a and 8b). As can be readily seen, the analysis of a 3X3 design is extremely cumbersome. I take advantage of the fact that the sub-categories of competence destruction constitute not just a categorical but an *ordinal* variable (a variable that

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To answer the first question, complementary assets are defined as mediating factors between the successful *completion* of the R&D process and the appropriation of rents (Teece, 1986). Installed manufacturing capacity (and its reliable functioning) and marketing efforts are common complementary assets in pharmaceuticals (and commonly mediate in the appropriation of rents, such as the case of Chiron's shortage of flu vaccine production [Financial Times, 2004] and the famous debate on higher marketing than R&D expenses in pharmaceuticals [U.S. Congress, Office of Teachnology Assessment, 1993]). Still, manufacturing process *design* and clinical trials execution are not complementary assets. The design of manufacturing processes is a standard component of R&D in any industry and has long been argued to need parallel coordination with product design in the product development literature (e.g., Graves, 1989; Ha and Porteus, 1995). In addition, prior to clinical trials, the patented molecules identified as drug candidates remain only that, candidates. As a standard, the process of clinical trials will discard approximately 80% of drug candidates as ineffective or unsafe for use in humans (PhRMA, 2003a).

To answer the second question, notice first that it is only recently that the execution of clinical trials has achieved a larger proportion of outsourcing (prior to 1996 it is estimated that only 8.5% of all clinical trials was outsourced [Azoulay, 2004]). Second, cancer as a therapeutic category is one of the least outsourced areas in terms of clinical trials (with a mean outsourcing level of 10.3% in the period 1995-1999, second only to ophthalmology [Azoulay, 2004]). Furthermore, even if clinical trial execution were outsourced, this competence is still firm-specific unless carried out in a spot-transaction manner (relational transactions with specific suppliers do represent a firm-specific competence). Interview material reveals that pharmaceutical firms do hold a list of preferred clinical trials execution suppliers (named Contract Research Organizations or CROs), and therefore engage in relational transactions. Furthermore, there is evidence that working repeatedly with a CRO does benefit the firm contracting the service (Boerner, 2002). Unfortunately, the standard source of information for clinical trials outsourcing, Fast Track Systems' CROCAS database, does not allow quantitative assessment of the frequency of switching among suppliers by outsourcing pharmaceutical firms.

[31] This means a design with 1 factor (firm categories) and 2 levels (incumbents and entrants). That is, this is a 2^1 quasi-experiment in factorial design, with 2 cells in total for comparative analysis.

[32] This means a design with 2 factors (firm categories and disruption levels) and 3 levels per factor (3 categories of firms and 3 levels of disruption to the R&D process). That is, this is a 3^2 quasi-experiment in factorial design, with 9 cells in total for comparative analysis.

measures low, medium and high levels of disruption, for preclinical drug design, manufacturing process design and the execution of clinical trials, respectively). I therefore concentrate on the contrast between low and high levels of disruption (i.e., the area with full competence destruction and the area with full competence re-use for incumbents) in this paper (see Figure 8c). I defer to future research for an assessment of competence in manufacturing process design.

Insert Figure 8 about here

Clearly, distinguishing between targeted small molecules and targeted large molecules is only particularly relevant for the analysis of competence disruption for manufacturing process design.[33] Therefore, for subsequent analysis, I distinguish only between cytotoxic and targeted drugs.

Measurement of Research Competence in each Sub-category of R&D

In order to measure the R&D competence in each level of disruption (preclinical drug design and execution of clinical trials) across firm categories, I make use of two different dependent variables, which requires the use of two different main datasets. I present details on both next and then present the feasibility of using them jointly.

[33] That is, Figure 7 only posits a clear change in disruption between targeted small molecules and targeted large molecules in that competence.

Research Competence in Preclinical Drug Design

I assessed differences across firm categories in their competence in preclinical drug design through information on phase I trial results for anti-cancer drugs documented from the American Society of Clinical Oncologists' (ASCO) Proceedings in the period 1991-2002, a dataset originally published in Roberts et al. (2004).[34] I matched drugs to the firms originating them as reported in the *Pharmaprojects* database. I started with the sample of 213 phase I trials originally analyzed in Roberts et al. (2004) (see Figure 9 for a replicate of the selection process of these 213 phase I cancer trials out of the 2460 phase I cancer trials identified through ASCO Abstracts, as reported in the original). I was then able to find a match for 187 (87.8%) trials.[35] I discarded 15 trials because the originator of the drug is a non-profit organization and ended with a sample of 172 phase I trials.

Whereas the original 213 trials corresponded to 149 unique drugs in Roberts et al. (2004), my final sample of 172 trials corresponds to 113 unique drugs. Although I use the anti-cancer drugs to infer the performance of the firms that originated them, the unit of statistical analysis in this section remains the trial. This is the case because trials that have a drug in common differ in their measures for control variables (to be described next). Figure 10 shows the distribution of number of trials per drug in the dataset. Still, controlling for replicate trials per drug in all models does not change results, either in direction or significance. Because the inclusion of such a control variable actually lowers the Adjusted R^2 of models, I omit it from regressions presented in the next section.

[34] I gratefully acknowledge full access to the dataset from the original authors, especially Thomas Roberts, M.D., Bernardo Goulart, M.D., and Stan Finkelstein, M.D.

[35] The remaining 26 (12.2%) trials lack information to permit a match to its originating firm (e.g., the publication reports the anti-cancer drug only in mentioning its broader drug class, such as *a* GM-CSF or *an* Interleukin-2).

Insert Figure 9 about here

Insert Figure 10 about here

I use this dataset to perform regression analysis on response rate during the phase I trial.[36] Response rate is measured as the proportion of patients enrolled in the trial who exhibit a reduction in the size of their tumor. I use this variable as a proxy for drug quality.[37] In addition to variables to identify the three categories of firms, I differentiate cytotoxic and targeted anti-cancer drugs. To construct the variable "Targeted," I measured its two sub-classes of drugs: targeted *small* molecules and targeted *large* molecules (the latter also commonly referred to as "biologics" or "biopharmaceuticals"). The identification of the latter is reliably documented in the *Pharmaprojects* database. It is the targeted small molecules that are difficult to identify since they are in many ways (e.g., molecular weight) similar to cytotoxic drugs. The main difference between them is that they were discovered through a process of "mechanism-driven" development. I therefore selected all drugs with mechanisms of action described in industry reports (e.g., Bear Sterns, 2002; Stephens Inc., 2002; UBS Warburg, 2001) as "mechanism-driven"

[36] Cancer is the only therapeutic category in which phase I trials recruit diagnosed patients and not healthy volunteers, although recruited patients can have any type of tumor. It is also the only therapeutic category in which randomized trials are never tested against placebos but rather against benchmark treatments by regulation.

[37] Response rates in cancer phase I trials can be argued to measure two firm capabilities together, that of designing the drug with high quality (efficacy) and that of designing the phase I trial itself, with no way to discern between them. Still, there is evidence that higher response rates in cancer phase I trials are significantly related to better results in subsequent phase III trials (Sekine et al., 2002), which supports the construct validity of my intended use for this proxy.

within anti-cancer drug development and identified them as targeted small molecules (in the end, mainly comprising angiogenesis and kinase inhibitors).

I also include as a control the variable "Two or fewer Tumor Types," a binary variable that represents the number of different indications (e.g., breast cancer, lung cancer, etc.) included in the trial. This variable is necessary because greater numbers of tumor types are significantly associated with lower trial efficacy, as shown in the original Roberts et al. (2004) and in interview material. Lastly, I include the death rate per clinical trial and its interaction with "Targeted" as controls as well. Death rate is measured as the proportion of patients enrolled in the trial who died due to toxicity.

Research Competence in Clinical Trial Execution

I implement the innovative differentiation of levels of disruption within R&D not without caveats. Although ideally I would have measured each competence independently, the sequential nature of the two steps of preclinical drug design and clinical trial execution makes the measure of firm competence in each step necessarily nested. That is, I first measure differences across firm categories in their competence in preclinical drug design alone. I then measure differences across firm categories in their competence in clinical trial execution *and* preclinical drug design jointly.[38] It is not until I compare the analyses of the two datasets that I can draw the conclusions I set out to explore.

[38] Although the ability of a firm to competently execute a clinical trial makes a significant difference in the advancement toward drug approval, so does the actual quality of the drug. If advancing toward drug approval depended only on the competence of executing clinical trials, a "skillful" firm could get a placebo approved for cancer treatment, a fact well known to be impossible.

I assessed differences across firm categories in the competences of preclinical drug design and clinical trial execution jointly directly through the *Pharmaprojects* database. I identify when each drug entered and exited clinical trials, and whether the drug was ultimately approved (or if it is still in clinical trials or was discontinued, in which cases I treat them as right-censored).[39] I use this dataset to perform event history analysis. Because the dates in *Pharmaprojects* are detailed down to the day, month and year (i.e., detailed enough to avoid tied events), I interpret the data as a continuous-time event occurrence and select Cox Models for their analysis (Singer and Willett, 2003). Cox Models are non-parametric and therefore impose the least assumptions on the data. I again use the same variables to identify the three categories of firms and the distinction between cytotoxic and targeted drugs. I include controls for firm age and size and for the cumulative introduction of drugs into clinical trials by each firm category (variable "Cumulative"). Furthermore, I control for the "novelty" of the drug. The variable "Drug Novelty" is defined as the inverse of the chronological place of introduction that the drug holds on the list of drugs within the same mechanism of action (a replicate of the measure included in Guedj and Scharfstein, 2004). Finally, I control for the presence of an R&D Alliance through a dummy variable with value 1 if the drug had an R&D alliance associated with it reported in the cancer sub-section of the *Windhover's Pharmaceutical Strategic Alliances* collection 1986-2003.

[39] Although information on a competing event, discontinuation of clinical trials, was also available, it could not be disaggregated into trials discontinued at the recommendation of the FDA or leading oncologists in charge of the trial, and those discontinued at the discretion of the sponsoring firm (this latter constitutes a firm-specific capability). Without disaggregating the two cases, no conclusions can be inferred and therefore, I consider only drug approvals in my analysis.

Comparison of the two Main Data Sources used for Joint Analysis

The comparison between the 113-drug sample and the 2,281-drug sample is shown in Table 1.

Insert Table 1 about here

I built a matrix with the proportions of drugs in each of the six classes resulting from all combinations of the three firm categories and two technologies (i.e., cytotoxic drugs from incumbents, targeted drugs from incumbents, cytotoxic drugs from diversifying entrants, and so forth) for the 113-drug sample versus the 2281-drug sample. This generated a 6X2 matrix in which to test differences in proportions. The Pearson Chi^2 test for differences in the distribution of proportions across the two samples is not significant (Pearson $chi^2[5] = 7.8$, $p < 0.17$). The lack of significance means that the proportions across the six classes are comparable in each sample. This result supports the representative nature of one sample versus the other and allows me to use them in joint analysis.

Testing the Reliability of Drug Assignment to Firms

Because the assignment of drugs to their originating firms is crucial for analysis, I further test the reliability of this information. *Pharmaprojects* reports for some drugs the number for the patent of the actual drug molecule. Of the 2,281 drugs, 419 have a patent reported for them.[40] Although this 419-drug sub-sample was not randomly selected, but

[40] Searching for patents for drug molecules is significantly difficult. An expert interviewee examined sample patents from this 419-patent list and corroborated their nature as patents for drug molecules (as opposed to use patents). Still, my attempt to expand the current sample even when supported by the MIT

rather the result of missing data, it is representative of the proportions of incumbents, diversifying and de novo entrants in the larger 2,281-drug sample (Pearson $chi^2[2] = 0.84$, $p < 0.65$).

The reliability of the firm name reported originally in *Pharmaprojects* is supported as 291 of the 419 patents (69.5%) have the same assignee as the firm listed as originator in the analysis.

Table 2 shows the distribution of types of drug owners and corresponding patent assignees for the 128 patents (30.5%) whose assignee is different from the firm reported as owner in *Pharmaprojects*.

A potential challenge to the use of the originator firms reported in *Pharmaprojects* is the possibility that incumbents conduct disproportionately more drug acquisitions from the other firm categories, because they are the firms at risk of underperforming in preclinical drug design. Intense drug acquisition would improve their performance measure in this R&D sub-category. Contrary to expectations, incumbents are the least present category within this 128-patent sub-sample (only 18% of the drugs mismatching originating firm and patent assignee have an incumbent as a firm). The highest proportion is of de novo firms (50%), with diversifying entrants in second place (32%). Although firms acquire drugs in equal proportions from for-profit and not-for-profit organizations (48.4% vs. 51.6% accordingly), the pattern is not random (Pearson $chi^2[2] = 17.73$, $p < 0.0001$) and is led by de novo firms acquiring drugs from universities. This pattern probably reflects the common dynamics of entrepreneurship

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Technology Licensing Office expert personnel proved extremely time- and resource-consuming and rendered the task impractical.

within biotechnology, which is heavily based on technology transfer out of university laboratories (Murray, 2002).

Insert Table 2 about here

ANALYSIS

I start by presenting Figures 11 and 12, which display the size and age distribution by firm category for the final sample, respectively.[41]

Insert Figure 11 about here

Insert Figure 12 about here

Next, I present the analysis of the 2281-drug sample to measure differences in the competences in preclinical drug design and clinical trials execution jointly. I then proceed to the analysis of the 113-drug sample to measure preclinical drug design.

Figures 13a and 13b offer a qualitative overview (prior to controls) of the differences in these competences measured jointly. The figure shows the cumulative probabilities of approval generated through the Cox Model Analysis. That is, the vertical

[41] The x-axis for both graphs represents a binary variable for market incumbency vs. market entry. I "disperse" the data points horizontally within each of these two categories for visual clarity only. Furthermore, instead of marking organizational experience per se in the graph, I use three different markers to distinguish among the three categories of firms directly.

axis represents higher probability of getting an approval, and of getting it faster. For clarity, the sample for this figure is stratified on targeted anti-cancer drugs only.

Table 3 then presents descriptive statistics. Table 4 offers results on the event history analysis for the entire sample, whereas Table 5 is stratified on targeted drugs.

Insert Figure 13 about here

Insert Table 3 about here

Insert Table 4 about here

Insert Table 5 about here

Note the presence of diversifying entrants and their similarity both in size and in age to the other two categories of firms at either end of the spectrum in Figures 11 and 12. More importantly, observe how in Figure 13, the performance of incumbents versus entrants looks drastically different unless the latter are separated into experienced vs. inexperienced (i.e., diversifying vs. de novo) entrants. When separated, diversifying entrants' performance seems similar to that of incumbents. Actually, it is experienced (i.e., incumbents and diversifying entrants) vs. de novo firms that are the most relevant categories for comparative analysis. Moreover, notice the direction of competitive advantage: when both preclinical and clinical (i.e., most and least disrupted) R&D sub-categories are taken into account, and entrants are disaggregated, both sub-categories of

experienced firms outperform de novo entrants. This implies that in this setting, competence re-use, the advantage stemming from organizational experience, overrides organizational inertia, the disadvantage.

The above-mentioned dynamics can be seen quantitatively in Table 4, Model 3, where all drugs are considered, but more specifically in Table 5, where models are stratified on targeted drugs only. In all models in Table 5, incumbents and diversifying entrants are considerably different from de novo firms, and diversifying entrants actually have a larger premium ($p < 0.02$ for the test of difference in coefficients for incumbents and diversifying entrants in Model 3 in that table).

Lastly, "Drug Novelty" is significant as expected but does not alter the results.

I advance now to the analysis of the differences in competence in preclinical drug design alone. A qualitative overview (prior to controls) for the measurement of competence in preclinical drug design is offered in Figure 14. This figure shows mean values on response rate and 95% confidence intervals. Descriptive statistics are provided in Table 6. Regression analyses are shown in Tables 7 and 8 for the full sample and the sub-sample stratified on targeted anti-cancer drugs, respectively.

Insert Figure 14 about here

Insert Table 6 about here

Insert Table 7 about here

Insert Table 8 about here

Notice the unexpected result that incumbents are at no disadvantage vs. entrants (aggregated or not) in the most disrupted area of R&D (as reflected by all interaction terms in Table 7 being no different from zero). Incumbents are actually at an advantage vs. all other firms in this sub-category of the R&D process (their main effect is significant in Table 8 with the stratified sample).

In all models, controlling for the number of tumor types is significant as expected, but does not change the direction or significance of coefficients.

DISCUSSION

In the introduction of this paper, I presented valid theoretical reasons why advancing the literature on creative destruction to decouple market incumbency from organizational experience is of primary importance. I also explained how this decoupling to appropriately assign the disadvantage of organizational inertia required the finer characterization of competence destruction to appropriately assign the advantage of competence re-use to all experienced firms in competition.

First of all, Figures 11 and 12 clearly show that the three categories of firms are present in the market. Figure 13 and the subsequent quantitative joint analysis of competences in preclinical drug design and clinical trial execution in Tables 3, 4, and 5 show how decoupling market incumbency from organizational experience does alter our conclusions regarding differences in R&D competitive advantage in creative destruction

studies. When both destroyed and re-usable competences are included in the analysis, distinguishing between diversifying entrants and de novo firms becomes relevant. In fact, the significant firm categories to compare become experienced (i.e., incumbents and diversifying entrants) vs. de novo firms.[42] Because the mechanisms at play are tied to organizational experience and not to market incumbency in particular, once the two are decoupled, experienced firms "cluster" together in performance.

Notice that even when the full drug portfolios are considered (i.e., cytotoxic and targeted anti-cancer drugs together, see models in Table 4), diversifying entrants behave so similarly to incumbents that they also exhibit a premium in performance above de novo firms.[43] They do, however, underperform incumbents in this case, likely as a result of incumbents' greater expertise in cytotoxic anti-cancer drugs, the old technology.[44]

Furthermore, note the reversed direction of performance: experienced firms (incumbents and diversifying entrants) outperform de novo firms. This implies that the advantage of competence re-use available from prior organizational experience outweighed the disadvantage of organizational inertia among experienced firms. Expert interviewees confirm these dynamics: although organizational inertia is a relevant impediment to radical innovation among experienced firms, in this setting, these firms have found ways to compensate for it.

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[42] Strictly speaking, the two categories of firms, incumbents and diversifying entrants, do not exhibit identical levels of research competence. This fact is reflected in the statistically significant difference between the coefficients of these two firm categories in Table 5. Such difference in coefficients is largely driven by the dissimilarities in the competences they possess for re-use.

[43] There is evidence that entrants to many markets under technological disruption outside pharmaceuticals invest in the old technology as well (e.g., Henderson, 1988). Recent research has connected this investment to underlying mechanisms such as R&D spillovers from their investment into the new technology (Snow, 2004).

[44] By definition, incumbents were, before the disruption started, the "surviving" market leaders, experts in the use of the old technology to develop products for this market.

Beyond the answer to my original research question, however, the analysis of the subsequent preclinical drug design competence offers additional insight into the dynamics of creative destruction. In an area of R&D described as fully disrupted, counterintuitively, incumbent firms outperform all other firms. Indeed, the least competent firm category appears to be de novo entrants.

Neither mechanism, organizational inertia or competence re-use, explains why incumbents outperform all entrants, including diversifying firms, in this particular area. There must be a competence accrued to incumbents only and that therefore only these firms can re-use. This point highlights a crucial inappropriate assumption in current studies of creative destruction: that, within R&D, the technology-specific side of R&D competence (e.g., mechanism-driven drug design used to perform preclinical design of targeted anti-cancer drugs) is the key to a firms' competitive advantage. There has been no recognition of the presence of an application-specific side of R&D competence (e.g., competence in the "science" of cancer as a disease). Under the assumption that the technological platform (i.e., technology-specific R&D competence) is the source of competitive advantage in R&D, once the existing technological platform for some area of R&D is destroyed by a radical technological change, incumbent firms are left empty-handed and at a serious disadvantage in that area. However, application-specific R&D competences have, by the start of the disruption, accrued only to incumbents. These competences might represent a unique source of competitive advantage for incumbents even in areas of R&D where the technology-specific R&D competences are destroyed.

With the above extension of our understanding of creative destruction, I propose to apply the larger argument already present in the corporate diversification literature,

that there are technology-specific and application-specific sides to competition (Roberts and Berry, 1985), into the R&D microcosms inside the firms. Inside R&D, there are also two sides to successfully researching and developing new products for a market. To research and develop targeted anti-cancer drugs necessitates a technology-specific side of R&D competence, that is, mechanism-driven drug discovery (as opposed to random drug discovery used to research and develop cytotoxic anti-cancer drugs). There is also, however, an application-specific side of R&D competence, that is, competence in the "science" of cancer as a disease. Just as the corporate diversification literature argues is the case for the entire innovation process, within R&D the differential importance of these two sides of R&D competence as a source of competitive advantage is contingent on the market.

For example, it is quite feasible that in the state of the market that transitioned from mechanical to electrical typewriters in the early 20th century (Utterback, 1994), it was trivial for IBM as a diversifying entrant to catch up with the application-specific R&D competence of building typewriters, but meaningful to re-use its technology-specific R&D competence at electrical automation.[45] Sperry Rand as an incumbent might not have had a strong source of competitive advantage in its unique competence in typewriter development and assembly in that case. For other markets, however, such as the market for anti-cancer drugs, the challenge of catching up on the application-specific side of the R&D competence might be considerable for all entrants.

[45] Although in 1961 when IBM introduced its famous *Selectric*, the first functional electrical typewriter to hit the market, the company had never been involved in typewriter development or manufacture, the company had certainly been using electricity for automation for some time. In fact, the company introduced its first tabulating equipment with electric key punch in 1923. Source: http://www-03.ibm.com/ibm/history/history/history_intro.html visited on November 4, 2005.

In fact, these two sides of R&D competence are so comparable in importance that de novo firms, the firms that usually cannot afford to emphasize the development of both competences, find emphasizing either side of R&D competence to be a viable business model. For example, in interviews, two de novo firms with equally successful corporate experiences (12 years since their foundings, over 100 employees, completed IPOs, similar 2-building installed facilities) reported taking opposite approaches. The first, betting on the innovative nature of their technological platform, had repeatedly changed targeted diseases (including leaving cancer to pursue immunological disorders and even congestive heart failure with an alliance partner). The other, betting on their application-specific R&D competence in anti-cancer drug development, changed technological platforms and left their original technological platform within their laboratory-scale manufacturing process with no intention of ever commercializing such a platform.

When we recognize that there is an application-specific side of R&D competence, we expand the amount of competences that incumbents can re-use during a period of radical technological change. Incumbent firms can re-use their full competences from the areas of R&D left undisrupted, but even in fully disrupted areas of R&D, they can still re-use their application-specific R&D competences.[46] In interviews, it is unclear whether

[46] It is critical to keep in mind, though, the contingent direction of the comparison of application-specific vs. technology-specific competences for firms competing in a period of radical technological change. The direction of the comparison of these two sides of R&D competence is contingent not only on the market, but also on the state-of-the-art of R&D in the market at the time the disruption takes place. During the biotechnology disruption to the R&D process for anti-cancer drugs, application-specific R&D competences could be a comparable source of competitive advantage for incumbent firms. However, a prior revolution took place in the same market with different results. This same market, which could be named a market for cancer treatment prior to the emergence of chemotherapy, was being serviced to a large extent by firms that had been producing x-ray and radiotherapy equipment since the turn of the 20th century (Lederman, 1981). In the 1940s, the first anti-cancer drug became available (Chabner and Roberts, 2005), and the market was radically disrupted by chemotherapy. The technology-specific R&D competence (chemotherapy) was radically different from the state-of-the-art of radiotherapy, and the new technology represented a significant improvement in treatment efficacy (Zubrod, 1979). Yet, the application-specific knowledge was not as deep as it is nowadays (little was known about cancer and used in the state-of-the-art radiotherapy-

the application-specific side of R&D competence consists of a deeper knowledge of cancer as a disease, of higher absorptive capacity in the knowledge of this disease[47] (Cohen and Levinthal, 1989, 1990), or of a different mechanism such as preemptive patenting due to first mover advantage (e.g., Fudenberg, et al., 1983). To the extent that a competitive advantage based on the application-specific side of R&D competence is connected to an enduring mechanism (e.g., higher absorptive capacity in that area), it would be an equally enduring source of competitive advantage.

It is important to look as well into the category of de novo entrants and explain their underperformance. The results we see for de novo entrants are not connected to a "liability of newness" (Stinchcombe, 1965). This author's classic theory is based on firm age, and this variable adopts no statistical significance in any of the models presented in this paper. The lack of significance of firm age as a predictor of research competence in a transition from an old to a new technology, however, is not a contribution to this theory but rather proof that we are outside the limits of the theory's boundaries. Stinchcombe (1965) stated that a combination of economic and technical conditions would explain cases contradicting his theory.[48] This assertion implies that his classic theory addresses

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based treatment), and therefore, incumbents did not possess a meaningful source of competitive advantage once the technology-specific R&D competence was radically disrupted. In fact, of the 143 firms listed in *Thomson's Register of American Manufacturers* for the year 1949 under the categories "Apparatus: Physicians," "Apparatus: Therapeutic," and "X-Ray Apparatus," a superset of the x-ray therapeutic and radiotherapy equipment manufacturers, none of them were ever listed as an anti-cancer drug manufacturer in the full *Physician's Desk Reference* collection of 1947-2005. Even firms in this superset such as General Electric X-Ray Corporation of Milwaukee, WI, the predecessor of today's General Electric Medical Systems Division, never launched a cytotoxic anti-cancer drug on the market, and after the advent of cancer chemotherapy instead diversified the exploitation of its technology-specific R&D competence into diagnostic equipment markets.

[47] That is, these firms do not know more about cancer but learn faster about it.

[48] The author declared for the deviant case of the water transportation industry that "clearly, the introduction of the steamship, diesel propulsion, and the steel hull reorganized the shipbuilding and water-transportation industries much more than I had anticipated" (p. 156).

"stable" markets, that is, it is not immediately applicable to the study of the transition of a market from its state under an old technology to its state under a new one.[49]

Further than the de novo firms' disadvantage of having no competences to re-use, their lower performance could be linked to the proposition that higher uncertainty is correlated with higher failure in the innovation process (Fleming, 2001). In the sample used in this study, for instance, 107 out of the total 918 drugs (12%) developed by de novo firms represent research in gene therapy,[50] the most "futuristic" and uncertain variant of targeted anti-cancer drug development.[51] In contrast, only 44 out of 864 drugs (5%) and 4 out of 499 drugs (1%) of diversifying entrants' and incumbents' anti-cancer drug portfolios, respectively, correspond to gene therapy research. This distribution of risk could be strategic on the part of all firm categories, where those with previously accrued competences (experienced firms) choose to stay in areas of targeted anti-cancer drug development where they can re-use those competences (areas which are, therefore, more certain). In contrast, de novo firms, knowing they are disadvantaged in competing directly against experienced firms with re-usable competences, choose to research "more uncertain" and hence "uncontested" areas of targeted anti-cancer drug development.

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[49] Outside of the original theory, it is difficult to contribute to its classic empirical tests (e.g., Carroll and Delacroix, 1982; Freeman, Carroll and Hannan, 1983). These classics refer to market entry, and my choice to isolate the R&D process makes my work a study of the *threat* of entry (Tirole, 1988). That is, mine is not a study of firms launching products in a market, but rather of firms advancing product candidates through their R&D process and thereby increasing their probability to soon have a product to launch into the market.

[50] As measured by identifying all drugs in the 2,281-drug sample that listed within the origin of material description the terms "biological, cellular," "biological, cellular, autologous" "biological, cellular, heterologous," "biological, nucleic acid, viral vector," "biological, nucleic acid, non-viral vector," and "biological, virus particles."

[51] In further work on the competence in manufacturing process design, de novo entrants seem to also generate the fewest innovations partly because they choose to engage in more uncertain research. In interviews, personnel in some of these firms report considering research in manufacturing process design too difficult to pursue in-house and therefore deciding to outsource manufacturing. But personnel in other de novo firms report that they chose rather to research a more futuristic manufacturing approach based on mammalian cells, an approach that still carries high uncertainty for implementation (Dorresteijn et al., 1997).

Nonetheless, to the extent we have concluded that "it may be worth tolerating the static efficiency loss attributable to the market power of [experienced] firms in exchange for their superior [research productivity]" (Henderson and Cockburn, 1996, p. 32), we will have to accept that it may be worth tolerating the loss of research productivity attributable to de novo firms throughout a technological disruption in exchange for their willingness to carry higher risks that might one day lead to more radical innovations.

Although there is nothing to be added to the study of young firms' liability of newness, there is an important point to be made regarding studies of Schumpeterian dynamics based on firm size. Such studies that examine competition between large and small firms have found inconsistent results (see Acs and Audretsch [1990] for a review). A look back at Figure 11 might shed light on this issue. Size does not perfectly correlate with market incumbency in the market for anti-cancer drugs. To the extent that the Schumpeterian dynamics these studies are trying to understand are focused on incumbents' empirical regularities, firm size will constitute an incomplete approach for several markets.

The results in the present paper are in line with the most recent evidence in other studies of innovation, such as the groundbreaking study on the biotechnology revolution offered by Zucker, Darby and Brewer (1998). In that study, the authors are interested in the category of "big pharma" firms, which are equivalent to all incumbents and a sub-set of diversifying entrants in my work. The authors find that "big pharma" firms encountered no disadvantage in the adoption of gene sequencing techniques. My study also parallels the most recent research in finance and entrepreneurial dynamics offered by Guedj and Scharfstein (2004). Here, the authors examine firms with portfolios of fewer

than 3 drugs, a category equivalent to a subset of all de novo firms in my work. They find firms with fewer than 3 drugs to be slower at discontinuing phase I trials for anti-cancer drugs that show poor prognosis, a decision that results in portfolios of drugs with poorer outcomes in phase II and III trials.

LIMITATIONS

It is extremely important to reiterate the *prospective* nature of my study. The transition from cytotoxic to targeted anti-cancer drugs is still taking place. Many years from now a *retrospective* study might find that, in the end, de novo entrants were the most successful competitors on all counts. If that were the case, this paper would still be of value as it shows that incumbents were not disadvantaged (and were actually advantaged) at the beginning of the revolution. Only over time, perhaps when some entrant firms catch up in the application-specific side of R&D competence, might the demise of incumbents begin. In the current literature on creative destruction, to my knowledge, few studies have examined the activity of incumbents over time during a period of radical technological change (namely, Cooper and Schendel, 1976; Christensen, Suarez and Utterback, 1999). The results in these studies are far different from those in the present paper. In the retrospective study offered by Cooper and Schendel (1976), the authors found that incumbents invested early, became disenchanted by the low quality results of the emerging new technology, and stopped investing. Incumbents only returned when it was too late to compete. In the study presented by Christensen et al. (1999), incumbents also missed the window of opportunity to invest in the new technology. In the present paper, incumbents invest early, get good (even

advantageously better) results throughout the R&D process, and continue investing in the radically new technology.

I should also emphasize that the tests presented here are comparisons of categories' means, and such a design does not preclude the possibility of an outlier (or set of outliers) emerging from any of the categories included. For example, this study finds no significant advantage accrued to de novo entrants yet, but that does not rule out the possibility that *one* de novo entrant might outperform all categories and represent the toughest competition. The successful cases of Genentech, a de novo entering the market for diabetes treatment in 1976, and of Amgen, a de novo entering the market for treatment of anemia in 1980, illustrate this point.

FUTURE RESEARCH

The course of my empirical analysis suggests some avenues for future research. An example is the originating firm vs. patent assignee analysis performed previously. In this analysis, most drug acquisitions performed by for-profit organizations were directed to diversifying instead of de novo firms (from all three categories of firms in almost equal proportions). These data suggest the possibility in future research of examining whether diversifying entrants outperform de novo firms not only as competitors but also as suppliers of upstream research activity.

My main findings also have implications for studies of creative destruction in general, beyond the analysis of the R&D process. For example, one of the most interesting recent propositions in creative destruction is the presence of cognitive biases among the top management teams of incumbent firms that interfere with their proper

strategic decision-making process. An important pioneering study is that of Tripsas and Gavetti (2000) on how Polaroid, an incumbent to the camera market, failed to capitalize on the radical technological transition from standard to digital cameras. The authors show that the management team insisted on holding on to the business model used for the old technology when it was no longer appropriate. Similarly, in the corporate venturing literature, Chesbrough and Rosenbloom (2002) show that a diversifying entrant also failed to successfully capitalize on a venture because the firm insisted on holding on to the business model of the past. To some extent, both studies can be traced to a broad-range theory of experienced firms: the attention-based view of the firm (Ocasio, 1997). The differences and similarities between these two contrasting cases of experienced firms (where one is and the other is not a market incumbent) illustrate the need to consistently decouple market incumbency from organizational experience.

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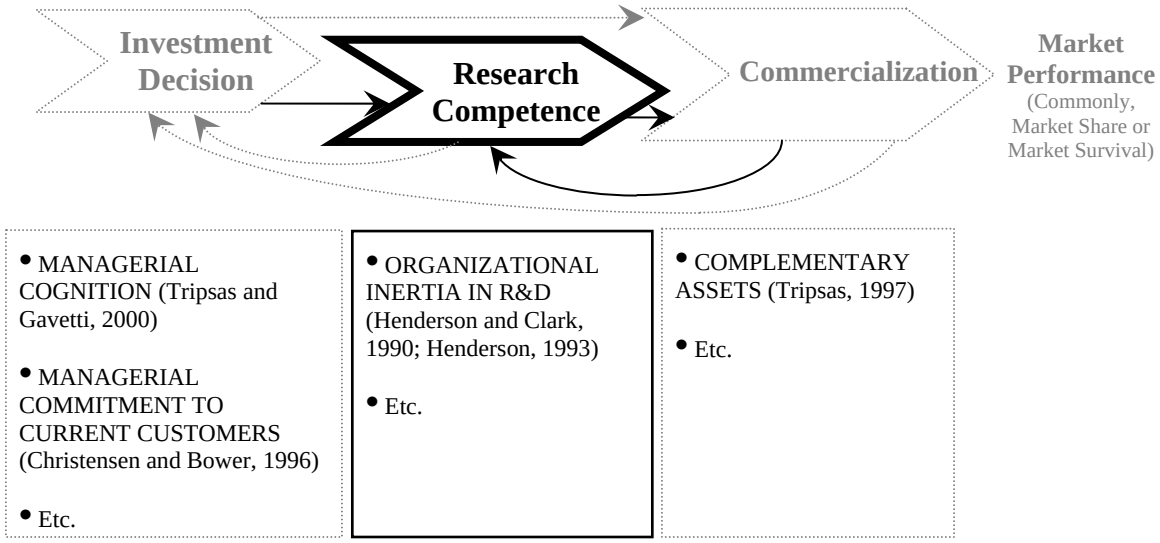
FIGURES

FIGURE 1
Place of the Present Study within the Literature on Creative Destruction[52]



[52] Notice the claim is not that firms do not iterate through their project execution (i.e., the claim is not that firms make a decision to invest and execute it without changes over time). The claim is rather that, per time unit (in most cases the budgetary period, whether yearly or quarterly) firms decide to invest, run R&D attempts and commercialization evaluations, examine their outcomes, and use (their interpretation of) the feedback gathered to act on the next time unit.

FIGURE 2
A Disconnect in the Creative Destruction Literature between Outcomes and underlying Mechanisms, when Market Incumbency and Organizational Experience are confounded

(2a). Common design in studies of creative destruction

	Market Incumbents	Market Entrants
	Low Research Competence	**High** Research Competence

(2b). Differences in the competence to research the radically new technology among firm categories, as seen when decoupling market incumbency from organizational experience

	Market Incumbents	Market Entrants
Experienced Firms	**Low** Research Competence (*incumbent*)	**High** Research Competence (*entrant*)
New Firms		

(2c). Mechanisms behind the differences in the competence to research the radically new technology among firm categories, as seen when decoupling market incumbency from organizational experience

	Market Incumbents	Market Entrants
Experienced Firms	***Incumbents*** • Inertia from Old Routines • Inertia from Current High Status Groups • Etc.	
New Firms		***Entrants*** • No Inertia from Old Routines • No Inertia from Current High Status Groups • Etc.

FIGURE 3
Identifying Incumbents and Diversifying Entrants within the Framework of the Corporate Diversification Literature

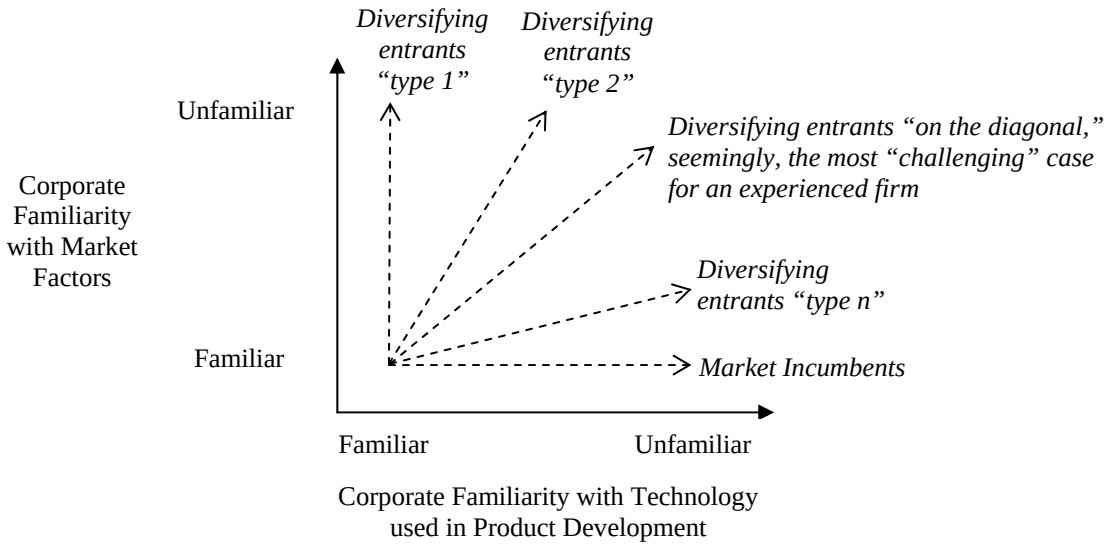


FIGURE 4
Comparison of Research Designs in the Creative Destruction Literature and in this Study

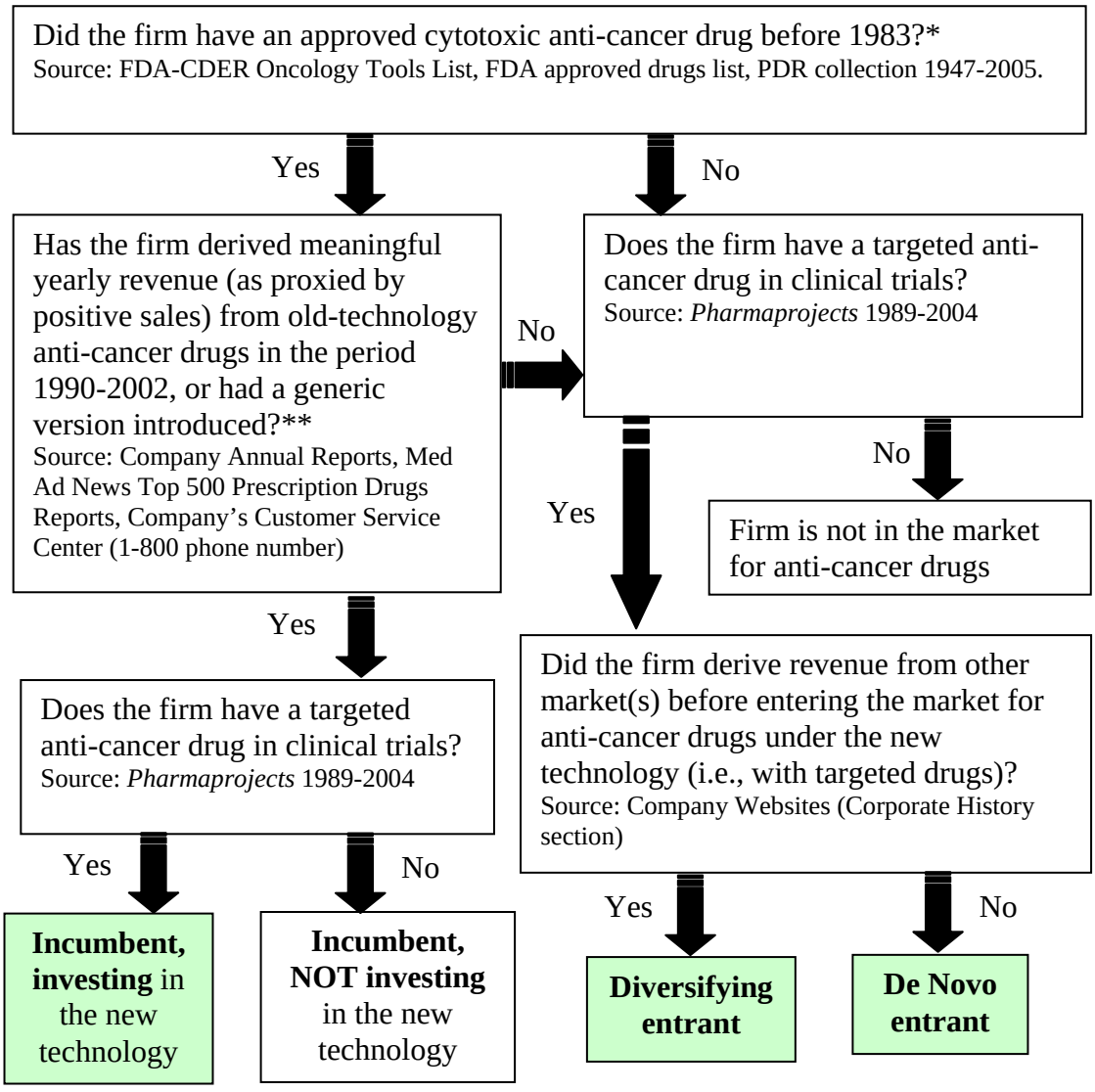
(4a). Common design in studies of creative destruction

	Market Incumbents	Market Entrants
	Low Research Competence	**High** Research Competence

(4b). Decoupling market incumbency from organizational experience

	Market Incumbents	Market Entrants
Experienced Firms	**?** Research Competence (*incumbent*)	**?** Research Competence (*diversifying entrant*)
New Firms		**?** Research Competence (*de novo entrant*)

FIGURE 5
Decision Tree to Categorize Firms



* This requirement ensures that the firm was an incumbent to the market prior to its investment in new-technology anti-cancer drugs (as opposed to just deciding to enter the market investing in both old and new technologies in parallel). 1983 was when the first Targeted Anti-Cancer Drug was launched on the market, and I therefore use it as a milestone.

** This requirement ensures that the firm did not leave the market and come back to it because of the new technology's effect on lowering barriers to entry. If a firm exits a market before the transition due to the radical technological change starts, then that firm is not in the market at the time of the radical change and therefore is not an incumbent. If it stays away from the market, then it is out of the scope of relevance for this study. If it comes back after several years, investing in the new technology, then it is a diversifying entrant.

FIGURE 6
The Effect of the Biotechnology Disruption on Anti-cancer Drug Development

		Mechanisms			
		Cytotoxic*	**Targeted**		
			TK inhibitors	Anti-angiogenesis	etc.
Molecule Size	**Small molecules**	Old Technology	New Technology	New Technology	New Technology
	Large molecules		New Technology	New Technology	New Technology

* Although producing a cytotoxic large molecule anti-cancer drug is technically feasible, it is economically impractical since cytotoxic anti-cancer drugs are expected to be of lower quality in the long-run, and large molecules are significantly more expensive to mass-produce than small molecules (in the estimated order of 50:1 according to interview material).

FIGURE 7
The Disruption of Biotechnology to
the Sub-categories of Competence within Anti-cancer Drug Development

Firm competence	**Type of drug**		
	Cytotoxic drugs (always small molecule)	**Targeted small molecule**	**Targeted large molecule**
Preclinical Drug Design	Baseline	Disrupted	Disrupted
Manufacturing Process Design	Baseline	Not Disrupted	Disrupted
Execution of Clinical Trials	Baseline	Not Disrupted	Not Disrupted

Note: Notice that the baseline of the disruption is the list of competences required to develop cytotoxic drugs and the state-of-the-art of R&D in this market up to the moment when the period of radical technological change began. It is against that baseline that the competences required to perform the different steps of R&D for targeted anti-cancer drugs, whether small or large molecule, are measured. For example, because designing the manufacturing process for targeted *small* molecule anti-cancer drugs is done in basically the same manner as for cytotoxic anti-cancer drugs, that cell reads "Not Disrupted." Because designing the manufacturing process for targeted *large* molecule anti-cancer drugs is done in an entirely different way (i.e., recombinant DNA and fermentation technology), that cell reads "Disrupted."

FIGURE 8
Standard Design of Studies on the Impact of Creative Destruction on R&D and the Design of the Current Project

(8a). 1X2 standard design of studies on the impact of Creative Destruction on the R&D process

	Firm Categories	
	Incumbents	**Entrants**
R&D Process		

(8b). 3X3 design resulting from the research elements proposed in this study and the specifics of the setting of choice

		Firm Categories		
Levels of Disruption		**Incumbents**	**Diversifying Entrants**	**De Novo Entrants**
High =	**Preclinical Drug Design**			
Medium =	**Manufacturing Process Design**			
Low =	**Execution of Clinical Trials**			

(8c). 2X3 design adopted for analysis in the remainder of this paper.

Levels of Disruption		**Incumbents**	**Diversifying Entrants**	**De Novo Entrants**
High =	**Preclinical Drug Design**			
Low =	**Execution of Clinical Trials**			

FIGURE 9
Replicate of "Figure 1. Trial Flow Used in Identifying Studies for Detailed Analysis**" from Roberts et al. (2004), p.2133**

FIGURE 10
Distribution of Replicate Trials per Unique Drug in the Final Sample for Measurement of Competence in Preclinical Drug Design

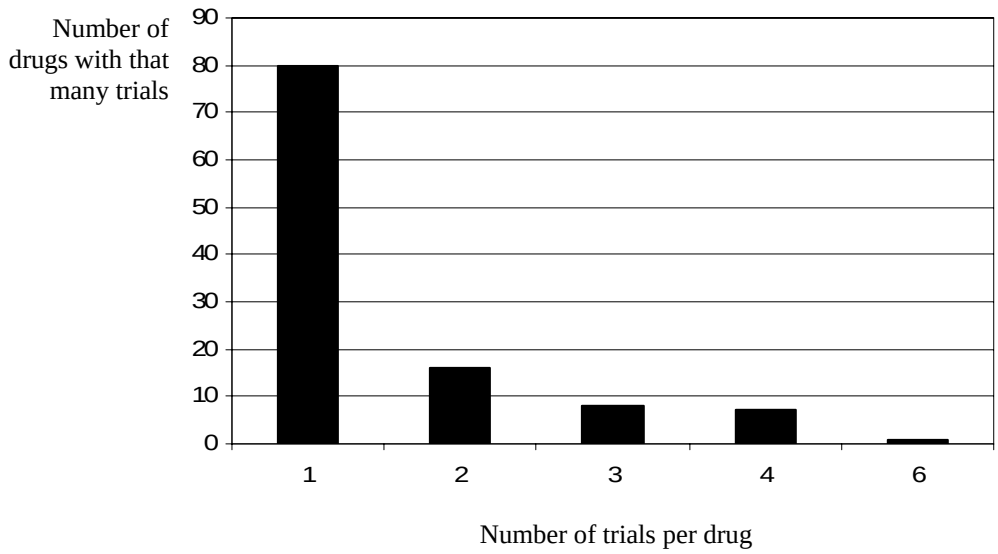


FIGURE 11
Distribution of Firms Competing in Targeted Anti-Cancer Drugs by Firm Category and Size

(■ incumbent, – diversifying entrant, • de novo entrant) .

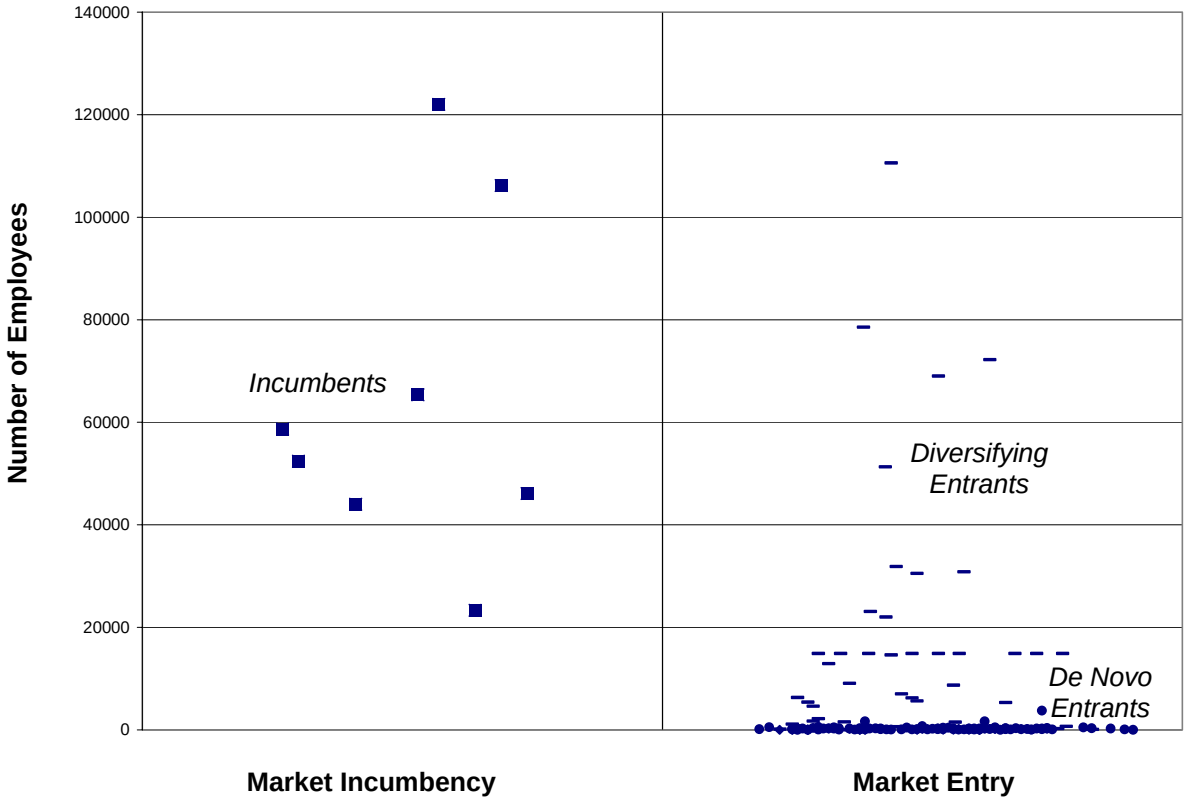


FIGURE 12
Distribution of Firms Competing in Targeted Anti-Cancer Drugs by Firm Category and Age

(■ incumbent, – diversifying entrant, • de novo entrant) .

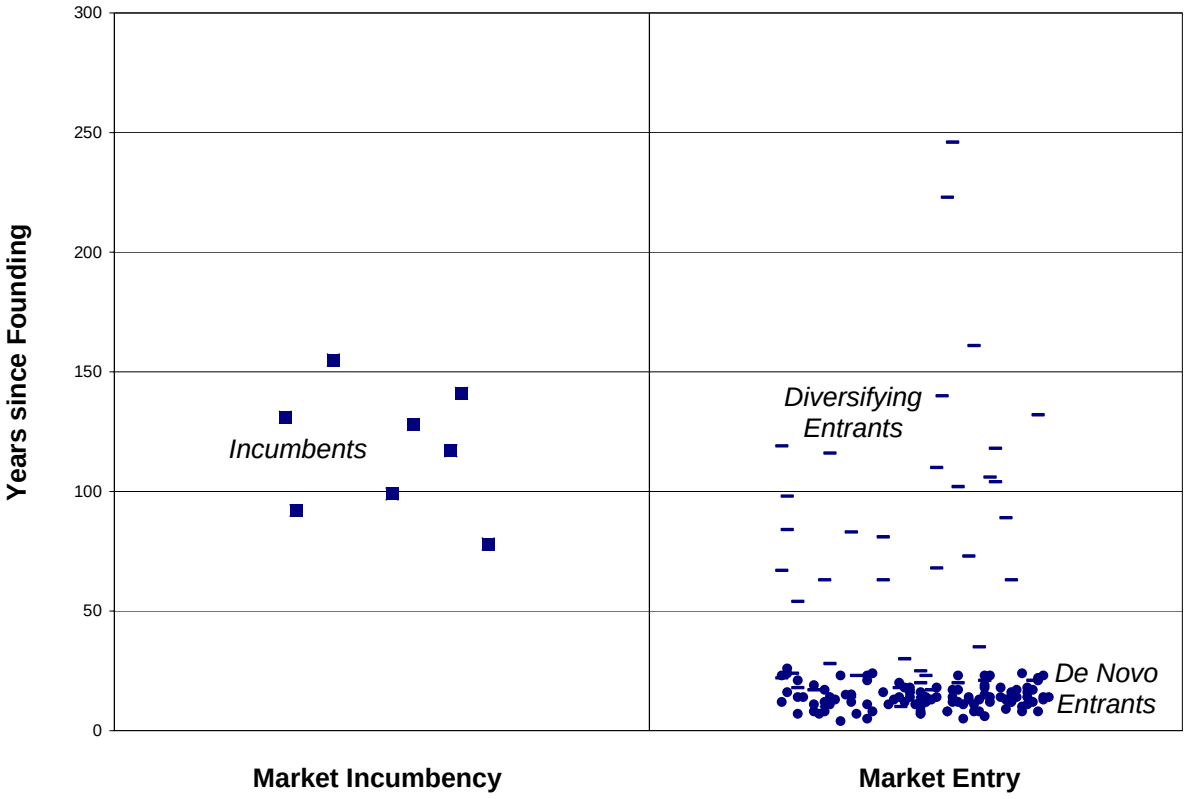
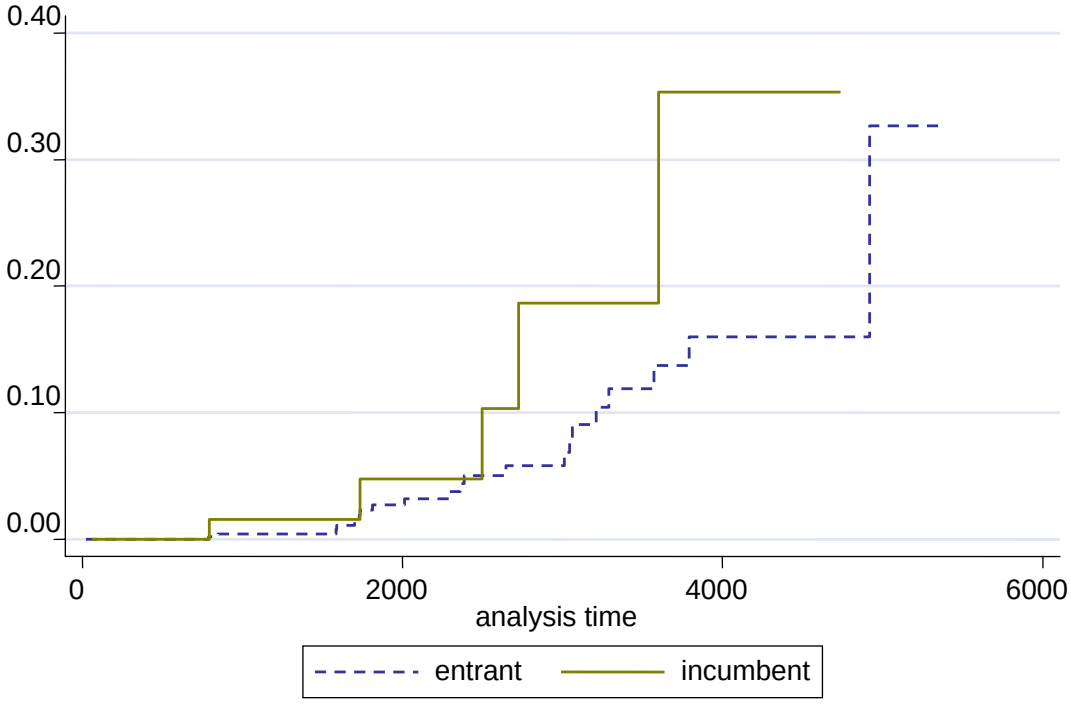


FIGURE 13
Cumulative Hazard (Nelson-Aalen) Graphs
Event modeled: Drug Approval *among Targeted Anti-Cancer Drugs Only*
(Spells = 991, events = 22)

(12a) Comparison of incumbents vs. entrants



(12b) Comparison of incumbents, diversifying and de novo entrants

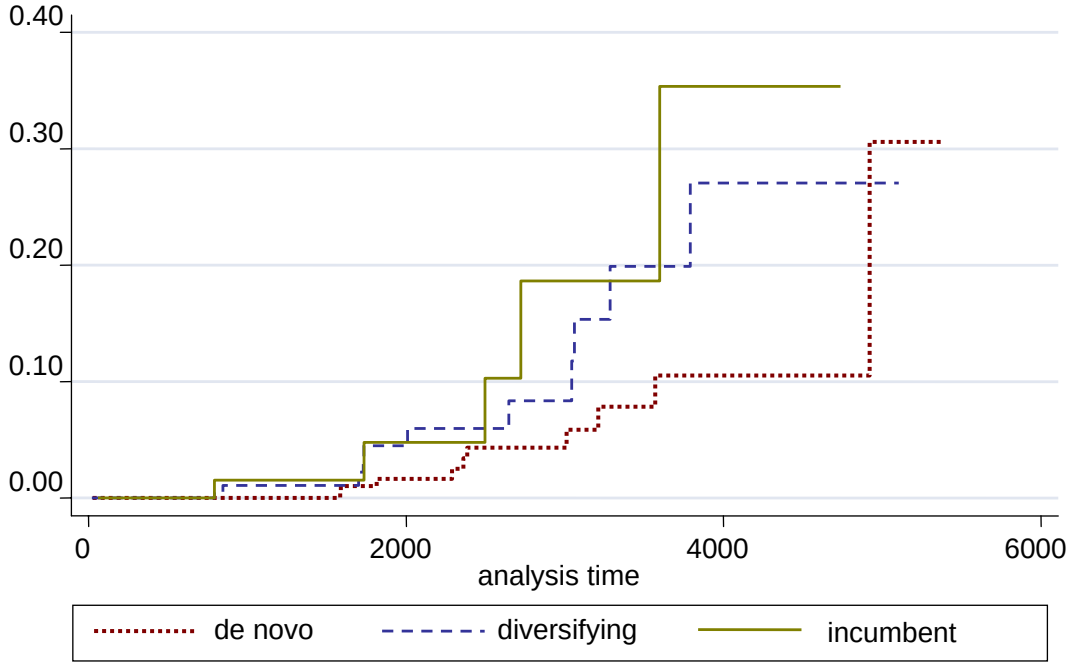
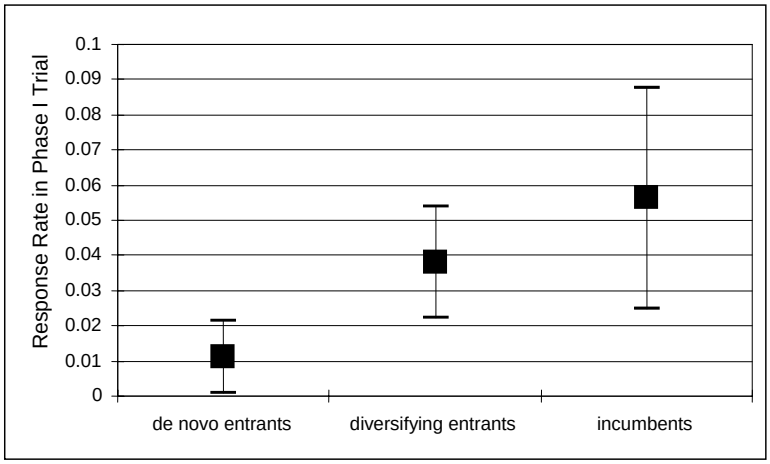
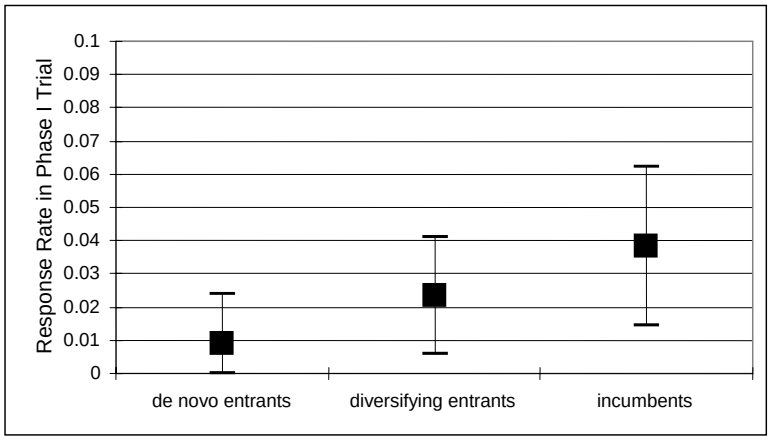


FIGURE 14
Differences in Means in Competence in Preclinical Drug Design (95% CI)

(14a). Mean response rates of *all*, cytotoxic and targeted anti-cancer drug phase I trials (N = 172 trials).



(14b). Mean response rates of *targeted* anti-cancer drug phase I trials only (N = 58 trials).



TABLES

TABLE 1
Comparison between 113-Drug Sample and 2,281-Drug Sample

Distribution of Types of Drugs across Firm Categories for the Two Samples

	Cytotoxic		Targeted		TOTAL	
	113-drug sample	2,281-drug sample	113-drug sample	2,281-drug sample	113-drug sample	2,281-drug sample
Incumbent	20	337	13	162	33	499
Diversifying	31	510	14	354	45	864
De Novo	18	443	17	475	35	918
TOTAL	69	1290	44	991	113	2281

TABLE 2
Types of Drug Owners and Patent Assignees for Cases when These do not Coincide (N = 128)

All counts are patents

	Category for Assignee in Patent for Drug Molecule							
	For-Profit Organizations (n_1 = 62)				**Not-for-Profit Organizations (n_2 = 66)**			
Category for Drug Owner	Incumbent	Diversifying Entrant	De Novo Entrant	Unclassified Firm	University	Research Center	Other (mainly Government)	TOTAL
Incumbent	0	15	1	4	2	1	0	23 (18%)
Diversifying Entrant	0	14	1	4	11	7	4	41 (32%)
De Novo Entrant	7	10	3	3	28	11	2	64 (50%)
TOTAL	7	39	5	11	41	19	6	128 (100%)

TABLE 3
Clinical Trial Execution, Descriptive Statistics and Correlation Matrix

	Count	Mean	StdDev	Min	Max
(1) Incumbent	499				
(2) Diversifying	864				
(3) Targeted	991				
(4) Firm Age		69.8	65.7	4	246
(5) Firm Size		30,200	39,937	10	122,000
(6) Cumulative		405	250	1	918
(7) Drug Novelty		27.6	40.6	1	222
(8) R&D Alliance	44				

	(1)	(2)	(3)	(5)	(6)	(7)	(8)	(9)
(1) Incumbent	1							
(2) Diversifying	-0.41	1						
(3) Targeted	-0.11	-0.039	1					
(4) Firm Age	0.44	0.31	-0.14	1				
(5) Firm Size	0.64	0.07	-0.12	0.80	1			
(6) Cumulative	-0.32	0.09	0.23	-0.24	-0.26	1		
(7) Drug Novelty	-0.007	-0.02	0.002	-0.02	-0.02	-0.28	1	
(8) R&D Alliance	-0.028	-0.05	-0.02	-0.05	-0.04	-0.08	0.03	1

TABLE 4
Clinical Trial Execution, Cox Model Analysis of Drug Approval
(2,281 Spells, 55 Events)
All Coefficients in *Log Odd Ratios*

	Model 1	**Model 2**	**Model 3**
Incumbent	0.90*	0.99*	1.72**
	(0.357)	(0.421)	(0.618)
Diversifying		0.194	0.66
		(0.447)	(0.491)
Targeted	0.01	-0.482	-0.296
	(0.325)	(0.493)	(0.495)
Incumbent x Targeted	-0.23	0.274	-0.11
	(0.661)	(0.759)	(0.771)
Diversifying x Targeted		1.10+	0.96
		(0.660)	(0.664)
Firm Age			-0.003
			(0.004)
Firm Size			-0.000002
			(0.000007)
Cumulative Introduction			-0.0008
			(0.001)
Drug Novelty			-0.01*
			(0.005)
R&D Alliance			0.62
			(0.538)
Log Likelihood	-315	-311	-304

+ p < 0.1, * p < .05, ** p < .01, *** p < .001 Standard errors in parentheses.

TABLE 5
Clinical Trial Execution, Cox Model Analysis of Drug Approval
Only Targeted Drugs
(991 Spells, 22 Events)
All Coefficients in *Log Odd Ratios*

	Model 1	**Model 2**	**Model 3**
Incumbent	0.69 (0.560)	1.31* (0.638)	1.42~ (0.912)
Diversifying		1.32** (0.487)	1.52** (0.560)
Firm Age			-0.006 (0.006)
Firm Size			0.000005 (0.00006)
Cumulative Introduction			0.0004 (0.001)
Drug Novelty			-0.01+ (0.006)
R&D Alliance			0.26 (1.05)
Log Likelihood	-110	-106	-103

~ p < 0.15, + p < 0.1, * p < .05, ** p < .01, *** p < .001 Standard errors in parentheses.

TABLE 6
Preclinical Drug Design, Descriptive Statistics and Correlation Matrix
(N = 172 Trials)

	Count	Mean	StdDev	(1)	(2)	(3)	(4)	(5)	(6)
(1) Response Rate		3.5%	7.7%	1					
(2) Incumbent	49			0.17	1				
(3) Diversifying	73			0.03	-0.54	1			
(4) Two or fewer Tumor Types	36			0.17	-0.03	-0.03	1		
(5) Targeted	58			-0.12	0.01	-0.18	0.20	1	
(6) Death Rate		0.5%	1.7%	0.08	0.19	-0.001	-0.04	-0.11	1

TABLE 7
Preclinical Drug Design, OLS Analysis of Response Rate during Phase I Trial
(N = 172)

	Model 1	**Model 2**	**Model 3**
Constant	0.03***	0.01	0.006
	(0.008)	(0.014)	(0.014)
Incumbent	0.03*	0.05**	0.05**
	(0.015)	(0.020)	(0.019)
Diversifying		0.02+	0.03+
		(0.018)	(0.017)
Targeted	-0.01	-0.003	-0.01
	(0.014)	(0.021)	(0.021)
Incumbent x Targeted	-0.009	-0.02	-0.02
	(0.027)	(0.031)	(0.031)
Diversifying x Targeted		-0.01	-0.02
		(0.030)	(0.029)
Two or fewer Tumor Types			0.04**
			(0.014)
Death Rate			-0.34
			(0.408)
Death Rate x Targeted			1.69*
			(0.791)
Adjusted R^2	0.0289	0.0349	0.0930

~ p < 0.15, + p < 0.1, * p < .05, ** p < .01, *** p < .001 Standard errors in parentheses.

TABLE 8
Preclinical Drug Design, OLS Analysis of Response Rate during Phase I Trial
Only Targeted Drugs
(N = 58)

	Model 1	**Model 2**	**Model 3**
Constant	0.014*	0.009	0.0009
	(0.006)	(0.007)	(0.007)
Incumbent	0.023*	0.029*	0.023*
	(0.011)	(0.012)	(0.010)
Diversifying		0.014	0.013
		(0.012)	(0.010)
Two or fewer Tumor Types			0.021*
			(0.009)
Death Rate			1.30***
			(0.302)
Adjusted R^2	0.0562	0.0619	0.3205

+ p < 0.1, * p < .05, ** p < .01, *** p < .001 Standard errors in parentheses.