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DIRECT AND MEDIATED TIES TO UNIVERSITIES:
‘SCIENTIFIC’ ABSORPTIVE CAPACITY AND INNOVATION PERFORMANCE
OF PHARMACEUTICAL FIRMS

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ABSTRACT
Extant literature on firm-university collaboration has emphasized two different strategies that firms in science based industries adopt in order to source scientific knowledge and expertise. On the one hand, firms engage in direct research collaborations with universities. On the other hand, firms establish indirect, mediated, ties to universities by engaging in research collaborations with dedicated biotech firms (DBFs) that are themselves strongly linked to universities - with the DBF taking the role of ‘broker’. We argue that the relative benefits of direct and mediated ties depend on the extent to which firms have organized their R&D to facilitate the absorption, assimilation, transformation and exploitation of scientific knowledge, which we coin ‘scientific absorptive capacity’. Drawing on patent and publication data in a panel of 33 vertically integrated pharmaceutical firms, we find that direct university collaboration is more beneficial for firms with relatively high scientific absorptive capacity, while only mediated ties are associated with greater innovative performance for firms with relatively low scientific absorptive capacity. The latter association is reduced if the mediated ties are with top universities. Our findings are suggestive of the importance of a ‘fit’ between the nature of a firm’s R&D organization and its strategy to access scientific knowledge.

Keywords: R&D collaboration, alliance portfolios, industry-science linkages, scientific absorptive capacity

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INTRODUCTION

Knowledge-intensive industries in general and science-based industries in particular, have been characterized by an intensification of the interactions between universities and firms (e.g. Hall et al., 2000; Cassiman et al., 2008). Firms increasingly look towards public science as one of the key sources for rapid and privileged access to new knowledge (Cockburn and Henderson, 2000; Zucker, et al., 1998; Mowery, 1998; Bruneel et al., 2010, Leten et al. 2011). This puts the issue of external knowledge sourcing from universities high on the corporate agenda, in order to keep at the forefront of the creation of new, state-of-the-art knowledge (Cohen et al., 2002; Mowery and Nelson, 1999; Balconi and Laboranti, 2006). Prior research on industry-science linkages has shown that research collaboration with university scientists is an important means for effective scientific knowledge sourcing and that this may yield a positive effect on a firm’s innovative performance (Zucker and Darby, 2001; Zucker, et al., 2002; George et al, 2002; Cassiman et al., 2008). More specifically, such business-university R&D collaboration may enhance firms’ capacity to generate high impact technologies and introduce new products to the market (Belderbos et al., 2004; Faems et al., 2005; Cassiman et al., 2008).

Extant literature on firm-university collaboration has emphasized two different strategies to source key scientific expertise. In the industry-science literature, the importance has been stressed of direct collaboration with universities (Cohen et al., 2002). The idea is that in knowledge-intensive industries it is important for firms to collaborate directly with universities in order to source state-of-the-art expertise developed at public research organizations and universities (Zucker and Darby, 2001; Zucker et al., 2002; Zucker and Darby, 2002; Cassiman et al., 2008). Direct collaboration with universities appears to be the realm of firms with substantial internal R&D capabilities (Belderbos et al., 2004). Active
involvement in scientific research (collaboration) is often conditional on the availability of human capital and the adoption of specialised organizational practices and routines in R&D (Gambardella, 1992; Cockburn et al, 1999).

On the other hand, studies in the innovation and strategic collaboration literature have emphasized that pharmaceutical firms collaborate with entrepreneurial dedicated biotech firms (DBFs) that are themselves strongly linked to universities and embedded in academic networks (Liebeskind et al., 1996; Powell et al., 1996; Zucker et al., 1998; George et al., 2002; Stuart et al., 2007). Hence, pharmaceutical firms also establish indirect, or ‘DBF-mediated’, ties to universities. Whereas both direct and indirect ties to universities have received attention in extant literature, there still is limited insight into the relative benefits of the two collaboration strategies. Addressing this issue forms the research objective of the current study.

The main premise of this paper is that the relative benefits of direct and mediated ties depend on the heterogeneous capabilities of pharmaceutical firms. We argue that differential performance benefits of the two collaboration strategies depend on the extent to which firms have strategically organized their R&D to facilitate the absorption, assimilation, transformation and exploitation of scientific knowledge. This is a specific form of absorptive capacity (Cohen and Levinthal, 1990; Zahra and George, 2002), i.e. ‘scientific absorptive capacity’, that is geared towards the absorption of state-of-the-art, academic expertise. Scientific absorptive capacity signals a firm’s scientific competence to the academic community, e.g. through publishing scientific papers, and facilitates firms’ abilities to get embedded and involved in the process of knowledge creation and knowledge exchange within the scientific community (Schmoch, 1997; Deeds and Hill, 1998). The build-up of scientific
absorptive capacity, however, requires long term investments in scientific research capabilities through the hiring of dedicated in-house scientists in order to bridge cognitive distance, and the adoption and implementation of specialised organizational practices in R&D, to bridge institutional distance to universities. This makes the build-up of scientific absorptive capacity a costly and complex process with pay-offs mostly expected in the longer term. Not every pharmaceutical firm commits itself to making these investments, and the degree of scientific absorptive capacity differs importantly across pharmaceutical firms (Gambardella, 1992; Fabrizio, 2009; Leten et al. 2011).¹

We argue that a strong scientific absorptive capacity enhances the relative effectiveness of direct university collaboration, whereas a relative lack of scientific absorptive capacity is associated with stronger performance consequences of indirect ties to universities. Our arguments and empirical tests specifically focus on the performance consequences of direct and DBF-mediated ties for vertically integrated pharmaceutical firms; biotechnology ventures are examined in their role as ‘brokers’ between university research and pharmaceutical firms. We test hypotheses on panel data (1995-2002) describing the innovation performance, R&D collaboration strategies, and scientific publication efforts of 33 pharmaceutical firms with their home base in the US, Europe and Japan.

¹ For instance, while Merck has always invested strongly in basic research and university collaboration, Pfizer tends to invest significantly less in scientific research. In our data, the ratio of Merck’s basic research publications to patents in the biopharmaceutical field is about 50 percent higher than Pfizer’s, and about 10 times the ratio for Johnson and Johnson.
Our research contributes to the industry-science links literature and the strategic collaboration literature by examining direct and indirect collaboration as alternative means for firms to source scientific knowledge. We inform the literature on strategic R&D organization (e.g. Cassiman and Valentini, 2009; Tzabbar et al., 2008) by highlighting the role of firm heterogeneity in organizing for scientific absorptive capacity, and by suggesting how this affects firms’ ability to benefit from different collaboration strategies with universities in science-based industries. Our analysis of the role of scientific absorptive capacity furthermore contributes to the literature on absorptive capacity by bringing in greater precision on the construct. The focus on a particular type of absorptive capacity in the context of university collaboration allows us to detail what type of external knowledge gets absorbed and what type of capabilities are required for absorption - aspects that have received limited attention in prior research (Zahra and George, 2002; Volberda et al., 2010).

Before proceeding, we note a number of caveats of our study. First, the empirical focus and data requirements of our analysis has restricted the number of firms included in the analyses to a limited number of large, vertically integrated pharmaceutical firms. Second, despite the use of multiple sources of information, it is likely that our data on direct university collaborations remains incomplete. Third, the difficulty in finding suitable instruments precluded controlling for potential endogeneity, such that we interpret the relationships under study as partial correlations. These issues suggest caution in the interpretation of our findings. We hope that future research can examine the generalizability of our findings in alternative empirical settings.
**BACKGROUND AND THEORY**

**Direct collaboration between firms and universities.** In the life sciences and the biopharmaceutical industry, public science forms one of the key sources of rapid and privileged access to new, state-of-the-art knowledge (Cockburn and Henderson, 2000; Zucker, et al., 1998; Mowery, 1998). In general, direct collaboration with universities tends to be in more uncertain areas and further away from commercialization. Although new scientific knowledge gets disseminated through publications, an important part of it tends to be non-codified and can only be exchanged through close interaction between individuals, through teams of university and firm scientists (Zucker et al., 1998; 2002; Cassiman et al., 2008). Tacit and sticky scientific knowledge can only be exchanged through direct links to the scientific community. Direct collaboration allows for the build-up of trust (Gulati, 1995a), which is an important prerequisite for the efficient exchange of tacit knowledge (Gilsing et al., 2008). Direct collaboration also reduces the likelihood of noise in information exchange and of fine-grained specificities getting lost, which mitigates the risk of misunderstanding (Ahuja, 2000).

Direct collaboration with universities offers firms exposure to fundamental scientific expertise and enables them to better decode advances in fundamental research and evaluate its quality and usefulness. This provides firms with opportunities for recombination and may enable them to develop state-of-the-art technology that cannot be easily imitated by others (Cassiman et al., 2008). Direct collaboration can be instrumental in speeding up the transfer of frontier academic knowledge to the firm (Fabrizio, 2009), providing first mover advantages in applied research and leading to higher value inventions. Firms can learn early about the most promising research opportunities, such as ‘embryonic inventions’, at an early stage through
interaction with university inventors or through membership of broader scientific networks (Santoro and Gopalakrishnan, 2001; Colyvas et al. 2002; Hertzfeld et al., 2006). Embryonic inventions require substantial additional work, typically from the side of firms, before they become of any use and may turn into something with commercial value (Thursby et al., 2001; Carayol, 2003; Santoro and Betts, 2003). If investments by firms are required in the further development of these inventions in view of future commercialization, their bargaining positions relative to universities in obtaining property rights through patents will be stronger (Crespi et al., 2010). Direct collaboration in this way may secure early access to promising new technologies that have the potential to contribute most to a firm’s innovation performance.

Firms that rely on direct collaboration with universities also have to cope with various kinds of barriers to knowledge exchange (Hall et al., 2001; Bruneel et al., 2010), which may mitigate the positive effects of direct collaboration with universities on a firm’s innovative performance. First, there can be a large cognitive distance between universities and firms (Noooteboom et al., 2007), as scientists’ focus on understanding fundamental problems and industrial researchers’ focus on application-related issues. As a consequence, these differences in cognition may create a risk that both parties do not sufficiently understand each other, with firms asking the ‘wrong’ knowledge questions and not being able to understand the answers they get, whereas scientists may misinterpret the questions or be unable to come up with an unequivocal answer (Gittelman and Kogut, 2003).

In addition, the institutional logic of scientific discovery is different from the institutional logic that characterizes industrial development of new technologies and their practical applications. Science forms a separate ‘epistemic community’ with its own practices and
routines that conflict with the routines and practices in firms that are specifically geared towards the upscaling and commercialization of inventions (Allen, 1977; Tushman, 1977). Scientists tend to focus on research that is considered to be interesting and valuable by the scientific community, whereas firms will make choices based on what is considered to be useful for the creation of new products, processes and/or services (Gittelman and Kogut, 2003; Nelson, 2004; Rothaermel and Deeds, 2006). University scientists will be keen on disclosing quickly in order to gain academic recognition and prestige, whereas industrial researchers may wish to keep information secret to facilitate value appropriation. Hence, institutional norms governing knowledge creation at universities differ profoundly when compared with firms. Such institutional distance may invoke a serious risk of opportunism as norms of reciprocity diminish if collaborating parties have incongruent goals and values (Deeds and Hill, 1998; Ouchi, 1980).

**Indirect ties between firms and universities.** Indirect ties imply that a firm is indirectly connected to a university through a common partner (Gulati, 1995b). The literature on network ties suggests that indirect ties offer firms the benefit of reducing the amount of time, costs and resources to gather and assimilate external information (Granovetter, 1985; Ahuja, 2000; Nahapiet and Ghoshal, 1998; Shane and Cable, 2002). More specifically, two advantages of indirect ties are identified, which we discuss in the context of firm-university linkages.

First, indirect ties can serve as an information-gathering device (Freeman, 1991), giving firms access to information about recent technological developments and developments in state-of-the-art scientific knowledge. Universities as indirect partners fulfill a ‘radar’ function by bringing broader information to the attention of the focal firm (Freeman, 1991; Ahuja, 2000).
Second, indirect ties can serve as an information-processing device (Leonard-Barton, 1984) helping firms to screens, absorb, filter and categorize new technological and scientific developments in a more efficient way (Ahuja, 2000). Given the large number of scientific discoveries in the life sciences, search costs for pharmaceutical firms run very high (Stuart et al., 2007). Indirect ties can support the identification, screening and classification of the most promising and relevant scientific findings. Although indirect ties operate by definition at a larger social distance in the firm’s network, the two-step reach may suffice in facilitating knowledge flows (Singh, 2003; Li and Rowley, 2002).

The general advantages of indirect ties suggested in the literature are in line with the description of the role of DBFs as tie ‘brokers’ in the biopharmaceutical industry. DBFs originate from universities and public research organizations (PROs) and generally possess expertise in the development of novel scientific approaches to drug development (see e.g. Liebeskind et al., 1996; Audretsch & Stephan, 1996; Powell et al., 1996; Zucker et al., 1998; Zucker et al., 2002; George et al., 2002; Murray and Stern; Stuart et al., 2007). DBFs maintain broad and deep formal and informal relationships with universities, while they are often simultaneously collaborating with downstream pharmaceutical companies. The more DBFs embed linkages to university research while simultaneously engaging in joint development activities with other firms, the more technology they are able to ‘convey’ relevant scientific knowledge to these downstream alliance partners such as pharmaceutical companies (e.g. Powell et al., 2005; Gilsing and Nootenboom, 2006). It has therefore been suggested that DBFs can serve as effective brokers between universities and (large) pharmaceutical companies (Stuart et al., 2007).
Pharmaceutical firms may be better able to learn from universities through DBF-mediated ties because DBFs have compatible values and related operational priorities. For academic scientists, collaboration with DBFs remain attractive as they have sufficient absorptive capacity and are familiar with the norms and institutionalized practices in academia (Gittelman and Kogut, 2003). Hence, DBFs can act as intermediary organizations that tap into the knowledge and capabilities of academic scientists and manage the selection of scientific inventions in order to create commercially valuable technological innovations (Audretsch and Stephan, 1996). They may serve as value-added ‘liaisons’ by obtaining intellectual property from universities and then monetize this through exchange with downstream partners, often after considerable investments in subsequent development of the technology. Brokering is an attractive role for DBFs because the more agreements and collaborations they have with universities, the more they may be able to attract revenue-generating alliances with downstream partners (George et al., 2002; Stuart et al., 2007).

The benefits of indirect ties notwithstanding, indirect ties also have drawbacks. Information obtained through indirect ties is imperfect and can be rather ‘noisy’ (e.g. Ahuja, 2000). It passes through a common partner, which may filter, interpret and attach meaning to this information in a different way than the focal firm would do. In this process, fine-grained specificities may fail to reach the focal firm. Furthermore, DBFs as the common-partner may obtain a powerful position if they can control the flows of information and resources between the focal firm and the indirect partner(s). This may enable them to extract extraordinary returns (Burt, 1992) and to share valuable knowledge and insights selectively with the focal firm.
Still, these drawbacks of mediated ties to universities may be offset by the benefits of obtaining insights into unfamiliar domains and key scientific developments. In particular those pharmaceutical firms with little scientific research involvement will lack knowledge of such insights and their implications.

**Hypotheses.** Based on the extant literature, it is evident that direct collaboration and indirect collaboration with universities are alternative strategies for firms to boost their innovation performance in a science-based industry. We argue that the extent to which one strategy provides more performance benefits than the other will vary among firms. We expect an important degree of heterogeneity in firms’ R&D strategy and organization, as prior research has shown that firms vary in their knowledge base profiles and their institutionalized practices and routines in R&D (D’Este, 2005; Bercovitz and Feldman, 2007; Cassiman et al., 2008; Cassiman and Gambardella, 2009). We argue that firms with a stronger focus on conducting basic research have a stronger capacity to absorb scientific knowledge and a better ability to bridge institutional distance with universities.

An important aspect of a R&D organization is the degree to which firms place particular emphasis on basic research rather than focusing only on applied research and development (Rosenberg, 1990; Bercovitz and Feldman, 2007; Fabrizio, 2009). When firms place an emphasis on basic research, they may hire in-house scientists, provide corporate support for their publication efforts in scientific journals and encourage them to comply with the norms and institutionalized practices in academia (Gittelman and Kogut, 2003). Such an adaptation of a firm’s R&D organization focusing on the role of ‘open science’ and fundamental research may help firms to attract high quality researchers at relatively low cost (Stern, 1999) and provide legitimacy and reputation in the academic community. This may facilitate privileged
access to frontier developments in relevant academic fields (Cockburn and Henderson, 1998). In general, such an R&D organization contributes to the build-up of ‘scientific absorptive capacity’: the capacity to understand, assimilate and utilize scientific knowledge.

The more a firm’s R&D organization is organized for accessing, analyzing and sharing state of the art scientific expertise - through own research activities, participation in academic conferences as well as through ongoing internal conversations and meetings between in-house scientists and applied researchers - the better it will be able to bridge cognitive distance with universities and develop a deeper understanding of the fundamental principles of the phenomena under study (Rosenberg, 1990; Orsenigo et al., 2001). Apart from bridging this cognitive distance, scientific absorptive capacity contributes to easier communication with university researchers and to bridging the institutional distance, providing legitimacy to the firm as a credible partner in basic research. Firm engaging in basic research will allow in-house scientists to participate fully in the distinct epistemic community that science represents (Gittelman and Kogut, 2003; Nesta and Saviotti, 2005), e.g. by attending conferences and publishing papers, creating a higher degree of congruence of the goals and values between the two collaborating parties that provides the basis for the build-up of trust in the relationship (Deeds and Hill, 1998). The role of trust is important in any collaboration but crucial between two parties from different institutional spheres, as it reduces the risk of opportunism that may in particular be present in collaborations between people with different backgrounds and diverging interests (Ouchi, 1980). In addition, trust contributes to the exchange of tacit knowledge and may help to alleviate the risk of conflict over the distribution of intellectual property rights (Bruneel et al., 2010).
A key mechanism in this process is formed by in-house scientists who can perform a critical brokerage role. They can serve as external gate-keepers contributing to the build-up of potential absorptive capacity through the acquisition of key external scientific expertise as well as its interpretation and comprehension (Zahra and George, 2002). In-house scientists will be able to understand novel causal relationships, whereas they can also assess which trajectories may probably become dead-ends and which ones will be much more promising (Fleming and Sorenson, 2004). In this way, in-house scientists can also serve as internal gatekeepers who contribute to the build-up of realized absorptive capacity: the transformation and exploitation of external scientific expertise (Zahra and George, 2002). Realized absorptive capacity is created by in-house scientists who bridge the gap between a firm’s scientific and applied research activities, through their understanding of the potential implications for applied research and their use of heuristics that enable them to assess the likelihood of success of certain innovation trajectories (Cassiman and Valentini, 2009; Gambardella, 1992). This entails a transformation capability that ‘translates’ basic scientific findings into implications for applied research and future innovation opportunities in downstream markets, suggesting that capabilities in fundamental research may increase the effectiveness of applied research (Cassiman and Veugelers, 2006; Dasgupta and David, 1994).

Within the context of the bio-pharmaceutical industry, a ‘transformational’ capability helps to connect early basic research with clinical testing and includes activities such as target identification and validation, in vitro and in vivo screening, and even early-stage human clinical trials (Pisano, 2006). Transformation is then followed by exploitation if firms develop high impact technologies (e.g. new molecular entities) building on more fundamental basic
research findings, materializing in the development of new and marketable innovations in downstream markets (Zahra and George, 2002; Cassiman et al., 2008).

For firms with high scientific absorptive capacity, indirect collaboration with universities, through DBF mediated ties, is likely to have fewer advantages. Engagement in mediated ties may imply that firms miss out on key benefits of direct collaboration such as access to complementary expertise and skills, the possibility to keep up with major technological developments and achieve potential research synergies (Caloghirou et al., 2001) and access to embryonic inventions (Santoro and Gopalakrishnan, 2001; Colyvas et al. 2002; Hertzfeld et al., 2006). Indirect collaboration with universities may also imply that DBFs will be the party to get early access to embryonic inventions, and may be able to obtain the property rights of such university-developed technology earlier (Colyvas et al., 2002; Hertzfeld et al., 2006; Crespi et al., 2010). Scientific knowledge sourced through DBF mediated ties are also likely to be of a more general and noisier nature (Ahuja 2000; Vanhaverbeke et al., 2012), while firms with high scientific absorptive capacity can access and absorb more specialised and fine-grained scientific knowledge developed at universities through direct collaboration.

The above arguments suggest that for firms with high scientific absorptive capacity direct collaboration with universities is more likely to be associated with improved innovation performance than DBF-mediated ties to universities. This leads to the following hypothesis:

**Hypothesis 1**: For pharmaceutical firms with high scientific absorptive capacity, direct collaborative ties with universities have a stronger association with innovative performance than DBF-mediated ties with universities.
For firms with low scientific absorptive capacity, direct collaboration with universities is less likely to bring innovation benefits. These firms do not have a R&D organization that is well equipped to bridge institutional differences with academia and may lack the ability to effectively assimilate scientific knowledge. A lack of scientific absorptive capacity implies that bridging of both cognitive and institutional distance is beyond their capabilities. In addition, engagement in university collaboration will dislodge scarce resources from more fruitful applied research within these firms.

Instead, for firms with low scientific absorptive capacity, DBF mediated ties are a good alternative to access scientific knowledge. DBF mediated ties to universities can serve both as a ‘cognitive bridge’ and ‘institutional bridge’, avoiding the need for fundamental adaptations to their R&D organization necessary for direct collaboration. For these pharmaceutical firms, it is the indirect connection with universities that contributes to the build-up of potential absorptive capacity as it serves as an external channel for both the acquisition of key scientific expertise as well as its assimilation through interpretation and comprehension by DBFs (Zahra and George, 2002). The direct connection with DBFs contributes to realized absorptive capacity, as this collaboration process involves ‘translating’ basic scientific findings into implications for applied research as well as their exploitation through application and incorporation into the pharmaceutical firm’s products and processes (Calantone et al., 2002; Lane and Lubatkin, 1998; Zahra and George, 2002).

The strategy of DBF mediated ties to universities is consistent with the notion that brokerage between two unconnected partners is more valuable when behavioral norms and routines are more distant and that there is tacit knowledge involved (Hargadon and Sutton, 1997; Burt, 2007). As universities and firms with low scientific absorptive capacity exhibit substantial
differences in their norms and institutionalized practices and as the exchange of tacit knowledge is involved, these conditions apply well in this context. It follows that DBF-mediated ties are most likely to contribute to the innovation performance of firms with low scientific absorptive capacity, in comparison with direct university ties. This suggests the following hypothesis:

**Hypothesis 2**: For pharmaceutical firms with low scientific absorptive capacity, DBF mediated ties with universities have a stronger association with innovative performance than direct collaborative ties.

**DATA AND EMPIRICAL METHODS**

**Sample and Data.** We constructed a panel dataset (1995-2002) on 33 of the largest EU, US and Japanese pharmaceutical firms. The focal firms are vertically integrated firms engaged in later stage trials and marketing as well as drug research and development. The firms were identified as applicants of biotechnology patents (see below) and listed on the 2004 EU Industrial R&D Investment Scoreboard, which contains the top 1000 R&D spending firms both in Europe and the rest of the world. We collected information on the firms’ patent applications at the European Patent Office (EPO) at the consolidated level, i.e. taking into account patents of the parent firms and all their consolidated (majority-owned) subsidiaries. We also collected information on the scientific publication efforts of the firms. We extracted publication data from Thomson Reuters Web of Knowledge, including peer-reviewed papers of the types article, letter, note and review. Alliance data were drawn from the CATI database (Hagedoorn, 2002) on strategic alliances as well as the RECAP (Recombinant Capital) database. The latter alliance database is a source on publicly announced alliances in the
biomedical field collected from press releases, SEC filings, and industry presentations.

Information on branded and non-branded product sales and ongoing developments projects
was extracted from the Pharmaceutical Industry Database (PhID) developed by Pammolli et al
(2011). Finally, we collected accounting data from the Worldscope and Compustat databases.

The focus on pharmaceutical firms and the combined data requirements imposed several
sample screens on the data. We excluded non-integrated specialized biotechnology firms
(DBFs) among the focal firms, as well as firms chemical firms and firms focusing on
instrument development. A number of larger European firms (e.g. Astra Zeneca, GSK) could
not be included because they were involved in mergers during the period, hampering
performance analysis over time, and for several firms no information was available in the
Pharmaceutical Industry Database. This limited the sample for analysis to 33 firms based in
the US, Europe and Japan, resulting in an almost balanced panel dataset with 248
observations. Given the selection from the R&D scoreboard, R&D budgets of the firms tend
to be large, amounting to several hundreds of million dollars in 2002 and with Pfizer investing
more than 5 billion dollars in R&D in that year. Total 2002 R&D expenditures of the firms
amounted to more than 31 billion US dollars.

**Variables and Measures.** We measured the innovative performance of the sample firms (the
dependent variable) in a particular year as the count of the number of forward patent citations
received by the patents applied for by the firm in the biotechnology field in the year. We
measured patent citations over a fixed time window of 5 years. This ‘weighting’ by the
forward patent citations allows controlling for variation in the value and technological
importance of patented inventions (Harhoff et al, 1999; Hall et al, 2005). Specifically in the
context of drug development, recent research (Hiou et al., 2012; Magazinni et al., 2012) found
a strong relationship between patent citations and the later success (FDA approval) of the drugs that were developed based on the patented molecular entity. This suggests that patent citations can be seen as a ‘forward looking’ indicator of success in drug development.

The key independent variables represent the number of direct collaborative and DBF-mediated ties to universities. The number of direct R&D collaboration agreements with universities is calculated by drawing on the RECAP database on pharmaceutical collaborations, complemented with information from the Lexis Nexis database covering press releases, articles and reports related to the focal firms. We extracted the information from Lexis Nexis through text mining techniques, collecting those articles (press releases, trade journals, newspapers) covering the focal firms in the relevant timeframe and containing relevant keywords (university, R&D, collaboration). We subsequently read the selected articles to determine if these were reporting on research collaborations not yet covered in the RECAP data. Throughout, we focused on research collaborations and excluded licensing and other non-collaborative agreements, while limiting the count to alliances in the biotech field to maintain consistency with the focus of the dependent variable. In total, we identified 151 direct collaborations between universities and the focal firms.

We counted the number of active collaborations and ties in a year. We identified the first and final years of the period during which the agreements were valid if information was available. In case no information was available on the dissolution of agreements, the length of the agreement was assumed to be five years (Stuart, 2000; Lavie, 2007). Similarly, the number of mediated ties to universities brokered by dedicated biotech firms was measured as the number of research collaborations in biotechnology between universities and the DBF partners of the pharmaceutical firms – the latter identified in the CATI database.
We note that despite the use of multiple sources of data (RECAP as well as LEXIS NEXIS) the identification of research collaborations with universities is very likely to be incomplete. Furthermore, a limitation of our study is that we cannot take the differential importance and scope of the collaborations into account. We conducted additional analysis to assess the quality of the direct tie indicator. We used information drawn from the firms’ scientific publications to identify publications co-authored with university scientists, using string search algorithms. The information drawn from copublications broadly confirmed the accurateness of the collaborations included in the analysis: close to 90 percent of the direct ties to universities could be traced in copublications between the firm and university. At the same time, the copublications identified a range of other research linkages between firms and universities. In auxiliary analysis, we explored an augmented direct collaboration measure that also drew on copublication data. We required that published coauthored research focused on basic research and included multiple (a minimum of 5) copublications – to assure systematic research collaboration of some scope. This resulted in close to 125 additional ties that could be included in the new direct collaboration variable. Despite this substantial increase, the new variable was highly (83 percent) and significantly correlated with the original variable. Substituting the new variable, in addition to a corresponding new top-20 university variable, in the estimating models produced similar results as those reported in the paper below.

The key moderator variable in our analysis is a firm's scientific absorptive capacity. It is measured as the number of basic scientific publications on which the firm or its subsidiaries are listed as the affiliations of one of the authors in a prior 4-year period. Engagement in in-house scientific research as evidenced by scientific publications is a clear indication of the
presence of in-house scientists and an R&D organization facilitating the absorption and utilization of scientific knowledge (e.g. Gambardella, 1992; Cockburn and Henderson, 1998). To ensure that we measure in-house absorptive capacity and in order to avoid potential overlap with the collaboration variable, we limit the publications to those that do not list universities as collaborating institutions.

Furthermore, we focus on publications that can be regarded as ‘basic’ research, rather than publications that reflect the results of clinical trials. Engagement in basic research is closely aligned with the concept of scientific absorptive capacity as it measures the involvement in scientific discovery. Among scientific articles in the ISI database, a large share report on applied research activities, which in the context of the pharmaceutical sector relates to clinical trials (Hicks, 1994). Using information on the journals in which firms’ scientific articles are published and the CHI classification scheme for basic versus applied research (Hamilton, 2003), we constructed the indicator by focusing on the subset of scientific articles appearing in journals that are classified as reporting mainly on basic scientific research. The CHI classification, which was prepared for the National Science Foundation, distinguishes four research Levels in biomedical research: 1: Clinical Observation; 2: Clinical Mix; 3: Clinical Investigation; 4: Basic Biomedical Research. The scientific absorptive capacity variable includes level 4 publications only. Finally, we scaled the number of publications by the number of prior patent applications to ensure that it is reflective of the orientation towards scientific research of the firms’ R&D activities.

One concern regarding the collaboration variables is that there is heterogeneity in the ‘quality’ of the university partners that may affect innovation outcomes. We therefore included a variable measuring what share of direct and mediated ties, respectively, is with universities
listed in the top 20 of publishing universities in the relevant domain.\textsuperscript{2} We collected data on the number of publications in relevant fields (biosciences, general and internal medicine, medical specialties, biomedical research, chemistry) during the period of investigation. We accessed Thomson Reuters Web of Knowledge and extracted the number of publications of these universities that we identified as direct or indirect partners. The top publishing institutions were Harvard University, University College London, University of Tokyo, John Hopkins, University of Toronto, University of Washington, UCLA, UC San Francisco, University of Pennsylvania, and Imperial College. Other universities in the top 20 include Stanford, Yale, and Ludwig Maximilian University (Berlin).

We include a set of time-variant firm characteristics that are likely to affect the innovative performance of firms. We control for a firm’s research and development expenditures in the biotechnology field in the past year, since the technological performance of firms is influenced by the amount of capital invested in R&D activities. As data on R&D expenditures dedicated to biotechnology is not available, we approximate the relevant R&D input by multiplying a firm’s total R&D expenditures by the share of its biotechnological activity in its overall portfolio of technological activities. The importance of biotechnology activity is approximated by the share of biotechnology patents in the total number of the firm’s patents. The variable is taken in natural logarithm.

The analysis also controls for potential differences across firms in the propensity to patent (at the European Patent Office) by including the ratio of patents to R&D expenditures. The

\textsuperscript{2} Applying a top 10 criterion produced comparable empirical results.
number of inter-firm R&D alliances, or precisely, the number of cooperative research agreements in the biotech field with partner firms that are not collaborating directly on biotech research with universities, is added to the models to control for the influence of inter-firm technology alliances.

Two other variables are introduced to control for other aspects of firm heterogeneity: a dummy variable indicating whether the firm has non-branded products on sale as an indicator of the firm’s involvement in generic drugs, and a variable indicating the share of the firm’s drug development projects that reached Phase III of clinical trials. The latter variable may have a negative association with innovation performance if the absence of a pipeline of drugs nearing approval and market introduction puts additional pressure on pharmaceutical firms to develop new promising compounds with promising applications. On the other hand, the presence of a strong pipeline may indicate unobserved heterogeneity in drug development expertise.

Finally, the models include the main effect of scientific absorptive capacity, year dummies to account for time-specific factors that may affect the number of firms’ patents and citations, and fixed effects to control for time-invariant firm traits. Explanatory variables are measured (one year) prior to the dependent variable.

Summary statistics and correlations for the variables are provided in Table 1. The descriptives distinguish between ‘low’ scientific absorptive capacity firms and ‘high’ scientific absorptive firms, based on the median value of scientific absorptive capacity in the sample. The descriptives show that on average direct collaboration with universities is more common for high scientific absorptive capacity firms, while the average number of indirect ties is larger for low scientific absorptive capacity firms, although these differences are not overwhelming.
High scientific absorptive capacity firms only have a slightly higher share of top publishing universities among their direct collaborations, while indirect ties with top universities are slightly more common among low scientific absorptive capacity firms. Average R&D expenditures are roughly equal across samples. The major difference, naturally, is in scientific absorptive capacity, reaching a ratio of 2.45 publications over patents for high scientific absorptive capacity firms, versus 0.8 for low scientific absorptive capacity firms. The coefficients of correlation between the independent variables are moderate and do not suggest multicollinearity concerns.

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Methods. Since the dependent variable takes non-negative integer values, nonlinear count data models, such as Poisson or Negative Binomial specifications, are preferred over linear regression models as they explicitly take into account the non-negativity and discreteness of the dependent variable. The LR test for the assumption of the Poisson model that the variance of the dependent variable equals its mean (e.g. Cameron and Trivedi, 2008) rejected the null hypothesis that the dispersion parameter is equal to zero at the 1 percent level. We therefore employ negative binomial models that allow for overdispersion and generate efficient estimates. A concern with negative binomial models is that the specific modelling of the variance does not guarantee consistent estimates. We examined the potential bias in the estimates by conducting a test for equality of the coefficients obtained from the fixed effects negative binomial model and the fixed effects Poisson model. We could not reject the null hypothesis that the coefficients on the focal variables obtained via the two models were equal.
We conducted split sample analysis to investigate the heterogeneous effects of alliances for firms with different levels of scientific absorptive capacity. We divided the sample into two subsamples: firms with high and firms with low scientific absorptive capacity. For the division of the sample we used the median value of the firms’ scientific absorptive capacity as cutoff point.\(^3\) Hypotheses 1 and 2 are then tested by examining the coefficients for mediated collaborative ties and direct university collaboration for each subsample. We employed a ‘split sample’ analysis rather than including interaction terms for scientific absorptive capacity because a split sample analysis is the more general test specification when comparing coefficients between groups of observations (Hoetker, 2007). A split sample test does not assume that unexplained variance is identical between the two groups of firms (with high or low scientific absorptive capacity) and also allows for the impact of other characteristics to differ systematically between the groups, which leads to consistent within-group estimates. In this case, we preferred not to assume that all other determinants of innovative performance are equal between high and low absorptive capacity firms.

Although the models include a broad set of controls variables, we cannot exclude the possibility of unobserved heterogeneity resulting in endogeneity bias. Given the difficulty of finding a proper set of instruments for the collaboration variables to test and control for

\(^3\) This ensures a roughly equal number of observations in the subsamples, but otherwise remains an arbitrary categorization. We return to this issue in the supplementary analysis section.
endogeneity, we cannot claim that our analysis establishes causality. Hence, we interpret the estimates as partial correlations.

EMPIRICAL RESULTS
The results of the fixed effects Negative Binomial Analysis relating firms’ innovative performance to their collaboration strategies are presented in Table 2. Models 3 and 4 report the results for high scientific absorptive capacity firms and models 5 and 6 for low scientific absorptive capacity firms. For comparison, baseline models on the full sample reported in models 1 and 2. The first of each of these model pairs is a baseline model with control variables only.

The full sample model 1 shows positive and significant coefficients of engagement in inter-firm alliances, R&D expenditures, patent propensity, and scientific absorptive capacity, while the share development projects in Phase III is associated with reduced innovative performance. Adding the direct and mediated tie variables in model 2, the coefficient on mediated ties is significantly positive, but no significant association is found between direct university ties and innovation performance. This pattern changes markedly if we split the sample into two groups based on firms’ scientific absorptive capacity.

For high scientific absorptive capacity firms, the coefficient on direct collaboration with universities is positive and significant effect (model 4), while the coefficient on mediated ties also is positive and significant (at the 10 percent level). For low scientific absorptive capacity firms, indirect ties to universities have a significantly positive association with innovative performance, whilst the coefficient on direct collaboration is negative but insignificant. For high absorptive capacity firms, a t-test on the equality of the coefficients for mediated ties and
direct ties reject the null hypothesis of equality (a p-value 0.07), in support of Hypothesis 1. Hypothesis 2, however, finds no support: although the coefficients between mediated ties and direct collaboration have opposite signs and the coefficient on mediated ties is significant at the 5 percent level, a t-test cannot reject equality of coefficients. This is due to the substantial imprecision with which the coefficient on direct collaboration is estimated.

The coefficients on the share of top universities in the collaboration portfolio of firms are generally not significant, with one exception: the share of top universities among mediated tie partners is negative and significant for low scientific absorptive capacity firms, mitigating the positive association between mediated ties and innovation performance. This effect is relatively strong: The coefficients suggest that the positive implications of mediated ties disappear if about one quarter of these are with top universities. We return to this finding in the discussion.

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Insert Table 2 about here
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Given that the expected value of the dependent variable in the Negative Binomial model is $E(y) = \text{Exp}(Xb)$, the coefficients $b$ represent the pseudo elasticity of innovative performance (the number of citation weighted patents) with respect to the independent variables. The pseudo elasticity is the proportional increase in innovative performance due to a one unit increase in the independent variables. Hence, the coefficient on direct ties in model 4 suggests that an additional direct university tie is associated with a performance increase of 14 percent for high scientific absorptive capacity firms. For low scientific absorptive capacity firms (model 6), an additional indirect tie is associated with a 2.3 percent increase in performance.
**Supplementary analysis.** We examined differences between high and low scientific absorptive capacity firms by separating firms at the sample median. The median value to split the sample is a focal point given the limited number of firms we have in our sample and a desired balance in degrees of freedom across subsamples. Requiring lower or higher thresholds than the median leads to an imbalance in sample size, such that insignificant findings could also be due to the limited degrees of freedom. We experimented with thresholds for the sample split defining high scientific absorptive capacity firms in a more stringent or less stringent manner. The possibility to do so is limited as the number of firms in one of the subsamples quickly reduces to less than 10. While broadening the group of firms in a subsample generally gave consistent but somewhat weaker results, a smaller number of firms in the subsamples resulted in insignificance of the collaboration variables, suggesting that the models suffer from imprecision in the estimates due to the reduced degrees of freedom. We conclude that the relatively limited empirical base prevents us from gaining clear insight into the level of scientific absorptive capacity at which the relative benefits of direct and mediated ties occur.

**DISCUSSION AND CONCLUSION**

In the literature, two different views on firm-university collaboration co-exist. In the industry-science literature the importance of direct collaboration between firms and universities, particularly in knowledge-intensive industries, is endorsed (Cohen et al., 2002; Zucker and Darby, 2001; Zucker et al., 2002; Zucker and Darby, 2002). On the other hand, in the innovation and strategic alliance literature the role of brokerage through DBFs as specialized go-betweens is emphasized (Powell et al., 1996; George et al., 2002; Pisano, 1991; Stuart et al., 2007). Despite their different emphasis, both streams of research tend to
regard pharmaceutical firms implicitly as possessing similar in-house resources and capabilities to absorb state-of-the-art, scientific expertise, i.e. as possessing similar ‘scientific absorptive capacity’. Our findings suggest that this assumption of homogeneity may not hold among vertically integrated pharmaceutical firms.

We found substantial heterogeneity in the importance of in-house scientific research among pharmaceutical firms (our indicator of scientific absorptive capacity). This heterogeneity was associated with differences in the performance consequences of direct university collaboration and DBF-mediated ties. Specifically, for firms with relatively high scientific absorptive capacity, the association between direct collaboration and innovation performance was significantly stronger than the association between mediated ties and performance. For firms with more limited scientific absorptive capacity only mediated ties were significantly associated with performance - although the relative imprecision of estimates lent no support for the hypothesis that the association between performance and mediated ties was stronger than the association between performance and direct ties.

Our empirical findings on the influence of the scientific strength of the universities with which firms maintain direct or mediated ties were mixed. We did not observe a significant association between innovation performance and the academic strength of universities with which the focal firms established direct collaborations. In contrast, for low scientific absorptive capacity firms, the association between mediated ties and innovation performance was importantly diminished when firms connect to top research universities. An explanation for the latter finding is that even mediated ties, when they connect to state-of-the-art scientific research at top universities, may still confront low scientific absorptive capacity firms with cognitive and institutional obstacles to benefit from these ties, such that resources allocated to
these collaborations reduce overall effectiveness of the R&D and knowledge sourcing strategy of the firm (Rothaermel and Deeds, 2006). It is conceivable that DBFs involved in collaboration with top institutions are closer to basic science and perhaps less able to perform their mediation and ‘translation’ function. In this regard, one aspect lacking in our analysis is the specific role the mediators (DBFs) and their characteristics play in the effectiveness of the mediated tie. In general, examining the role of mediator characteristics presents itself as an interesting avenue for future research.

Our study is subject to a number of limitations suggesting that we have to interpret our findings with caution. It is likely that our measures of direct and indirect ties are incomplete and do not identify all (indirect) ties between firms and universities. In addition, the limited sample size of 33 firms may prevent capturing pharmaceutical firms’ heterogeneity regarding their scientific absorptive capacity in full. Both factors may play a role in the lack of precision in the estimate on direct ties for low absorptive capacity firms. The restricted empirical base also prevented us from gaining clear insight into the level of scientific absorptive capacity at which the relative benefits of direct and mediated ties occur, and limit the generalizability of our findings. Finally, our research is suggestive of associations between firm characteristics, collaboration strategies and innovation performance, but does not establish causal relationships.

With these caveats in mind, collectively our findings are suggestive of the importance of a ‘fit’ between the nature of a firms’ R&D organization and its collaboration strategy to access scientific knowledge. The existence of an alternative strategy to source scientific knowledge through indirect ties appears an overlooked issue in the industry-science literature and counters the common idea that in science-based industries, one should be proximate to, and
collaborate directly with public research organizations (Zucker and Darby, 2001; Zucker et al., 2002; Arundel and Geuna, 2004; Cassiman et al., 2008). Vertical specialization in the biopharmaceutical industry and the importance of DBFs in basic scientific research in close collaboration with universities provides pharmaceutical firms with an alternative route to benefit from scientific developments, without emphasizing investments in a science-oriented R&D organization.

Our research provides reflections on the still poorly understood relationship between the process of absorptive capacity and interorganizational networks (Volberda et al., 2010). Our findings are consistent with the notion that firms with high scientific absorptive capacity can rely on in-house scientists to perform a critical brokerage role by serving as external gatekeepers, contributing to the build-up of potential absorptive capacity (i.e. the acquisition and assimilation of key external scientific expertise) and as internal gate-keepers, contributing to the build-up of realized absorptive capacity (i.e. transformation and exploitation of key external scientific expertise). Firms with low scientific absorptive capacity externalize the absorption process through DBF mediated ties, while their collaboration with and the ‘translation function’ of the DBF is likely to enhance the creation of realized absorptive capacity (Zahra and George, 2002). The literature on absorptive capacity until now has focused on the different steps in the absorption process, such as recognizing, assimilating and applying external knowledge (Cohen and Levinthal, 1990) or the sequence of potential and realized absorptive capacity (Zahra and George, 2002). A clear understanding of what specific kind of knowledge gets absorbed, and what constitutes the specific capabilities to absorb this particular knowledge is much less developed (Volberda et al., 2010). Here we contribute by focusing on the absorption of scientific knowledge that requires critical in-house scientific
capabilities as reflected by the degree to which firms’ researchers are conducting basic scientific research independently.

Our study informs the literature on strategic R&D organization by highlighting the role of firm heterogeneity in organizing for scientific absorptive capacity, and how this affects firms’ ability to benefit from different collaboration strategies with universities in science based industries. Earlier studies have demonstrated that capabilities in basic R&D are associated with synergies between in-house R&D and external technology acquisition such as licensing and technology acquisition (Cassiman and Veugelers, 2006; 2009; Hagedoorn and Wang, 2012). Our results align with the notion that a choice for a particular organization of R&D will have important consequences for the effectiveness of different external knowledge sourcing strategies (e.g. Cassiman and Valentini, 2009) and that firms should strive for complementarity between internal R&D resources and capabilities, and alternative external collaboration strategies (Tzabbar et al., 2008; Rothaermel and Alexandre, 2009).

As noted above, the limitations of the current study suggest that more research is needed on the relationships between scientific absorptive capacity and direct and mediated ties to universities to establish the generalizability of our findings. Such research preferably focuses on a larger and more varied set of focal firms, while exploring more refined measures of collaboration. An interesting question is whether generalization is possible to other industries to the extent that these are also characterized by a key role of public research in industrial innovation and the presence of intermediary firms. Examples of this may be formed, among others, by microelectronics, advanced materials and nanotechnology (Lavie and Drori, 2011; Baba et al., 2009). Replication and extension of this type of study on (in)direct R&D collaboration with universities in other sectors and for broader sets of firms will help build
more insights into the importance of the various types of research collaborations and the
influence of public research on firms’ innovation performance.

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Table 1. Descriptive statistics and correlations
Table 2. Results of fixed effects negative binomial models of the innovative performance of pharmaceutical firms, 1995-2002

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<td>(0.0114)</td>
<td>(0.0170)</td>
<td>(0.0184)</td>
<td>(0.0152)</td>
</tr>
<tr>
<td>Biotech R&amp;D Expenditures</td>
<td>0.0861*</td>
<td>0.0825</td>
<td>0.0521</td>
<td>0.0409</td>
<td>0.2401**</td>
</tr>
<tr>
<td></td>
<td>(0.0501)</td>
<td>(0.0508)</td>
<td>(0.0712)</td>
<td>(0.0732)</td>
<td>(0.1016)</td>
</tr>
<tr>
<td>Patent Propensity</td>
<td>1.4290**</td>
<td>1.4870**</td>
<td>5.9890***</td>
<td>6.0473***</td>
<td>0.2614</td>
</tr>
<tr>
<td></td>
<td>(0.6584)</td>
<td>(0.6596)</td>
<td>(0.9018)</td>
<td>(0.9687)</td>
<td>(0.8542)</td>
</tr>
<tr>
<td>Scientific Absorptive Capacity</td>
<td>0.3226***</td>
<td>0.3370***</td>
<td>0.3053***</td>
<td>0.2909***</td>
<td>0.3916</td>
</tr>
<tr>
<td></td>
<td>(0.0814)</td>
<td>(0.0869)</td>
<td>(0.0974)</td>
<td>(0.1060)</td>
<td>(0.2740)</td>
</tr>
<tr>
<td>Phase 3 Development Projects Share</td>
<td>-0.8922</td>
<td>-1.1560**</td>
<td>-1.7559*</td>
<td>-1.5880*</td>
<td>0.1461</td>
</tr>
<tr>
<td></td>
<td>(0.5585)</td>
<td>(0.5724)</td>
<td>(0.9012)</td>
<td>(0.9032)</td>
<td>(0.6994)</td>
</tr>
<tr>
<td>Generic Drug Sales (Dummy)</td>
<td>0.0621</td>
<td>0.0832</td>
<td>0.0206</td>
<td>0.1375</td>
<td>-0.2424</td>
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<tr>
<td></td>
<td>(0.1886)</td>
<td>(0.1895)</td>
<td>(0.3423)</td>
<td>(0.3510)</td>
<td>(0.2521)</td>
</tr>
<tr>
<td>Year Dummies</td>
<td>Included</td>
<td>Included</td>
<td>Included</td>
<td>Included</td>
<td>Included</td>
</tr>
<tr>
<td>Constant</td>
<td>-0.1358</td>
<td>-0.1450</td>
<td>0.1035</td>
<td>0.0676</td>
<td>-0.6516</td>
</tr>
<tr>
<td></td>
<td>(0.3904)</td>
<td>(0.3899)</td>
<td>(0.5854)</td>
<td>(0.5842)</td>
<td>(0.6832)</td>
</tr>
</tbody>
</table>

No. of Observations | 248 | 248 | 127 | 127 | 121 | 121

No. of Firms | 33 | 33 | 17 | 17 | 16 | 16

Log Likelihood | -722.16 | -717.48 | -333.17 | -330.37 | -372.00 | -366.53

Wald Chi-square | 75.74*** | 86.65*** | 87.12*** | 97.21*** | 40.97*** | 56.98***

Notes: Standard errors in parentheses, * p<0.1, ** p<0.05, *** p<0.01