Network failure: Biotechnology firms, clusters and collaborations far from the world biotechnology superclusters

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This article traces the trajectory of biotechnology firms, clusters and collaborations in Australia between 2003 and 2014. Combining descriptive analyses, network visualizations and statistical modelling of longitudinal data collected from multiple sources, we investigate Australian firms' ability to overcome the three challenges characterizing biotechnology: first, accessing new knowledge and intellectual property; second, raising early-stage funding for timely product development; and third, bringing products to market. Like biotechnology firms worldwide, Australian firms adopt a network approach to success, relying on different types of collaborative ties with diverse partners to access complementary resources and facilitate learning and innovation. The aspiration here is a virtuous cycle, where networks promote innovation and innovation promotes networks, as occurs in the world superclusters. In contrast, our analyses show that the collaborations of Australian biotechnology firms produce not so much a virtuous cycle, as a dead end. Specifically, local collaborations with public research organizations generate network effects in meeting the challenges of new knowledge and early-stage funding, but do not extend to the challenge of bringing products to market. We link this 'network failure' to the limitations of public research organizations as anchor tenants with the capability to catalyze collaborations with distant partner organizations directed towards commercialization, in particular giant multinational pharmaceutical corporations. Our study enriches the substantial literature on networked innovation, which is biased towards celebrating the benefits of networks and collaborations for innovation and performance, particularly in biotechnology.

1. Introduction

Biotechnology has long been presented as the exemplar of a networked form of organization (Casper 2007; Gay and Dousset 2005; Liebeskind, et al. 1996; Powell, et al. 1996; Powell and Sandholz 2012) that is distinct from markets and hierarchies, grounded in trust and suited to advanced technology industries (Powell 1990). Dedicated biotechnology firms (DBFs) routinely form collaborative ties with diverse types of partners, thereby generating inter-organizational networks. An extensive literature celebrates how such networks promote learning, innovation and performance, giving rise to a virtuous cycle where networks promote innovation and innovation promotes networks (Baum, et al. 2000; Liebeskind, et al. 1996; Powell 1996). In contrast, this article presents an analysis of network failure, where collaborations produce not so much a virtuous cycle, as a dead end.

Existing research highlights three critical challenges for DBFs in leveraging their collaborative ties to succeed. These challenges are largely sequential: first, accessing a science base that generates new knowledge and intellectual property (Swann and Prevezer 1996; Zucker, et al. 2002); second, obtaining early funding for the timely development of a viable product (Bertoni and Tykvová 2015; Powell, et al. 1996); and third, navigating commercial and regulatory demands in taking the product to market (Powell, et al. 2005; Stuart, et al. 2007). Each challenge requires collaboration with other organizations that deliver complementary resources and expertise for resolution. While the challenges are interrelated, particular types of organizations are pivotal for particular challenges: most obviously, public research organizations for new knowledge, venture capital for product development, and giant multinational pharmaceutical corporations ('Big Pharma') for commercialization.

This article describes and analyzes how biotechnology firms in Australia address the challenges of new knowledge, product development and getting to market, paying particular attention to their collaborative networks between 2003 and 2014. Inspired by the literature on the network dynamics of biotechnology firms in the US (Powell, et al. 2005) and encouraged by diverse policy initiatives aiming to foster biotechnology in Australia, our project originally aimed to better understand the dynamics of growth among Australian firms (Ernst & Young 2006; Gilding 2008; Herpin, et al. 2005). Above all, it asked whether the

network dynamics that informed the creation and success of US biotechnology clusters, most famously the Boston and San Francisco Bay Area 'superclusters' (Nature Biotechnology 2007) also informed collaborations, clusters and networks in Australia. Beyond Australia, regional governments of many countries have a stake in this question, given their efforts to build biotechnology clusters and networks by policy design. A substantial literature maps their progress and challenges (Breznitz 2013; Fontes 2005; Gilding 2008; McKelvey, et al. 2003; Rees 2005; Trippl and Todtling 2007; Zylberberg, et al. 2012)

This article builds upon these studies. Australia makes an ideal case study, as its policymakers have developed a portfolio of policies aimed at emulating the US superclusters. At the same time, its distance from potential and actual partner organizations amplifies the challenges for its regional clusters (Gilding 2008). We demonstrate that between 2003 and 2014 Australian DBFs adopted a similar network approach to success as observed in biotechnology clusters worldwide. We find that the collaborations formed by Australian DBFs with local PROs yielded benefits in meeting the challenges of creating new knowledge and raising funds for product development, but did not provide pathways for meeting the challenge of commercialization. We link this 'network failure' to the absence of 'anchor tenants' (Powell, et al. 2012) with the capability to catalyze collaborations directed towards commercialization through deals with Big Pharma. Our findings indicate that the existing literature has been unrealistic about the prospects of regional clusters, distant collaborations and the benefits of networks far from the world's superclusters.

In section 2, we introduce the literature on biotechnology networks and clusters, including the US superclusters, the trajectories of regional clusters worldwide, and the Australian experience in particular. Section 3 describes our analytical approach, integrating three elements allowing for triangulation of our findings: in-depth descriptive analyses, network visualizations and statistical modelling of longitudinal data. Section 4 presents the findings of our threefold analysis to illustrate the trajectory of biotech collaborations in Australia in meeting the challenges of new knowledge, early-stage funding and commercialization. Finally, we discuss the implications of the findings for our understanding of networked innovation in regional biotechnology clusters in section 5.

2. Literature review

2.1 Biotechnology networks

Powell (1990) identifies networks as a form of organization distinct from market and hierarchy, where exchange depends upon trust. In turn, networks are especially suited to sourcing information through their connections between people and organizations. Specifically, 'information passed through networks is "thicker" than information obtained in the market, and "freer" than communicated in a hierarchy' (Powell 1990: 304). As a result, networks are of critical importance for high-technology industries in times of rapid innovation and uncertainty. During the 1990s and early 2000s biotechnology met these conditions in abundance and became the exemplar of a new networked form of organization (Casper 2007; Gay and Dousset 2005; Liebeskind, et al. 1996; Powell, et al. 1996).

Biotechnology refers to the use of biological sources, systems and processes for commercial purposes (Orsenigo 2001). In the 1990s and early 2000s it was commonly presented in Schumpeterian terms, as a 'competence-destroying innovation' built upon a different knowledge base to that of the pharmaceutical industry (Powell, et al. 1996: 117), giving rise to a 'biotech revolution'. Since then, this heroic account has given way to a more incremental view, which describes how drug development increasingly demanded a wider and more dynamic knowledge base, including inorganic chemistry, molecular biology and immunology (Hopkins, et al. 2007; Nightingale and Martin 2004). The upshot was the proliferation of small DBFs, which forged interorganizational collaborations directed towards development and commercialization. In this context, biotechnology is often described as a 'field' rather than an industry or sector, because the concept better captures the variety of organizations and actors that engage with each other across the extended product cycle (Powell, et al. 2005).

Powell et al. (2005) describe the logic of collaboration and networks in biotechnology as 'multiconnectivity'. Following this logic, DBFs form partnerships with diverse organizations, including public research organizations (PROs), government agencies, venture capital, Big Pharma and other bioscience firms. These partnerships are directed towards diverse purposes at different points of the pharmaceutical value chain, including

research and development (R&D), finance, complementary resources and skills, and commercialization. The establishment of one type of partnership fosters other types of partnerships (Miozzo and DiVito 2016), for example where ties with PROs facilitate partnerships with bioscience firms (Stuart, et al. 2007).

Collaborations in biotechnology are not just a vehicle to access missing resources, but also for learning and innovation (Baum, et al. 2000; Liebeskind, et al. 1996; Powell 1996). Rapid technological change means that no single firm can dominate the field on its own. Rather, innovation occurs across the network, at the interstices between DBFs, PROs, government agencies, venture capital, Big Pharma and other bioscience firms. For example, joint authorship of scientific papers serves 'to improve research and development productivity', maintaining ties with PROs, attracting talent and accessing external knowledge for innovation (Polidoro and Theeke 2012: 1135). In turn, firms develop their skills and routines for effective collaboration (Rothaermel and Hess 2007). The faster the learning, the better the performance – both because it pre-empts competitors addressing the same therapeutic needs and because the clock is ticking on patent protection (Hopkins, et al. 2013; Xu 2009).

Collaborations are also vehicles for reputation, legitimacy and judgements around performance (Higgins, et al. 2011; Nicholson, et al. 2005; Stuart, et al. 1999). In turn, because situations defined as real are real in their consequences – a classic sociological dictum – network ties influence performance. This is especially the case in biotechnology because its business model makes conventional business performance measures, such as profitability and revenue, mostly irrelevant. Specifically, biotechnology firms direct their efforts towards building the value of their product pipelines with a view to deals with Big Pharma and profitable exits. In the absence of conventional measures, 'value inflection points' (an industry term) are events that signal pipeline progress. They include raising substantial risk capital (DeCarolis and Deeds 1999), successful completion of clinical trials (Fazeli 2004; Hopkins, et al. 2013) and deals with Big Pharma (Nicholson, et al. 2005). At a more modest level, patent applications and authorship of scientific papers allow firms to highlight their 'innovation's uniqueness and to mitigate the threat of substitution' (Polidoro and Theeke 2012: 1135), thereby contributing to market value (Simeth and Cincera 2016). More

generally, partnerships across the board signal timely access to ideas and funds, reduced risk and promise of windfall gains.

2.2 Biotechnology superclusters

A powerful spatial logic informs biotechnology collaborations and networks. Above all, proximity facilitates tacit knowledge transfer (DeCarolis and Deeds 1999; Owen-Smith and Powell 2004; Swann and Prevezer 1996; Zucker, et al. 2002), which encourages start-ups to establish themselves nearby key partner organizations, most often PROs. Biotechnology worldwide is concentrated in the US. This is directly related to the three challenges; in particular, the US is an exemplar when it comes to continuous development of the science base, access to venture capital, and ease of movement between science and commerce (Pavitt 1998; Prevezer 2001; Senker 1996). In turn, biotechnology in the US is also concentrated around clusters.

The US superclusters warrant particular consideration, because they shape the aspirations of regional clusters and policymakers worldwide. Powell and his colleagues map collaborations in the Boston and Bay Area between the formative years of 1988 and 1999. In 1988 the Boston cluster was relatively sparse, 'stitched together' through DBFs' ties with PROs, notably MIT and Harvard, allowing access to a rich science base (Owen-Smith and Powell 2006). Partner organizations outside Boston, notably government agencies, venture capital and Big Pharma, were more diverse and offered benefits that were unavailable locally, including capital, specialist expertise and downstream support in new product development. A decade later, the regional network was more diverse and connected. DBFs now had ties not only with local venture capitalists, but also formed ties with each other, led by the most successful firms Genzyme and Biogen. In short, there occurred a transition from dependence upon PROs to a 'more market-oriented regime', where biotech firms played 'a connective role similar to the ones held by large companies in the trans-local network' (Owen-Smith and Powell 2004: 13).

In contrast, in 1988 DBFs and their local partners in the Bay Area formed small disconnected components, most commonly around venture capitalists, and to a lesser extent around PROs such as Stanford. During the 1990s, ties with venture capital underpinned rapid

growth and connectivity, supplemented by ties between DBFs, led again by the most successful firms, Genentech and Chiron. In contrast, ties with PROs remained secondary. By the end of the decade, venture capitalists played 'an important connective and prospecting role in this network', but the narrowness of their network portfolios indicated that innovation mostly arose from 'the dense and multiplex cluster of biotech to biotech ties' (Owen-Smith and Powell 2006: 72).

The Boston and Bay Area superclusters differed in what Powell et al. (2012) describe as their 'anchor tenants'. This concept draws an analogy from real estate, where a large department store in a shopping mall draws in customers who then patronize smaller specialty shops. In the biotech cluster, the anchor tenant 'sustains multiple principles of evaluation – in this case, world-class science, biomedical discovery, unmet medical need, or financial opportunity – and in so doing continually recombines and repurposes diverse activities' (Powell, et al. 2012: 439). In the Boston region anchor tenants were PROs; in the Bay Area they were venture capitalists.

There are common themes in the trajectories of the superclusters, nothwithstanding their differences. First, both locations featured outstanding PROs, which delivered the science base for new knowledge. Second, both locations featured sophisticated venture capital, which provided early-stage funding for product development. Third, both locations relied upon trans-local ties with Big Pharma in order to take their products to market. Their access to Big Pharma commercialization capabilities was facilitated by connections with PROs (Stuart, et al. 2007), Big Pharma's creation of local 'observatories' (Cooke 2005; Porter, et al. 2005), and successful DBFs' tendency to forge local ties with other DBFs, creating pathways between DBFs and Big Pharma for interactive learning and knowledge transfer.

2.3 Regional clusters

Since the mid 1990s regional governments around the world have forged policy frameworks directed towards emulating the superclusters. Their ambitions are overwhelmingly grounded in their PROs (Cooke 2007), which are a prerequisite of a successful cluster. In Portugal, for example, biotechnology firms originate in universities and research centres of the two major

cities (Fontes 2005). In Sweden, co-location deals are most commonly between firms and universities (McKelvey, et al. 2003). In Austria, local universities generate most spinoffs (Trippl and Todtling 2007). In Israel, the industry congregates around leading research institutes (Kaufmann, et al. 2003). In Southern Italy, a regional university underpins the activity of most firms, both as 'a key source of knowledge' and a vehicle to access 'other types of resources' (Capaldo, et al. 2015: 1392).

Some studies note that PROs on their own provide a poor foundation for biotechnology clusters. In the US, Powell et al. (2012) observe that regions dominated by a single type of organization, such as PROs, struggle to progress as clusters, perhaps because these organizations dominate at the expense of other players. In Italy and Europe generally, Orsenigo (2001) notes weak interactions between universities and industry. In Israel – celebrated as the 'startup nation' – Breznitz describes the local life sciences cluster, unlike ICT, as a 'knowledge-based cluster', dependent upon PROs. In turn, investment by venture capital is weak, and the industry 'appears to be stuck at the R&D stage', with 'almost no companies at the development, manufacturing, marketing, and sales stages' (2013: 33-5).

Whatever the case, regional clusters routinely experience local 'deficits' of ideas, expertise and money, above and beyond the local science base. These deficits extend much further downstream than those of the superclusters. As a result, regional governments and policymakers make 'repeated interventions' to substitute for local deficits, especially in relation to early-stage capital (Hopkins, et al. 2019: 1113). The results are often disappointing: for example, Wong (2011) describes the limits of Asia's 'developmental state' and Bertoni and Tykvová (2015) find that government investment vehicles in Europe have no impact on DBF invention and innovation (although they do boost the impact of private venture capital).

Local deficits cause regional biotech firms to cast a wider net in their pursuit of trans-local and international collaborations. In Canada, for example, national and international collaborations provide biotechnology firms 'with vital access to basic research, production expertise and finances that are locally scarce' (Rees 2005: 298). In Portugal, firms practice 'precocious internationalism' in the positive sense in order to 'overcome some of the relative disadvantages of their location' (Fontes 2005: 917), including forging ties with

distant venture capital. In Austria, cluster development depends upon 'distant knowledge sources' for 'scientific knowledge, managerial know-how as well as venture capital and qualified labour' (Trippl and Todtling 2007).

There are substantial challenges for regional clusters in forging trans-local and international collaborations directed towards later-stage commercialization. In Sweden, McKelvey reports that local Big Pharma 'are truly international firms and do not seem to have much connections with the Swedish development of, and markets for, knowledge' (2003: 498). In the UK, Hopkins et al. (2013) observe insufficient financial resources for UK biotech firms seeking to bring projects to late-stage development. In Portugal, Fontes highlights the importance of international mobility, facilitating 'extensive exposure of individuals and organizations to more advanced contexts' (2005: 915). In Germany, Al-Laham and Souitaris (2008) identify network structures that promote international research alliances: specifically, clusters with many international linkages, R&D collaborations with local research institutes and national partners, and a central position in the national research network.

A growing literature on 'territorial knowledge dynamics' is optimistic about the prospects of navigating distant collaborations. Crevoisier and Jeannerat (2009), for example, frame this process as a shift from the 'proximity paradigm' based upon cumulative knowledge to 'multi-location milieus' grounded in combinatorial knowledge. Similarly, Butzin and Widmaier observe that 'in a world of endless possibilities and global knowledge sources', regional players must be able to take knowledge from its geographical origin and 'anchor it within a regional context' (2016: 223). For biotech firms, this demands absorptive capacity (Gertler and Levitte 2005: 487) and the ability to 'recontextualize and diffuse' imported knowledge in place (Vale and Carvalho 2013: 1021). This literature focuses overwhelmingly upon the creation of new knowledge rather than its commercialization. It is uncertain whether 'precocious internationalism' or 'multi-location milieus' provide a foundation for commercially successful regional clusters.

2.4 Biotechnology in Australia

From the 1980s Australian governments – federal and state – adopted a neo-liberal policy framework, which privileged markets over government (Pusey 1991). In line with this policy, they sold major government enterprises, including CSL, a producer of vaccines and blood-related products. During the same period, governments adopted the vision of becoming an 'innovation economy' (Australia 2001; Dodgson, et al. 2011; Henderson 2015; Victoria 2001). Consistent with the neo-liberal framework, this vision was guided by the principle of market failure: that is, government spending was directed towards activities in which it was believed that private firms were disinclined to invest (Dodgson, et al. 2011).

Advocates of the innovation economy – politicians, policymakers, scientists and industry players – consistently promoted biotechnology as a particular opportunity for Australia. This was on account of its 'strong regional research capability' (Barlow 2010: 4; Petersen and Krisjansen 2015), exemplified by distinguished scientists (from the inventor of penicillin Howard Florey, to the inventor of the human papillomavirus vaccine Ian Frazer), Nobel Prizes (seven in medicine and physiology since World War 2), and world-class public research organizations (such as Monash University in Melbourne, a pioneer of IVF technologies worldwide). The advocacy of Australia as a biotechnology hub reached its high watermark in the early 2000s. For example, a landmark federal government report – *Backing Australia's Ability: An Innovation Action Plan for the Future* – declared the ambition 'to strengthen Australia's research capability, to ensure the flow of new ideas which underpin innovation, to create critical mass in leading research fields, and to build competitive advantage in ICT and biotechnology' (Australia 2001: 15). Similarly, the state government of Victoria announced its aspiration to become one of the world's five top biotechnology locations by 2010 (Victoria 2001: 2).

In turn, governments took measures to support the vision of a biotechnology hub. Above all, they concentrated their investment in research and development (strengthening Australia's science base), on the basis that private firms under-invest in knowledge creation due to its inherently uncertainty and only partially excludability. High-profile initiatives included the launch of three new dedicated research institutes: the Institute for Molecular Bioscience at the University of Queensland in 2000, the Bio21 Molecular Science and

Biotechnology Institute at the University of Melbourne in 2002, and the Australian Stem Cell Centre at Monash University in 2003.

Governments also directed support to firms in the early stages of their development to help them survive the so-called 'valley of death'. In particular, they operated a succession of direct grants programs and venture capital co-investment schemes (Cumming and Johan 2009; Cumming and Johan 2016). Government commitment to these activities – consistent with the logic of market failure – was justified in terms of 'spillover effects', but was qualified, parsimonious and uneven. This was exemplified in a Productivity Commission (2007: 588) report, which concluded that the main direct grants scheme (Commercial Ready) 'supports too many projects that would have proceeded without public funding assistance', whereupon the government axed it (McNaughton 2009). Similarly, a government-funded venture capital co-investment program called the Innovation Investment Fund was validated for its effectiveness in 'supporting firms that would otherwise not exist' and compared favourably with government venture capital programs in Europe (Cumming and Johan 2016: 56), but struggled to obtain legitimacy and scale (AVCAL 2017).

Throughout the period, a small but steady stream of evidence-based research questioned the 'promissory' rhetoric of politicians, policymakers, scientists and industry players (Petersen and Krisjansen 2015). In the first instance, studies noted deficits pertaining to the fund-raising challenge, notably the underdevelopment of venture capital and the over-resort to IPOs as a substitute (Herpin, et al. 2005; Lerner and Watson 2008; Vitale and Sparling 2004). As firms and clusters struggled to progress, researchers identified a wider variety of deficits, including those pertaining to the challenges of new knowledge and getting to market. Barlow (2010) compared unfavourably the science base of the three main clusters in Australia (Melbourne, Sydney and Brisbane) with San Diego, one of the largest clusters in the US outside the superclusters. Gilding (2008) highlighted the 'tyranny of distance' in navigating later-stage commercialization, as a result of which international collaborations with Big Pharma were 'far-flung and diffuse', and thereby 'precarious and vulnerable'. More generally, Marceau (2007) questioned the effectiveness of government policy in addressing the science base, early-stage capital and commercialization.

From the late 2000s, the promissory rhetoric of advocates for Australian biotechnology became more qualified, but nonetheless persisted. In 2011, for example, a government report from the state of Victoria described biotechnology as a 'vitally important' industry and an 'area of competititive advantage for the State, with the potential to make a major contribution to future economic growth and increased productivity' (Victorian Government 2011: 6). Similarly, a 2016 industry report described biotechnology as 'front and centre of Australia's post-mining boom economic transition' and a 'pivotal contributor to Australia's economy' (Grant Thornton 2016). Yet, there is a gap between rhetoric and reality. The prospects of Austrialian DBFs remain uncertain. This article is the first longitudinal study of biotechnology networks in Australia and provides a more robust foundation for regional policy-makers with ambitions of emulating the superclusters.

3. Methodology

3.1 Research design and data collection

The design of this study draws heavily upon the landmark longitudinal research by Powell and colleagues in the US that mapped the trajectories of biotech firms, clusters and networks between 1988 and 2002 (e.g., Padgett and Powell 2012; Powell, et al. 2002; Powell, et al. 1996; Powell, et al. 2005). That project tracked the development of the entire US biotechnology field, but directed particular attention to the formation of the Boston and Bay Area superclusters (Owen-Smith and Powell 2004; Owen-Smith and Powell 2006; Porter, et al. 2005). Following the US project, we map the development of the entire Australian biotechnology field from 2003 to 2014. We start in 2003 because in this year its DBFs were roughly the same age, size and scale as DBFs in the US superclusters in 1988 (Herpin, et al. 2005; Owen-Smith and Powell 2006; Powell, et al. 1996). In addition, we direct particular attention to the three main concentrations of biotechnology in Australia, in Melbourne, Brisbane and Sydney.

We also follow the US project in our definition of DBFs as 'independently operated, profit-seeking entities involved in human therapeutic and diagnostic applications of biotechnology', where biotechnology refers to the use of biological sources, systems and

processes. That is, we do not include firms in veterinary, agricultural or environmental biotechnology, because they 'draw on different scientific capabilities and operate in quite different regulatory climates' (Powell, et al. 2005: 1148). We assembled a list of all 214 DBFs active in the time period under investigation amounting to 1592 DBF-year observations. We collected information on the DBFs and their collaborations from a variety of sources. Unlike the US project, there was no private industry directory available on which we could rely. Rather, all information was manually assembled from a range of sources, including the online membership directory of the peak industry organization AusBiotech, company websites, government reports, the business press and stock exchange reports. Patent information was retrieved from the EPO Worldwide Patent Statistical Database (PATSTAT). Information on scientific publications was collected from Web of Science, and journal impact factors (JIF) were obtained from the Journal Citation Reports provided by Clarivate.

Following the example of Powell et al., we collected data on different types of interorganizational collaborations, defined as 'any contractual agreement to exchange or pool resources' between a biotechnology firm and a partner organization (2005: 1149). We validated the assembled data on DBF collaborations through a survey of all biotechnology firms in 2004 (response rate 51 percent), 2007 (28 percent) and 2009 (18 percent). The survey consistently indicated that the public record over-states collaboration, presumably because firms are motivated to promote collaborations as signals of value creation, but unmotivated to promote their termination for the same reason. These dynamics informed the declining response rate, as the industry's fortunes declined. On this account, a conservative view of collaborations is adopted for all years under investigation, requiring strong evidence of a current partnership.

We combine rich descriptive analyses, data visualizations and statistical modelling to provide a comprehensive analysis of how Australian DBFs addressed the three challenges, that is, accessing and creating new knowledge, raising early-stage funding, and commercialization.

3.2 Dependent variables

For our statistical models, we consider three distinct dependent variables, one aligned with each of the challenges that DBFs need to overcome. Concerning new knowledge and acquiring a science base, we follow Aharonson et al. (2008) and consider DBFs' *number of patent applications* in a given year as a proxy for DBF inventive productivity. Patent application rates do not necessarily reflect new product development output or commercialization (Trajtenberg 1990), but they are a useful indicator of DBFs' new knowledge.

With regard to early-stage fund-raising, we capture whether or not a DBF was able to forge a *risk capital deal* as a dependent variable. This variable was coded as 1 for a given year if a DBF entered a collaboration with a financial partner or made an Initial Public Offering (IPO), as both events reflect significant financing events for DBFs.[1]

Concerning their ability to scale up and get to market, we investigate whether or not a DBF was able to forge a *deal with Big Pharma* in a given year as a critical value inflection point. To reduce potential endogeneity problems (Abdallah, et al. 2015), we introduce a time lag and measure all dependent variables in year t+1.

3.3 Independent variables

Following Powell and colleagues, we distinguish between different types of collaborations, delivering different types of resources and capabilities, specifically R&D, financial, licensing, commercial and grants. In some instances, single partnerships deliver multiple resources and capabilities. In these instances, the partnership type is classified as commercial. Moving beyond Powell and colleagues, we also consider co-authorship of scientific articles as a type of collaborative partnership that signals science capability, enhances R&D productivity and highlights the uniqueness of innovations (Polidoro and Theeke 2012). Moreover, we distinguish between different types of partner organizations: PROs (including universities, research institutes and hospitals), financial institutions (principally venture

[1] We aggregated the two because there were only 16 instances in which DBFs went public in the period under observation. Robustness checks using only agreements with financial partners yielded similar results to the ones presented in section 4.

capital), government agencies, as well as private bioscience firms, namely Big Pharma (all firms included in the Pharmexec Top 50 Pharmaceutical companies list between 2003 and 2014), second-tier pharmaceutical firms, overseas DBFs, and other bioscience firms. Finally, we have a category for other partner organizations, typically private non-bioscience firms and not-for-profit organizations.

Further following Powell and colleagues, we classify DBFs by their location in Australia. All are located in (or occasionally nearby) major population centres: the state capitals of Melbourne (Victoria), Sydney (New South Wales), Brisbane (Queensland), Perth (Western Australia) and Adelaide (South Australia), and the national capital of Canberra (in the Australian Capital Territory). We also identify the relative location of partner organizations, distinguishing between local, interstate and international. Most studies, including the US project which provides the template for this study, distinguish between local and trans-local ties (e.g., Owen-Smith and Powell 2004). Local ties, which are characterized by propinquity and enabling face-to-face communication, generate local networks, commonly described as clusters. Trans-local ties are any ties above and beyond local ties, forging networks that extend cluster capabilities. Yet this duality obscures the difference between collaborations within the same jurisdiction – and thereby the same national innovation system – and those located in other national jurisdictions. As a result, the current study introduces a further distinction between interstate and international ties, which is especially relevant in the in the Australian context characterized by the 'tyranny of distance' (Gilding 2008). This distinction captures not only the effects of national innovation systems, but also different degrees of geographic, jurisdictional and cultural distance in trans-local ties.

We use these detailed distinctions in our descriptive and visual analyses. Moreover, we incorporate them into our statistical models as the following independent variables. First, we account for the overall number of *collaborations*, which reflects DBFs' network centrality (Powell, et al. 1996). We also consider the *proportion of international collaborations* of a DBF as well as *network portfolio diversity* calculated as Blau's heterogeneity index (Blau

1977) accounting for the different types of partnerships (Powell, et al. 1996).[2] Moreover, we consider *partner popularity*, calculated as the average number of collaborations formed by the partner organizations of a DBF with other DBFs in the sample.

Based on the three challenges we identified, we further account for the following specific collaborative arrangements. Most relevant to the science base, we consider *R&D collaborations* and *co-authorships* – in an aggregated fashion as well as differentiated in terms of local, interstate and international collaborations. In a similar manner, we account for *financial collaborations* instrumental for the timely development of a viable product. We also consider whether DBFs received *AusIndustry grants.* Finally, we consider the number of DBF collaborative ties with other *domestic DBFs* and the number of their connections with *international private bioscience partners* – specifically, Big Pharma, tier two pharma, other biotech firms, and other bioscience firms – as potential drivers of commercialization success.

For our statistical models, we followed previous research (Alnuaimi, et al. 2012; Jong and Slavova 2014) and calculated all independent variables described here by aggregating observations over a three-year window.

3.4 Control variables

To account for the underlying science base, we control for DBFs' annual number of *publications* weighted by JIF following the procedures described in McFadyen and Cannella (2004) and Toole and Czadmtziki (2010) and aggregating observations over a three-year window. Moreover, we created a dummy variable to capture whether the *founder* of a DBF was affiliated with a PRO before or during the creation of the DBF as a reflection of academic entrepreneurship.

We further control for DBF *age* measured in years since incorporation and for whether a DBF is *listed* on the Australian Stock Exchange (ASX). In the absence of more detailed information, we control for DBF *size* as a dummy variable comparing (0) small to

[2] We also calculated a diversity index for types of partners, which was highly correlated (r = 0.78) with our measure of network diversity for types of ties and, therefore, decided not to include both into our statistical models.

(1) medium to large firms. This distinction was determined using the selection criteria and classification systems adopted by Bureau van Dijk (MintGlobal database) and the Australian Securities and Investments Commission (ASIC), including assets, revenue and number of employees. We control for whether a DBF was active in (0) human therapeutics or (1) *diagnostics* and whether it belonged to the Melbourne, Sydney, or Brisbane cluster.

Consistent with our dependent variables, we also account for the number of *patent applications*, whether or not a DBF was able to forge a *risk capital deal* or a *Big Pharma deal* aggregated over a three-year window. Table 1 provides an overview of all variables used in our statistical models.

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3.5 Methods of analysis

Descriptive analyses include consideration of DBFs, partner organizations, partnership types and geographic location. Visualizations provide a vehicle to consider network structure, including main components, density and connectivity. All network visualizations were created using Visone 2.17. For statistical analyses we used Stata 14.

Our sample for the statistical estimations consisted of unbalanced pooled cross-sectional panel data with DBF-years representing observations. Due to the introduced lag structure, we needed at least four observations per DBF to specify our models. Therefore, 175 DBFs (987 DBF-year observations) enter the statistical analyses. Following previous studies on the role of networks for innovation and using comparable dependent variables (e.g., Guan and Liu 2016; Liang and Liu 2018; Yayavaram, et al. 2018), we rely on a random-effects specification[3] for our statistical models to control for unobserved heterogeneity. An advantage of the random effect specification is that it allows us to account for time-invariant predictors of our dependent variables. Moreover, as emphasized by Guan and Liu (2016) using a similar observation period to ours, the fixed effect specification can lead to biased estimates for panel data covering relatively short periods of time (Greene 2003). We estimate

[3] Many scholars employ a Hausman test to decide between random and fixed effects estimation (e.g., Gilsing et al. 2008). However, as detailed by Liang and Liu (2018), this approach is increasingly criticised as being neither necessary nor sufficient for deciding between random and fixed effects (e.g., Bell and Jones, 2015; Clark and Linzer, 2015).

cluster-robust standard errors to adjust for potential within-firm correlation to account for the non-independence of repeated observations on each DBF.

Our first dependent variable, the number of patent applications, is a count variable. As we observed overdispersion, we utilize negative binomial rather than a Poisson model to investigate the factors affecting Australian DBFs' ability to overcome the science base challenge. Specifically, we run negative binomial panel models using the generalized estimating equation (GEE) algorithm to be able to include cluster-robust standard errors.[4] Risk capital and Big Pharma deals are measured as binary dependent variables. Accordingly, we rely on logistic panel regression.

Descriptive statistics and correlations between all variables used in the statistical models can be found in Table A1 in the appendix. An inspection of the correlation coefficients revealed high correlations between DBFs' number of international private bioscience partners and their overall number of collaborations (r = .72) and the number of JIF-weighted publications and co-authorships (r = .90), raising concerns of multicollinearity. To further substantiate these concerns, we ran OLS regressions to generate variance inflation factors (VIFs) for all variables (Hair, et al. 2010). The highest VIF was 6.77 with an average of 2.40 (independent variables in Models 2 below) and 6.92 with an average of 2.28 (independent variables in Models 3) for models including all four variables. When dropping collaborations with international bioscience firms and JIF-weighted publications, the highest VIF drops to 4.35 with an average of 1.99 (Model 2) and 4.46 with an average of 1.99 (Model 3). Based on these figures, we decided not to include collaborations with international bioscience firms and number of JIF-weighted publications in our statistical models but integrate them into our descriptive and visual analyses.

[4] In STATA 14, cluster-robust standard errors cannot be computed for negative binomial panel regressions. Robustness checks using a pooled cross-sectional model specification with cluster-robust standard errors yielded largely comparable results.

4. Firms, clusters and networks 2003-14

In the following, we present the results of our threefold analysis, grounded in descriptive statistics, network visualizations and inferential statistics. We first describe the overall distribution and trajectories of Australian DBFs between 2003 and 2014. Then, we analyze how Australian DBFs were able to address the three challenges – access to new knowledge, funding for product development and commercialization – through their collaborative partnerships.

4.1 Firms

Between 2003 and 2014, 214 therapeutic and diagnostic DBFs operated in Australia. In 2003 there were 130; the number progressively rose to 167 in 2006 and then declined to 104 in 2014. There were 84 startups and 110 exits across the period. Between 2003 and 2006, startups exceeded exits, whereas from 2007 exits exceeded startups.

All DBFs were located in or nearby six cities: five state capitals – Melbourne, Sydney, Brisbane, Perth and Adelaide – and the national capital Canberra. As illustrated in Figure 1, three-quarters of the firms were concentrated in the eastern seaboard cities of Melbourne, Sydney and Brisbane.

--- Insert Figure 1 about here ---

Startups between 2003 and 2006 were concentrated in Melbourne and Sydney; exits between 2007 and 2014 were concentrated in Melbourne and Brisbane. Overall, Melbourne was the main location of biotech firms across the period, peaking at 64 DBFs in 2006 and bottoming at 40 in 2014. Brisbane tumbled from 34 DBFs in 2006 to 10 in 2014. Sydney replaced Brisbane as the second largest concentration of firms, peaking at 31 DBFs in 2006 and easing to 27 in 2014.

During the same period, success indicators linked to the three challenges followed the same broad trajectories. Patent applications by Australian DBFs crashed, from 49 in 2003 to four in 2014. The number of early-stage risk capital deals peaked at 27 in 2005 and bottomed at two in 2014. The number of firms in partnership with Big Pharma almost doubled from 16 in 2003 to 29 in 2006, but then fell to 23 in 2014.

There were just three successful exits across the period. In 2007, the Melbourne-based wholesaler Sigma Pharmaceuticals acquired Melbourne-based Orphan Holdings for A$107 million. In 2011, the Dutch bioscience corporation Qiagen acquired Melbourne-based Cellestis for A$341 million. In 2014, the Irish Big Pharma Shire PLC acquired Melbourne-based Fibrotech for A$75 million. There were also some firms that promised breakthrough therapeutics; notably, Melbourne-based Biota (for avian flu), Acrux (for testosterone replacement) and Mesoblast (for regenerative stem cell therapeutics). Yet none of these firms delivered on that promise and in each case, their valuations declined dramatically after an ephemeral peak.

4.2 Science base

The science base is a pre-condition for biotechnology clusters to emerge and flourish (Feldman 2000; Swann and Prevezer 1996). Superclusters in the US are distinguished by outstanding PROs; more generally, clusters worldwide are underpinned by R&D collaborations and joint publications with local PROs. In Australia, a majority of DBFs originated in a PRO. Specifically, 133 DBFs (62 percent) had a founder drawn from a local PRO. Moreover, 72 DBFs (34 percent) actively engaged in the publication of scientific articles, of which more than a quarter were published in elite journals (among the top 5 percent based on JIF for each year of observation). Between 2003 to 2014, they published 687 papers, of which 88 percent were co-authored. Two thirds of co-authorships were with scientists from Australian PROs. Overall, 146 PROs nationwide collaborated with DBFs through different types of partnerships. Of these PROs, 51 were located in Melbourne, 45 in Sydney and 18 in Brisbane. PROs were responsible for more than two-thirds of local ties with DBFs.

By implication, PROs were the ‘glue’ that held clusters together. In particular, major universities, such as Monash University (Melbourne), the University of Sydney and the University of Queensland (Brisbane), were the most connected organizations in each city. Following Owen-Smith and Powell (2004), we demonstrate the pivotal role of PROs for regional clusters by removing them from data visualizations of local collaborations. Data visualizations for 2006, the peak of biotechnology activity across the period, highlight how

collaborations give rise to networks, forging pathways between DBFs. In Melbourne, 78 percent of DBFs are reachable through the 'main component' of DBFs and partner organizations; in Brisbane, 79 percent are reachable; and in Sydney 52 percent are reachable. When PROs are removed from visualizations, this connectivity dissolves as local networks decompose into multiple disconnected components across all three clusters. This pattern becomes even more pronounced across the period. In 2014, the connectivity of firms largely disappears in the absence of PROs. Figure 2 illustrates this for the Melbourne cluster. For all visualizations, comparable figures for Sydney and Brisbane can be found in the online supplement.

--- Insert Figure 2 about here ---

Notwithstanding the dominance of PROs in local networks, DBFs also routinely forged ties with interstate and international PROs in order to access specialist capabilities as required. In 2006, for example, Australian DBFs had 227 ties with local PROs, 123 ties with interstate PROs and 109 ties with international PROs. On the one hand, the roughly equivalent number of trans-local ties (232) over local ties (227) highlights the search for specialist knowledge irrespective of location. On the other, the greater number of domestic ties (350) – local and interstate combined – over international ties (109) highlights the pivotal role of PROs in the Australian biotechnology field. Across the period, the number of ties with PROs diminished across the board, but the weightings of local, interstate and international ties stayed the same.

Our statistical analysis highlights the importance of local collaborations, particularly co-authorships and R&D collaborations with local PROs, to access new knowledge. Table 2 contains the results of the negative binomial regression models for DBF patent applications as an indicator of their inventiveness. The Wald χ^2 statistics indicate that all models were highly significant ($p < 0.01$). Model 1 contains the control variables; Models 2 and 3 add the independent variables. Model 2 shows that the number of co-authorships with scientists from PROs significantly influences patent applications, but the number of R&D collaborations does not. Model 3, which introduces a distinction between local, interstate and international partnerships, shows that the number of local co-authorships significantly influences patent

applications. Domestic (local and interstate) financial ties also positively influence inventiveness. Otherwise, there are no network effects influencing DBFs' inventiveness.

--- Insert Table 2 about here ---

4.3 Early fund-raising

Local venture capital is a common theme among the US superclusters, but not among aspiring regional clusters worldwide. In Australia between 2003 and 2014, early-stage fund-raising was overwhelmingly a domestic phenomenon. Specifically, venture capital and other providers of early-stage finance operated at both local and interstate levels. At the local level, DBF ties with financial entities were the second most common form of collaboration, after PROs. At the national level, ties with financial entities were the third most common form of collaboration, after ties with federal government agencies headquartered in Canberra and ties with interstate PROs. Providers of early-stage finance were rarely international. In 2006, for example, Australian DBFs had 114 ties with financial entities altogether, of which 50 were local, 55 were interstate, and only 9 were international.

The providers of early-stage finance were diverse, but public investment is a common theme. Consider, for example, the 41 domestic providers of early-stage finance in 2006. Of 41 providers (concentrated in Melbourne and Sydney), nine (located in Melbourne, Sydney and Brisbane) were responsible for more than half of all ties. Of these providers, four were boutique venture capital firms, two were listed firms specializing in biotech, two were listed financial firms with a suite of investments, and one, the Queensland Investment Corporation (QIC), was a state government investment fund. Brisbane-based QIC was the single most connected provider of early-stage capital; Melbourne-based Uniseed, a university-funded boutique venture capital firm, was the second most connected; and two other boutique firms – GBS in Melbourne and Start-Up Australia in Sydney – were co-funded by the Australian Government through the Innovation Investment Fund.

As illustrated in Figure 3, ties between Australian DBFs and domestic finance providers rose between 2003 and 2006, but thereafter declined. Throughout the period, networks arising from these ties were sparse, heavily dependent upon a few well-connected finance providers, such as QIC, Uniseed, GBS and Start-Up Australia. At the local level,

these patterns were amplified, as additional visualizations for Melbourne, Sydney and Brisbane in the online supplement illustrate. Collaborative ties between DBFs and venture capital potentially presented opportunities for introductions to additional financial providers. Otherwise, PROs – through their pivotal position in regional clusters (Figure 2) – had the potential to instigate connectivity within the network and bring emergent DBFs and financial providers closer together.

Aside from support for venture capital, government agencies also provided modest support for early-stage product development in the form of direct grants. In the mid 2000s the federal agency AusIndustry was the most connected organization in the Australian biotechnology network through four different schemes. In 2006, it funded 64 DBFs (roughly one-third of all firms), concentrated in Melbourne (24), Brisbane (12) and Sydney (11). Some state governments also provided grants on a smaller scale. The closure of the Commercial Ready scheme effectively amounted to the withdrawal of government from direct grants for early-stage support. The number of federal government grants provided by AusIndustry fell from 64 in 2006 to zero in 2014, and state government grants fell from 18 to six. By implication, the institutional logic of government support for biotechnology shifted further towards the creation of new knowledge at the expense of early-stage development of a timely product.

--- Insert Figure 3 about here ---

We use statistical modelling to investigate network effects on DBFs' ability to access early-stage financing. Table 3 presents the results of the logistic regression models explaining whether or not DBFs were able to forge a risk capital deal as required for the timely development of a viable product. The Wald $\chi 2$ statistics indicate that all models were highly significant ($p < 0.01$). Model 1 contains the control variables; Models 2 and 3 add the independent variables. Results indicate that financial collaborations and public listing at the Australian Stock Exchange increase the chances of risk capital deals. In addition, having a founder with a PRO background and collaborative ties to domestic DBFs have a positive impact. Other than that, there are no network effects influencing DBFs' ability to forge a risk capital deal.

--- Insert Table 3 about here ---

4.4 Commercialization

Clusters depend upon trans-local ties with Big Pharma for later-stage development and commercialization, but the most successful generate their own biopharmaceutical corporations ('Big Biotech') and attract observatories from Big Pharma. Melbourne-based CSL, which is primarily a manufacturer of blood products and vaccines, is the only Australian Big Pharma included in the Pharmaexec Top 50 list, with more than 13,000 employees in 27 countries. Over the entire period from 2003 to 2014, CSL had collaborations with 12 Australian biotech firms (five based in Melbourne), more than any other Big Pharma worldwide. Of these collaborations, seven (three in Melbourne) were directed towards later-stage commercialization. CSL's local ties highlight the advantages of geographical proximity and its promise as a vehicle for commercialization. Yet CSL became no more embedded – locally or nationally – across the period. On the contrary, in 2006 it had three commercial ties with three Australian DBFs (two in Melbourne) and in 2014 it had none.

In this context, DBFs turned their attention towards international partnerships, overwhelmingly concentrated in the US and Europe (as illustrated in Figure 4). Between 2003 and 2006, the number of DBF international ties more than doubled, from 210 to 463; thereafter they declined to 350 in 2014, albeit more gradually than domestic partnerships. As a result, the proportion of DBFs with international ties rose from 40 percent in 2003 to 69 percent in 2014, and the proportion of international ties rose from 34 percent of all ties to 56 percent in the same period. More than half of these ties were with private bioscience firms, mainly commercial; most of the balance were with PROs, mainly research and development. Only a tiny proportion of international collaborations were with Big Pharma. In 2006, for example, DBFs had 281 ties with private bioscience firms and 109 with PROs not located in Australia. Of ties with private bioscience firms, 42 were with Big Pharma, 43 with second-tier pharmaceutical firms, 46 with other biotech firms and 150 with other bioscience firms. At the same time, ties with international bioscience firms and PROs presented potential pathways to deals with Big Pharma.

--- Insert Figure 4 about here ---

Between 2003 and 2014, 65 DBFs – more than a quarter of all firms – forged ties with Big Pharma. In nearly all instances (58), their ties included commercial or licensing

elements. As noted, Melbourne-based CSL collaborated with 12 Australian DBFs across the period, but Big Pharma in the US and Europe also forged multiple ties. GSK (London) collaborated with nine DBFs; Merck (New Jersey) and Merck AG (Germany) with eight; and Pfizer (based in New York), Johnson & Johnson (New Jersey) and AstraZeneca (London) with seven. In short, proximity facilitated ties, but distance did not prevent them.

Across the period, a handful of DBFs seemed on the verge of breakthrough: for example, Biota (in collaboration with GSK, based in London), Acrux (with Eli Lily, based in Indiana) and Mesobast (with Teva, based in Israel). Yet none of these partnerships delivered on their promise. In turn, there were no Australian firms that progressed to become Big Biotech firms, in the manner of Genzyme in Boston and Genentech in the Bay Area, investing to form their own local ecosystems and anchoring their capabilities within these ecosystems. In close connection, Australian DBFs, unlike those in the US superclusters, barely formed local partnerships with each other.

Notwithstanding active creation of international ties, data visualizations in Figure 5 highlight how they did not generate network connectivity, in contrast to local and national ties. In 2003 ties with international bioscience firms were spread thinly. In 2006 a main component of ties emerges, but consists largely of 'strings' where single DBFs collaborate with a bioscience firm, which then collaborates with another DBF, which collaborates with another bioscience firm, and so on. In 2014, the main component persists, but includes fewer DBFs. Figure 5 also highlights the large number of isolated DBFs without connections to international bioscience firms across the period. In the online supplement, we present the respective visualizations broken down to the cluster level, where the observed fragmentation becomes even more obvious.

--- Insert Figure 5 about here ---

Table 4 presents the results of the logistic regression models predicting whether DBFs were able to forge a deal with a Big Pharma as a critical value inflection point for commercialization. The Wald χ^2 statistics indicate that all models were highly significant ($p < 0.01$). Model 1 contains the control variables; Models 2 and 3 add the independent variables. Few results are significant. The proportion of international ties increase the chances of scoring a Big Pharma deal. The effects for prior patent applications, risk capital

deals and partner popularity are marginally significant and positive. Other than that, there are no network effects fostering commercial success.

--- Insert Table 4 about here ---

5. Discussion

In this article, we identify three critical challenges for biotechnology firms: access to new knowledge and intellectual property, early-stage fund-raising for the timely development of a viable product, and commercial efforts aimed at bringing a product to market. In the US, firms pursue 'multiconnectivity' to meet these challenges (Powell, et al. 2005). In doing so, they create different types of collaborative ties with diverse partners to access complementary resources and cutting-edge knowledge in a field that no firm can dominate on its own. In turn, collaborations facilitate clusters and networks. In this connection, the US superclusters are characterized by local access to outstanding PROs and sophisticated venture capital, both of which have the capacity to serve as 'anchor tenants' with the legitimacy and capability to catalyze collaborations among diverse partners (Powell, et al. 2012), including trans-local ties with Big Pharma (Stuart, et al. 2007). In the longer run, superclusters also benefit from local observatories created by Big Pharma and the tendency of successful DBFs to forge local ties with other DBFs, creating pathways for interactive learning and knowledge transfer. This is a virtuous cycle, where networks promote innovation and innovation promotes networks.

The goal of this study was to apply and test the above logic for the Australian biotechnology field, which we trace over a twelve year period starting in 2003 when it was at a comparable stage of development to that of the US field in 1988 (Powell, et al. 2005). Based on in-depth descriptive analyses, network visualizations and statistical modelling of longitudinal data, we demonstrate that Australian biotechnology firms and clusters followed a distinctive trajectory. In particular, our analysis provides evidence that Australian DBFs adopted the same logic of multiconnectivity, forging collaborations with diverse organizations directed towards new knowledge, funding for timely product development and getting to market. Yet we find that multiconnectivity has no immediate benefits for Australian DBFs. Rather, the network effects for Australian biotechnology are specific to

each challenge, in terms of partners, partnership types and location. In short, Australian DBFs adopt a similar network approach as DBFs in the superclusters, but do no achieve the same network effects. The upshot is that biotechnology collaborations do not produce a virtuous cycle (as per the superclusters), but rather a dead end.

Consider the three challenges in turn. With regard to the creation and accessing of new knowledge, our descriptive and visual analyses show that collaborations between DBFs and PROs underpin regional clusters and domestic networks throughout the period. PROs produce more connectivity in Australian clusters between 2003 and 2014 than was the case in the fast-growing US superclusters during the 1990s (Owen-Smith and Powell 2006). Our statistical models show that local R&D collaborations and local co-authorships positively influence new knowledge creation, but interstate and international collaborations and co-authorships do not. This is consistent with the literature, which identifies proximity as a pre-condition for the transfer of tacit and complex knowledge (DeCarolis and Deeds 1999; Zucker, et al. 2002). In this sense, the regional science base in Australia generates network effects (consistent with the experience of the world superclusters), and PROs demonstrate potential as anchor tenants (consistent with the trajectory of the Boston supercluster). Overall, local collaborative networks support Australian DBFs in meeting the first challenge of creating and accessing new knowledge.

Regarding early funding for the timely development of a viable product, our results shift attention from regional to national collaborations and grants. Our descriptive and visual analyses show that provision of early-stage funding for DBFs in Australia is dominated by domestic partnerships with financial entities, both local and interstate. These financial entities have strong ties with public agencies, including the government co-funded Innovation Investment Fund. Otherwise, in the mid 2000s the federal government agency AusIndustry is the most connected organization in the Australian biotechnology network (comparable to the central position of the National Institutes of Health in the US biotechnology network), until its main grant scheme is axed in 2007. Our statistical models show that AusIndustry grants are not conducive to risk capital deals however. In contrast, ties with Australian PROs (through local co-authorships and academic founders), domestic DBF collaborations and interstate financial collaborations positively influence early-stage

funding. These findings demonstrate the dependency of DBFs on domestic partnerships for risk capital. They also highlight the distinction between engaged partnerships where partner organizations actively interact with each other, for instance exchanging strategic advice, as occurs in venture capital (including government co-investment schemes), and more transactional arrangements as exemplified by direct grants (Bertoni and Tykvová 2015; Cumming and Johan 2016). The influence of local co-authorships and academic founders in accessing risk capital confirm the potential of PROs as anchor tenants within the Australian biotechnology industry, extending beyond knowledge creation to early-stage funding. Moreover, the influence of interstate financial and domestic DBF collaborations suggest the promise of a larger national innovation system, where venture capital, government co-investment programs and more mature DBFs facilitate network effects in crossing the 'valley of death' that afflicts DBF start-ups (Dodgson, et al. 2011; Herpin, et al. 2005; Marceau 2007). Overall, local and domestic collaborations support Australian DBFs in meeting the second challenge of accessing early-stage funding for development of a viable product.

For the final challenge of commercialization, our results shift attention once more, from domestic to international collaborations. One reason for this is that there is just one multinational pharmaceutical corporation located in Australia. The fact that it has more partnerships with Australian DBFs than any other Big Pharma during the observed period confirms the benefits of proximity and the difficulty of collaborating at a distance (Boschma 2005). Our descriptive and visual analyses show that that as DBFs become more mature, they form relatively more international collaborations. These collaborations, unlike domestic collaborations, are thinly spread, giving rise to sparse networks. Our statistical models show, consistent with Al-Laham and Souitaris (2008), that the overall proportion of existing international ties improves the chances of forging Big Pharma deals. This suggests possible network effects but, given weak connectivity, may simply reflect 'precocious internationalism' (Fontes 2005) in the form of punishing travel schedules and dogged effort. In short, local collaborations fail to translate local and domestic network effects that benefit knowledge creation and early funding into international network effects necessary for getting to market, and international collaborations fail to make up for it.

Previous studies propose many different explanations for the disappointing progress of Australian DBFs, including the depth of the science base (Barlow 2010), underdeveloped venture capital (Barlow 2010; Vitale and Sparling 2004), misdirected government policy (Marceau 2007), and geographic distance from the headquarters of Big Pharma (Gilding 2008). The diversity of explanations reflects significant challenges at every point of the value chain. Our study directs particular attention to the gap between network effects in creating new knowledge and accessing early funding on the one hand, and taking products to market on the other. Australian PROs serve as anchor tenants in meeting the first two challenges, but not the third. In this sense, they are weak anchor tenants for biotechnology clusters in Australia. This finding is consistent with other research that highlights the limitations of PROs as anchor tenants (Breznitz 2013; Powell, et al. 2012)

In particular, our study highlights the absence of network effects in securing deals with Big Pharma. The challenge of securing deals with Big Pharma can partly be understood in terms of the 'tyranny of distance' (Gilding 2008), but it is much more than this. It requires attention to institutions, facilities and practices that mitigate geographic distance, extending the reach of local and domestic organizations and their absorptive capacity. This might include local observatories (as found in the superclusters), international exchange programs between PROs and Big Pharma (designed to make PROs more robust anchor tenants), or incentive schemes for more mature DBFs to forge collaborations with start-ups (following the example of the superclusters). Such initiatives would demand public investment, patience to allow the long biotechnology product pipeline to take its course, and bipartisanship to survive the short-term election cycle. These conditions seem unlikely in the long-standing Australian policy climate, with its partisanship around industry policy, its narrow understanding of market failure and its intermittent engagement with the innovation economy agenda (Dodgson, et al. 2011).

In conclusion, our analysis suggests that advocates of the innovation economy – politicians, policymakers, scientists and industry players – have overstated their case for biotechnology as a prospective industry for countries far from the world biotechnology superclusters and Big Pharma. In close connection, the literature on 'territorial knowledge dynamics' is excessively optimistic about the prospects of navigating distant collaborations

and combinatorial knowledge across ‘multi-location milieu’ (Butain and Widmaier 2016; Crevoisier and Jeanneret 2009). Distant collaborations cannot seamlessly substitute for local deficits. Regional public research organizations struggle to catalyze collaborations with diverse partners across the entire value chain. Strategies to build absorptive capacity and embed distant capabilities are poorly understood. Collaborations do not automatically translate into virtuous cycles, and may become dead ends. The ambitions of regional policymakers and industry players have been mostly disappointed. We need a better understanding of network failure in order to fashion new industries far from the world advanced technology hubs.

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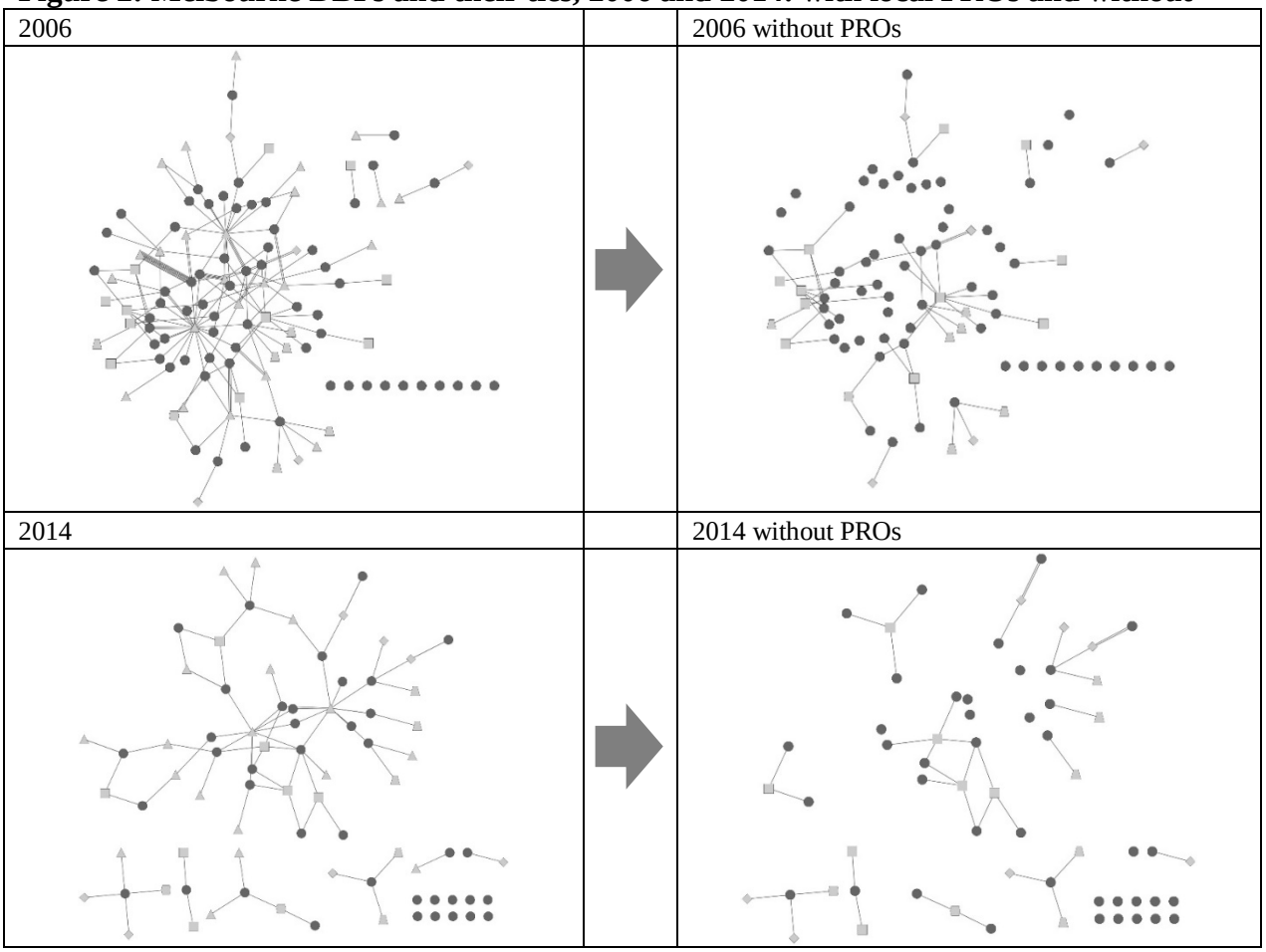
Figure 1: Regional biotechnology clusters, Australia, 2003-2014

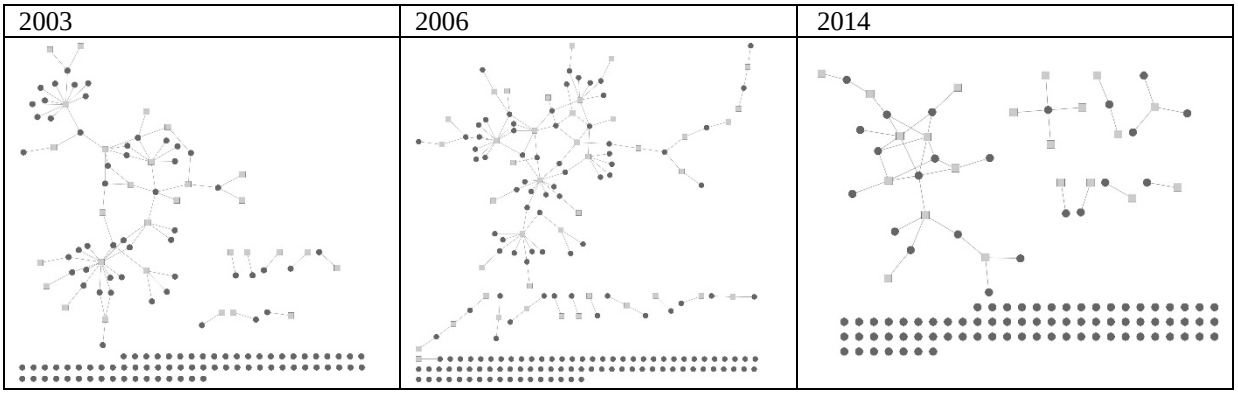
Note. = 2003 DBFs; = 2006 DBFs; = 2014 DBFs; node size = aggregated number of biotechnology firms per year.

Figure 2: Melbourne DBFs and their ties, 2006 and 2014: with local PROs and without



Note: Dark grey circles = DBFs; light grey triangles = PROs; light grey squares = FIN; light grey diamonds = private bioscience firms; light grey hexagon = GOV; light grey trapeze = other

Figure 3: Ties of Australian DBFs with domestic financial entities in 2003, 2006, and 2014

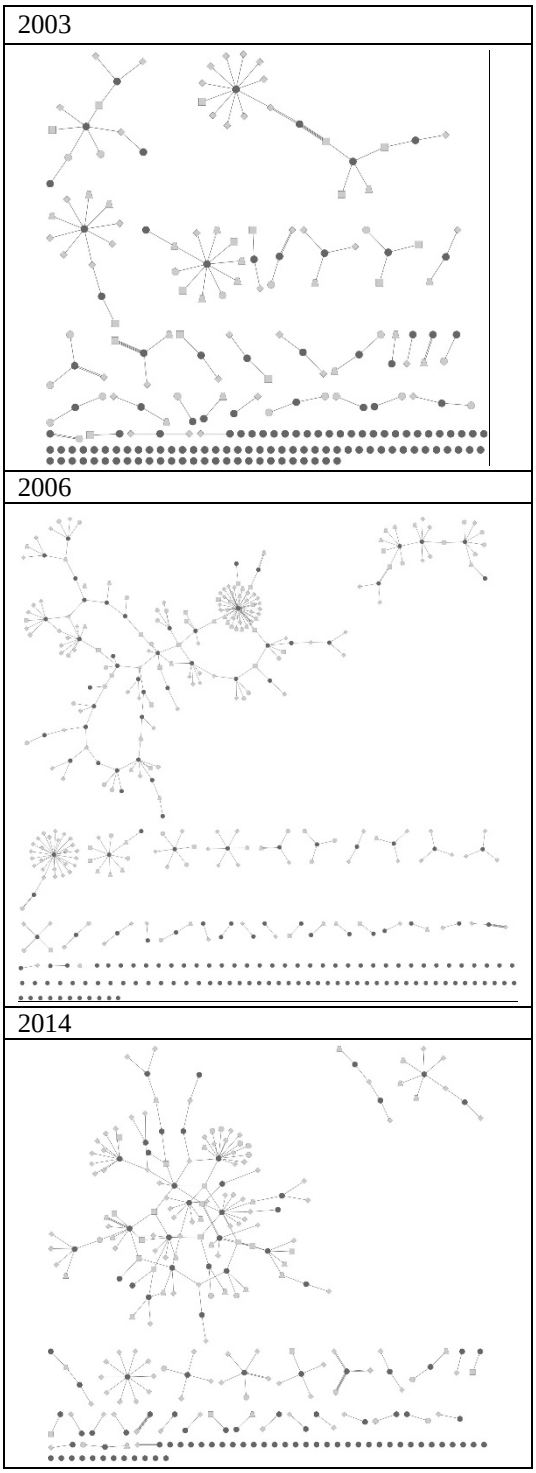


Note: Dark grey circles = DBFs; light grey squares = domestic FIN

Figure 4: Aggregated DBF international collaborations, Australia, 2003-14

Note. ● = biotechnology firms; ■ = partner firms; node size = number of aggregated firms. Only international locations with 10 partners or more (greater than 1 percent of all partner organizations) between 2003-14 are included.

Figure 5: Ties of Australian DBFs with international bioscience firms in 2003, 2006, and 2014



Note: Dark grey circles = DBFs; light grey circles = international DBFs; light grey diamonds = international private bioscience firms; light grey squares = international big pharma; light grey trapeze = international second-tier pharmaceutical firms

Table 1: Overview of variables used in the statistical models

Variable	Description
Dependent variables	
Patent applications	Number of patent applications captured in t+1; reflective of inventiveness
Risk capital deal	Dummy variable capturing whether a DBF was able to forge a risk capital deal in t+1
Deal with Big Pharma	Dummy variable capturing whether a DBF was able to strike a deal with a Big Pharma partner captured in t+1
Independent variables	
AusIndustry grants	Number of AusIndustry grants averaged over three years
Collaborations	Overall number of collaborations averaged over three years; reflective of degree centrality in the network
Proportion of internat. collab.	Ratio of international collaborative ties to the overall number of collaborations averaged over three years
Network portfolio diversity	Blau's heterogeneity index for types of ties averaged over three years
Partner popularity	Average number of collaborations that all of a DBFs' partners had with other DBFs in the sample averaged over three years
Domestic DBF collaborations	Number of collaborations with other Australian DBFs averaged over three years
R&D collaborations (overall, local, interstate, international)	Number of (overall, local, interstate, or international) research and development collaborations averaged over three years
Co-authorships (overall, local, interstate, international)	Number of (overall, local, interstate, or international) co-authorships averaged over three years
Financial collaborations (overall, local, interstate, international)	Number of (overall, local, interstate, or international) financial collaborations averaged over three years
International private bioscience collaborations	Number of collaborations with international private bioscience firms averaged over three years
Control variables	
JIF-weighted publications	Number of publications weighted by JIF averaged over three years
Academic founder	Dummy variable capturing whether at least one of the founders of a DBF previously held a research position at a domestic PRO
Age	Age of a DBF measured in years since incorporation
Listed	Dummy variable capturing whether a firm is public (i.e., listed at the Australian Stock Exchange ASX) or private
Size	Dummy variable capturing the size of a DBF with (0) small biotechnology firms and (1) medium to large firms
Diagnostic	Dummy variable distinguishing diagnostic (1) from human therapeutic (0) biotechnology organizations
Melbourne cluster	Dummy capturing whether a DBF was located in the Melbourne cluster
Sydney cluster	Dummy capturing whether a DBF was located in the Sydney cluster
Brisbane cluster	Dummy capturing whether a DBF was located in the Brisbane cluster
(Prior) patent applications	Number of patent applications averaged over three years (t-2 to t)
(Prior) risk capital deal	Dummy variable capturing whether a DBF was able to forge a risk capital deal between t-2 and t
(Prior) Big Pharma deal	Dummy variable capturing whether a DBF was able to forge a Big Pharma deal between t-2 and t

Table 2: GEE negative binomial regression models for patent applications

Variables	Model 1		Model 2		Model 3	
	Coefficient	SE	Coefficient	SE	Coefficient	SE
Age	-0.006	-0.017	-0.027	-0.017	-0.027	-0.019
Founder	0.038	-0.232	-0.036	-0.195	-0.061	-0.190
Listed	0.806**	-0.258	0.312	-0.309	0.246	-0.308
Size	0.953**	-0.209	0.457^{+}	-0.240	0.430^{+}	-0.235
Diagnostic	-0.405	-0.436	-0.292	-0.340	-0.368	-0.347
Melbourne cluster	-0.175	-0.332	0.077	-0.248	0.085	-0.272
Sydney cluster	0.360	-0.393	0.525^{+}	-0.284	0.563^{+}	-0.293
Brisbane cluster	-0.675^{+}	-0.36	-0.473	-0.347	-0.371	-0.374
Prior patent applications			0.401**	-0.067	0.355**	-0.072
Risk capital deal			-0.558*	-0.235	-0.611**	-0.225
Big Pharma deal			0.296	-0.260	0.254	-0.243
AusIndustry grants			0.255	-0.196	0.278	-0.218
Collaborations			-0.015	-0.031	-0.024	-0.032
Partner popularity			-0.021	-0.024	-0.020	-0.025
Network portfolio diversity			0.491	-0.560	0.264	-0.514
Proportion of international ties			0.133	-0.402	0.847^{+}	-0.469
Domestic DBF collaborations			0.060	-0.316	0.116	-0.298
R&D collaborations			0.057	-0.046		
Local R&D collaborations					0.137^{+}	-0.079
Interstate R&D collaborations					0.183	-0.140
International R&D collaborations					0.008	-0.059
Co-authorships			0.153*	-0.062		
Local co-authorships					0.200*	-0.100
Interstate co-authorships					0.291	-0.199
International co-authorships					0.021	-0.137
Financial collaborations			0.187^{+}	-0.109		
Local financial collaborations					0.384*	-0.195
Interstate financial collaborations					0.248^{+}	-0.130
International financial collab.					-0.280	-0.322
Constant	-4.323**	-0.946	-4.718**	-0.848	-4.710**	-0.831
Year dummies	included		included		included	
Observations	987		987		987	
Number of unique DBFs	175		175		175	
Wald chi^2	128.34**		523.69**		554.99**	

Note: SE = cluster-robust standard errors; $^{+}p < 0.1$; * $p < 0.05$; ** $p < 0.01$.

Table 3: Logistic panel regression models of risk capital deals

Variables	Model 1		Model 2		Model 3	
	Coefficient	SE	Coefficient	SE	Coefficient	SE
Age	0.012	-0.030	-0.004	-0.031	-0.006	-0.026
Founder	1.054**	-0.348	1.017**	-0.377	1.207**	-0.403
Listed	1.049*	-0.414	1.097*	-0.496	1.065*	-0.478
Size	-0.044	-0.383	-0.351	-0.488	-0.250	-0.463
Diagnostic	-0.273	-0.423	0.060	-0.502	0.043	-0.470
Melbourne cluster	0.370	-0.408	0.302	-0.424	0.745^{+}	-0.407
Sydney cluster	0.156	-0.458	0.040	-0.495	0.162	-0.477
Brisbane cluster	0.552	-0.460	0.219	-0.532	0.625	-0.533
Patent applications			0.138	-0.171	0.193	-0.137
Prior risk capital deals			-0.246	-0.593	-0.182	-0.425
Big Pharma deal			-0.031	-0.383	-0.084	-0.374
AusIndustry grants			0.249	-0.531	0.396	-0.481
Collaborations			-0.033	-0.058	-0.044	-0.067
Partner popularity			-0.013	-0.036	-0.017	-0.035
Network portfolio diversity			-0.446	-0.852	-0.802	-0.901
Proportion of international ties			0.301	-1.007	0.455	-1.006
Domestic DBF collaborations			1.284*	-0.562	1.514**	-0.458
R&D collaborations			-0.052	-0.077		
Local R&D collaborations					-0.180	-0.168
Interstate R&D collaborations					0.487^{+}	-0.274
International R&D collaborations					-0.198	-0.135
Co-authorships			0.129	-0.11		
Local co-authorships					0.413*	-0.198
Interstate co-authorships					-0.351	-0.533
International co-authorships					0.112	-0.264
Financial collaborations			0.507**	-0.158		
Local financial collaborations					0.216	-0.363
Interstate financial collaborations					0.486*	-0.232
International financial collab.					0.759^{+}	-0.446
Constant	-6.200**	-1.152	-6.021**	-1.202	-6.172**	-1.276
Year dummies	included		included		included	
Observations	987		987		987	
Number of unique DBFs	175		175		175	
Log likelihood	-207.89		-197.18		-192.53	
Wald chi^2	41.03**		93.33**		179.16**	

Note: SE = cluster-robust standard errors; $^{+}p < 0.1$; * $p < 0.05$; ** $p < 0.01$.

Table 4: Logistic panel regression models of deals with Big Pharma

Variables	Model 1		Model 2		Model 3	
	Coefficient	SE	Coefficient	SE	Coefficient	SE
Age	-0.001	-0.021	-0.007	-0.015	-0.001	-0.019
Founder	0.516	-0.330	0.333	-0.271	0.445	-0.324
Listed	1.523**	-0.509	0.421	-0.508	0.328	-0.552
Size	0.801^{+}	-0.411	0.382	-0.380	0.413	-0.383
Diagnostic	-1.197*	-0.585	-0.790	-0.521	-0.772	-0.551
Melbourne cluster	0.232	-0.413	-0.054	-0.363	0.051	-0.419
Sydney cluster	-0.871	-0.582	-0.763	-0.563	-0.893	-0.581
Brisbane cluster	-0.154	-0.525	-0.399	-0.457	-0.181	-0.510
Patent applications			0.171	-0.124	0.242^{+}	-0.146
Prior risk capital deals			0.778^{+}	-0.422	0.775^{+}	-0.432
Big Pharma deal			0.376	-0.409	0.247	-0.423
AusIndustry grants			-0.253	-0.435	-0.050	-0.452
Collaborations			0.007	-0.038	-0.002	-0.039
Partner popularity			0.059^{+}	-0.031	0.056^{+}	-0.031
Network portfolio diversity			1.498	-0.942	1.055	-0.977
Proportion of international ties			1.320*	-0.651	1.704*	-0.756
Domestic DBF collaborations			-0.142	-0.398	-0.212	-0.418
R&D collaborations			0.051	-0.057		
Local R&D collaborations					0.078	-0.155
Interstate R&D collaborations					0.381	-0.236
International R&D collaborations					-0.026	-0.091
Co-authorships			0.113	-0.073		
Local co-authorships					0.199	-0.144
Interstate co-authorships					0.124	-0.224
International co-authorships					0.020	-0.225
Financial collaborations			-0.071	-0.215		
Local financial collaborations					0.079	-0.321
Interstate financial collaborations					-0.355	-0.262
International financial collab.					0.298	-0.412
Constant	-5.267**	-0.969	-6.373**	-0.944	-6.459**	-0.949
Year dummies	included		included		included	
Observations	987		987		987	
Number of unique DBFs	175		175		175	
Log likelihood	-207.19		-195.11		-192.55	
Wald chi^2	92.99**		212.77**		240.51**	

Note: SE = cluster-robust standard errors; $^{+}p < 0.1$; * $p < 0.05$; ** $p < 0.01$.

Appendix

Table A1: Descriptive statistics and correlations

		Mean	S.D.	1	2	3	4	5	6	7	8	9	10	11	12	13
1	Patent applications	0.374	1.016													
2	Risk capital deal	0.059		0.048												
3	Deal with Big Pharma	0.069		0.164	0.068											
4	Age	9.569	6.573	0.065	0.014	0.085										
5	Founder	0.660		-0.030	0.089	0.001	-0.189									
6	Listed	0.354		0.262	0.131	0.217	0.465	-0.148								
7	Size	0.178		0.334	0.075	0.218	0.270	-0.056	0.536							
8	Diagnostic	0.188		-0.088	-0.021	-0.090	-0.031	-0.031	-0.091	-0.082						
9	Melbourne cluster	0.370		0.043	0.032	0.107	0.097	-0.145	0.210	0.098	-0.090					
10	Sydney cluster	0.208		0.050	-0.011	-0.070	-0.011	0.067	-0.008	0.009	0.034	-0.392				
11	Brisbane cluster	0.175		-0.065	0.032	-0.020	-0.056	0.174	-0.073	0.001	-0.059	-0.353	-0.236			
12	(Prior) patent applications	0.489	0.885	0.484	0.130	0.221	0.125	-0.042	0.390	0.420	-0.127	0.071	0.063	-0.077		
13	(Prior) risk capital deal	0.252		0.096	0.143	0.155	-0.047	0.083	0.249	0.144	-0.119	0.149	-0.033	-0.016	0.178	
14	(Prior) Big Pharma deal	0.169		0.148	0.037	0.208	0.210	-0.047	0.345	0.355	-0.121	0.186	-0.145	-0.002	0.250	0.173
15	AusIndustry grants	0.225	0.384	0.211	0.126	0.094	-0.104	0.067	0.147	0.260	-0.121	-0.058	0.038	0.081	0.266	0.261
16	JIF-weighted publications	2.105	5.443	0.257	0.048	0.201	0.317	-0.055	0.324	0.351	-0.130	0.022	0.004	0.037	0.447	0.067
17	Collaborations	6.802	7.162	0.290	0.067	0.244	0.387	-0.039	0.560	0.478	-0.015	0.145	-0.018	-0.047	0.376	0.201
18	Network portfolio diversity	0.445	0.290	0.188	0.082	0.157	0.134	0.147	0.381	0.302	-0.186	0.135	-0.054	0.014	0.284	0.289
19	Partner popularity	6.712	7.206	-0.033	0.040	-0.030	-0.256	0.154	-0.218	-0.117	-0.079	-0.012	-0.048	0.264	-0.051	0.033
20	Prop. of internat. collab.	0.300	0.323	0.127	0.014	0.155	0.414	-0.140	0.535	0.363	0.142	0.122	-0.003	-0.111	0.215	0.028
21	Domestic DBF collaborations	0.049	0.242	0.174	0.092	0.127	0.178	-0.068	0.167	0.224	-0.022	0.072	0.021	-0.049	0.257	0.153
22	Internat. private bioscience collab.	1.767	3.022	0.147	0.028	0.145	0.372	-0.050	0.507	0.417	0.100	0.068	-0.038	0.008	0.211	0.054
23	R&D collaborations	1.480	2.443	0.290	0.064	0.219	0.228	-0.061	0.461	0.350	-0.040	0.171	-0.038	-0.120	0.356	0.188
24	Local R&D collaborations	0.542	0.918	0.215	0.050	0.163	0.173	0.009	0.309	0.259	-0.008	0.121	0.010	-0.086	0.266	0.167
25	Interstate R&D collaborations	0.305	0.618	0.258	0.091	0.187	0.060	-0.035	0.370	0.276	-0.062	-0.017	0.007	-0.092	0.292	0.143
26	International R&D collaborations	0.632	1.563	0.225	0.035	0.172	0.231	-0.086	0.394	0.286	-0.033	0.204	-0.068	-0.101	0.286	0.139
27	Co-authorships	0.778	1.806	0.256	0.071	0.203	0.330	-0.009	0.364	0.367	-0.118	0.062	-0.015	0.029	0.399	0.074
28	Local co-authorships	0.347	0.857	0.206	0.088	0.192	0.327	0.008	0.260	0.276	-0.113	0.050	0.003	-0.021	0.313	0.125
29	Interstate co-authorships	0.214	0.630	0.237	0.020	0.147	0.251	0.005	0.329	0.338	-0.080	0.048	-0.038	0.065	0.330	0.046
30	International co-authorships	0.218	0.718	0.189	0.054	0.152	0.219	-0.036	0.316	0.296	-0.091	0.054	-0.008	0.040	0.341	-0.004
31	Financial collaborations	0.653	0.952	0.075	0.139	0.064	-0.020	0.192	0.073	0.085	-0.185	0.105	-0.062	0.135	0.113	0.500
32	Local financial collaborations	0.292	0.528	0.005	0.077	0.044	-0.117	0.194	-0.075	-0.032	-0.206	0.186	-0.061	0.016	0.034	0.340
33	Interstate financial collaborations	0.293	0.607	0.125	0.133	0.038	0.027	0.124	0.136	0.133	-0.077	-0.019	-0.067	0.187	0.161	0.396
34	International financial collab.	0.068	0.263	-0.026	0.045	0.057	0.101	0.020	0.102	0.064	-0.075	0.050	0.055	0.023	-0.031	0.211

Note: N = 987 firm-year observations for all variables; all correlations coefficients larger than .062 in absolute values are significant ($p < 0.05$)

Table A1: Descriptive statistics and correlations (contd.)

		14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
15	AusIndustry grants	0.106														
16	JIF-weighted publications	0.223	0.121													
17	Collaborations	0.411	0.209	0.476												
18	Network portfolio diversity	0.244	0.255	0.268	0.393											
19	Partner popularity	-0.097	0.314	-0.069	-0.176	-0.049										
20	Prop. of internat. collab.	0.340	-0.060	0.154	0.500	0.268	-0.380									
21	Domestic DBF collaborations	0.122	0.071	0.163	0.271	0.134	-0.034	0.059								
22	Internat. private bioscience collab.	0.419	0.052	0.239	0.667	0.203	-0.230	0.550	0.093							
23	R&D collaborations	0.266	0.160	0.199	0.587	0.304	-0.112	0.296	0.327	0.313						
24	Local R&D collaborations	0.225	0.151	0.222	0.403	0.277	-0.062	0.079	0.286	0.153	0.753					
25	Interstate R&D collaborations	0.219	0.184	0.190	0.424	0.316	-0.063	0.135	0.192	0.244	0.596	0.375				
26	International R&D collaborations	0.196	0.090	0.106	0.513	0.188	-0.114	0.363	0.268	0.302	0.885	0.441	0.316			
27	Co-authorships	0.266	0.086	0.904	0.506	0.283	-0.096	0.193	0.166	0.296	0.221	0.222	0.207	0.133		
28	Local co-authorships	0.246	0.069	0.706	0.424	0.260	-0.078	0.113	0.217	0.225	0.238	0.288	0.146	0.145	0.829	
29	Interstate co-authorships	0.200	0.082	0.716	0.375	0.224	-0.067	0.133	0.089	0.219	0.063	0.047	0.189	-0.004	0.793	0.458
30	International co-authorships	0.201	0.064	0.803	0.436	0.205	-0.088	0.233	0.081	0.284	0.217	0.172	0.182	0.166	0.830	0.491
31	Financial collaborations	0.094	0.211	0.086	0.167	0.320	0.046	-0.063	0.024	0.011	0.056	0.070	0.077	0.016	0.056	0.119
32	Local financial collaborations	0.030	0.145	0.047	0.033	0.251	0.091	-0.157	0.013	-0.107	-0.019	-0.004	0.038	-0.043	0.025	0.086
33	Interstate financial collaborations	0.045	0.230	0.094	0.179	0.238	0.031	-0.056	0.016	0.053	0.099	0.120	0.087	0.049	0.065	0.108
34	International financial collab.	0.174	-0.059	0.000	0.125	0.105	-0.088	0.215	0.022	0.131	0.012	-0.019	0.000	0.030	0.001	0.008

Note: N = 987 firm-year observations for all variables; all correlations coefficients larger than .062 in absolute values are significant ($p < 0.05$)

Table A1: Descriptive statistics and correlations (contd.)

		29	30	31	32	33
30	International co-authorships	0.570				
31	Financial collaborations	0.009	-0.010			
32	Local financial collaborations	-0.007	-0.034	0.697		
33	Interstate financial collaborations	0.042	-0.001	0.760	0.148	
34	International financial collab.	-0.048	0.037	0.466	0.172	0.147

Note: N = 987 firm-year observations for all variables; all correlations coefficients larger than .062 in absolute values are significant ($p < 0.05$)