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Endowing university spin-offs pre-formation: Entrepreneurial capabilities for scientist-entrepreneurs

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ABSTRACT

University spin-offs are important mechanisms for creating and capturing value from scientific inventions. Academic scientists are uniquely positioned to shape such opportunities long before the university spin-off is founded. To better understand how science-based university spin-offs can be endowed for success, the *pre-formation* stage of 30 ventures co-founded over a 40 year period by a star-scientist-entrepreneur is analysed by matching his 363 co-invented US patents granted to 1476 co-authored publications and these 30 ventures. Employing the extended case method, including the analysis of extensive archival data, iterative interviews, and this unique, longitudinal, multi-level dataset, existing dynamic capabilities theory is confronted and extended with evidence as to how a star-scientist-entrepreneur senses and shapes and seizes opportunities to endow university spin-offs pre-formation. A process model is developed depicting four pre-formation entrepreneurial capabilities with which these science-based university spin-offs are endowed for success. Recommendations are made for scientist-entrepreneurs, investors, university leadership, and for innovation policymakers.

1. Introduction

Universities generate a large and growing proportion of scientific inventions (Edwards et al., 2003; Leih and Teece, 2016; Martin and Tang, 2007; Roberts et al., 2015). University spin-offs are important mechanisms for creating and capturing value from these inventions (Leih and Teece, 2016; Maine and Seegopaul, 2016; Shane, 2004). Academic scientists are uniquely positioned to shape such opportunities long before the university spin-off is founded (Clarysse and Moray, 2004; Clarysse et al., 2011; Maine and Thomas, 2017; Murray, 2004; Rasmussen et al., 2011). While scholars have noted that the location and growth of science-based ventures can be linked to the presence of highly productive academic scientists (Maine et al., 2014a; Zucker et al., 1998), the process by which scientists endow university spin-offs remains unknown. And, though understudied, the entrepreneurial capabilities of scientists are much maligned. In fact some scholars have cast doubts on whether scientists should play a leading role in the commercialization of science through spin-off formation (Gurdon and Samsom, 2010; Stuart and Ding, 2006; Vohora et al., 2004). This study is motivated by the research question: *How can scientist-entrepreneurs endow university spin-offs pre-formation?*

The extended case method (Burawoy, 2009) is employed to confront and extend dynamic capabilities theory by elucidating the manner in which an exemplar star-scientist-entrepreneur (SSE) senses, shapes, and seizes opportunities to endow university spin-offs pre-formation. A process model of entrepreneurial capabilities leading to the emergence of 30 science-based university spin-offs is developed. An exemplar SSE was identified as an outlier based on the 30 science-based university spin-offs he had co-founded, their level of success, and after initial data collection showed that his career patenting output exceeded most firms in the emerging nanobiotechnology industry. The research leading to the formation of a science-based university spin-off may precede the founding of the venture by a decade or more. Thus, although the first spin-off co-founded by the focal scientist-entrepreneur was formed in 1987, extensive data including papers, patents, and ventures with the scientist as a co-author, co-inventor, and co-founder was gathered for

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the period 1974–2014, allowing for a longitudinal examination of the progression of science from research laboratory to science-based university spin-off.

A sensing and shaping capability was linked to seizing capabilities *pre-formation* through matching patents and papers to ventures. The patent-paper-venture matching provided objective data on the timeline from invention to spin-off formation, through analysing and linking patents to their associated papers and spin-off ventures. Interviews and secondary sources provided evidence on technology-market matching – a key sensing and shaping capability – which was then anchored in time via patent-paper-venture matching to the corresponding seizing capabilities. A method was developed to identify platform technologies from papers, along with a technique to identify matched patents which were broad, blocking, and relevant (Maine and Thomas, 2017). Data on the founding and financing of ventures was sourced from the US Securities and Exchange Commission (SEC) filings, archived documents, company reports, and press releases (**see appendix 1**). The entrepreneurial capabilities leading to well-endowed science-based university spin-off emergence were verified and refined through interviews with the scientist-entrepreneur, senior personnel at the MIT Technology Licensing Office (TLO), a lab alumni and academic co-founder, a business co-founder identified and nurtured by the scientist-entrepreneur, a venture capitalist who was also CEO of a co-founded spin-off, and an IP counsel of a co-founded spin-off (**see appendix 2**).

This study contributes to the academic entrepreneurship and dynamic capabilities literatures in several substantial ways. First, through the extended case method, detailed evidence of the commercialization activities of a star-scientist-entrepreneur is used to confront and extend dynamic capabilities theory to the individual level pre-formation (Table 1, Fig. 1). Consistent with existing dynamic capabilities theory (Eisenhardt and Martin, 2000; Helfat and Peteraf, 2015; Teece, 2007; Teece et al., 1997) both a sensing and shaping capability as well as seizing capabilities are observed at the firm-level. Extending dynamic capabilities theory, at the individual level the key *pre-formation* sensing and shaping capability of technology-market matching and the *pre-formation* seizing capabilities of claiming and protecting IP, attracting and mentoring the founding team, and strategic timing are identified and elucidated. A process model of these four entrepreneurial capabilities which lead to well-endowed science-based university spin-offs is developed, identifying the role of the scientist-entrepreneur, his academic collaborators, the university's technology licensing office, and the external environment. Second, the novel method of patent-paper-venture matching is developed which enables a detailed longitudinal examination of the processes of science commercialization from the flow of research outputs and personnel from the lab to the emergence of science-based university spin-offs. Through this method, we reveal how the coordination, sequencing, and timing of commercialization decisions by the SSE (along with his collaborators and the TLO), helps prepare the nascent venture in the pre-formation and early post-formation stages of venture emergence. Third, this research adds to the growing literature on science-based entrepreneurship by providing empirical evidence and longitudinal analysis of the emergence and performance of 30 science-based university spin-offs. In doing so, a nuanced perspective on a crucial and understudied period in the lifecycle of science-based university spin-offs (Druilhe and Garnsey, 2004; Phan, 2004; Rasmussen, 2011) is provided. From this analysis, we offer recommendations for scientist-entrepreneurs, investors, university leadership, and policymakers to further facilitate the commercialization of university science.

2. Literature review

Despite an extensive literature on academic entrepreneurship, the pre-formation stage of science-based university spin-offs remains something of a black-box. This is problematic because constraints to the commercialization of public science – and the capabilities required to overcome them – are poorly understood (Maine et al., 2014a; Pisano, 2010). Enabling further commercialization of science from universities requires a deeper understanding of the capabilities demonstrated by highly successful scientist-entrepreneurs, and the ecosystems within which they operate. In this section, relevant literature on academic entrepreneurship, scientist-entrepreneurs, dynamic capabilities, and entrepreneurial capabilities is reviewed.

2.1. Academic entrepreneurship

Universities contribute to economic growth through academic entrepreneurship, and more specifically, through university spin-off emergence (Roberts et al., 2015; Rothaermel et al., 2007; Shane and Stuart, 2002; Siegel and Wright, 2015). This mechanism is particularly important for the commercialization of breakthrough technologies which have the potential to create new industries or transform existing ones. Though the importance of this phenomena of university spin-off emergence is broadly recognized, extant studies have concentrated at

Table 1
Theory-building through the extended case method.

Dynamic Capabilities Theory	Gaps/Critiques/Calls for action	Confirmatory findings from the case	Extensions – Entrepreneurial Capabilities *Pre-formation* (Fig. 1)
Can be disaggregated into the capacity *(1) to sense and shape opportunities* *(2) to seize opportunities* (3) to maintain competitiveness through enhancing, combining, protecting, and when necessary, reconfiguring the enterprises. Teece (2007)	A call for more *process-oriented studies to extend dynamic capabilities theory* (Schilke et al., 2018). A call for *"focusing on the entrepreneurial function embedded in dynamic capabilities* i.e. managerial capabilities for sensing and seizing opportunities." (Protogerou et al., 2012, pp. 641), and "How do star scientists and technology gatekeepers influence the development of sector-based entrepreneurial capabilities?" (De Massis et al., 2018, pp. 14). The pre-formation stage leading to the creation of a new venture are seen as a neglected issue both in the spin-off literature (Druilhe and Garnsey, 2001; Mustar et al., 2006; Rothaermel et al., 2007; Rasmussen and Wright, 2015; Colombelli et al., 2016) and in entrepreneurship theory (Phan, 2004; Rasmussen, 2011; Hopp and Greene, 2018).	Sensing and shaping opportunities (firm-level): Technology-market matching (Fig. 4) Seizing opportunities (firm-level): Claiming and protecting the invention, Attracting and mentoring the founding team, Strategic timing (Table 2 and Table 3)	Technology-market matching (Table 2, Fig. 4 - bold) Claiming and protecting the invention (Table 2 - bold) Attracting and mentoring the founding team (Table 2 - bold, Table 3) Strategic timing – Importance of timing in spin-off processes (Table 2 and Fig. 4)

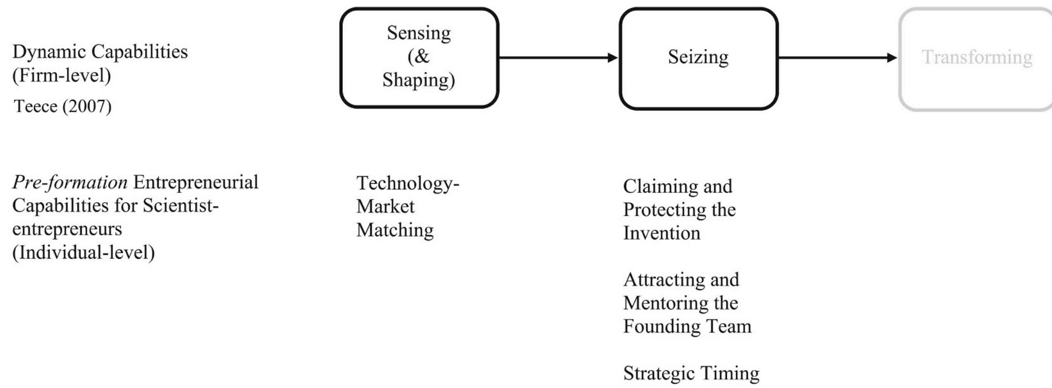

Fig. 1. Linking entrepreneurial capabilities to dynamic capabilities.

the macro/institutional level leading to the critique that the micro-level remains understudied (Fuller and Rothaermel, 2012; Siegel and Wright, 2015). Moreover, the vast majority of the academic entrepreneurship literature examines university spin-offs post-formation (Mustar et al., 2006; Rothaermel et al., 2007). Yet much remains unknown. For example, though it is well recognized that academic scientists are the key decision makers developing the technology and shaping the commercialization strategy in the very early stages with the technology having been developed in their scientific lab (Jain et al., 2009; Krabel and Mueller, 2009; Perkmann et al., 2013), further elucidation is needed to understand how scientists can endow university spin-offs for success.

Science-based academic entrepreneurship draws into sharp distinction the need for micro-level (early stage) evidence in the academic entrepreneurship literature (Rasmussen, 2011). Science-based university spin-offs face challenges that are well recognized – in particular, high uncertainty and high commercialization costs coupled with long timelines from invention to revenue generation (Agrawal, 2006; Maine and Seegopaul, 2016; Pisano, 2010; Shane, 2004). Although some potential strategies to overcome these challenges have been identified, all remain insufficiently understood. In particular, little is known about the pre-formation stage, and the role that a scientist-entrepreneur may play in endowing a university spin-off with the resources required for a higher likelihood of success. This gap has been noted by other academic entrepreneurship scholars, who call for qualitative research on sector-based entrepreneurial capabilities, and specifically ask "How do star scientists and technology gatekeepers influence the development of sector-based entrepreneurial capabilities?" (De Massis et al., 2018, pp. 14).

2.2. Scientist-entrepreneurs and the commercialization of public science

Science-based university spin-offs require significant resources and capabilities in their pre-formation and early post-formation stages. The lack of such endowments result in most university spin-offs failing within a decade of founding (Dimov and De Clerq, 2006; Timmons, 1990). Few science-based university spinoffs succeed in raising substantial VC financing or reaching an initial pubic offering (IPO) (Fini et al., 2018; Maine and Thomas, 2017). Highly productive scientists are thus at an advantage in being able to attract much needed resources to these spin-offs through their reputation and signalling effects (Stuart and Ding, 2006). Highly productive scientists have also been labelled "elite" or "stars" and several scholars have shown that such scientists contribute disproportionately to the discovery of scientific inventions from universities (Baba et al., 2009; Lotka, 1926; Zucker et al., 1998). This productivity has led them to be identified in several ways: having an above average level of productivity in generating scientific publications and patents (Baba et al., 2009; Lawson and Sterzi, 2014; Schiffauerova and Beaudry, 2011; Subramanian et al., 2013), being Nobel prize winners (Higgins et al., 2011), or having identified and characterized specific DNA sequences (Zucker et al., 1998 & 2002). Beyond the underlying theme of productivity in patents and papers, these scientists are often actively involved in commercializing their discoveries (Fuller and Rothaermel, 2012; Rothaermel et al., 2007; Stuart and Ding, 2006), possibly because of their ability to signal the quality of research and to attract resources towards nascent science-based spin-offs. In fact, the founding of firms in emerging science-based industries is disproportionately co-located with star scientists (Maine et al., 2014a; Zucker et al., 1998), and spin-offs co-founded by star scientists are more likely to reach an IPO (Fuller and Rothaermel, 2012). Thus, highly productive scientists contribute disproportionately to academic entrepreneurship in scientific fields.

2.3. Dynamic capabilities

Dynamic capabilities theory seeks to explain why some firms are able to show better performance in a changing environment (Eisenhardt and Martin, 2000; Helfat and Peteraf, 2015; Teece, 2007; Teece et al., 1997). While researchers have made significant progress in identifying the antecedents, moderators and mechanisms leading to firm performance, much work remains (Schilke et al., 2018). The predominant focus of most studies on dynamic capabilities has been at the firm-level. While this focus is essential, valuable insights can also be gained by examining individual-level capabilities (Felin et al., 2012; Helfat and Peteraf, 2015). This emphasis on individual-level capabilities is particularly enlightening in the pre-formation stage of new ventures because "it is entrepreneurs who bring agency to opportunity", Shane (2003), by sensing, shaping, and seizing opportunities.

Decisions taken during this pre-formation stage shape later stages in the life cycle of science-based university spin-offs (Druilhe and Garnsey, 2004; Phan, 2004; Rasmussen, 2011). Path-dependent decisions on key elements of science commercialization such as intellectual property (IP), founding team, and target markets are often taken during this stage. For example, the quality of patent protection achieved pre-formation and the manner in which the patents are licensed out by the inventors and their institutions impact the ability of the licensee science-based venture to commercialize the technology. Academic scientists from whose research labs these inventions emerge, are key stakeholders in the pre-formation stage. While extant researchers have suggested that most academic scientists are neither well-suited nor trained for science commercialization (Gurdon and Samsom, 2010), a few outlier star-scientist-entrepreneurs have emerged. Their unusual success in co-founding a large number of science-based university spin-offs can shed light on the entrepreneurial capabilities they possess and enrich the dynamic capabilities framework (Table 1, Fig. 1).

2.4. Entrepreneurial capabilities

Productive streams of research have investigated the influence of dynamic capabilities in firms post-formation (Eisenhardt and Martin, 2000; Teece et al., 1997). Moving from the level of the firm to the individual, research on entrepreneurial capabilities has also focussed predominantly on the post-formation stage (Alvarez and Barney, 2007; Shane, 2000; Shane and Venkataraman, 2000). However, the pre-formation stage is where critical decisions which affect the future success of the spin-off may be taken by the scientist and his or her academic collaborators (Druilhe and Garnsey, 2004; Rasmussen, 2011; Rasmussen et al., 2011; Shane, 2004). The entrepreneurial capabilities of a founder and of a founding team can impact venture success (Eesley et al., 2014; Gruber et al., 2008; Maine et al., 2015), and we argue that this is particularly true for scientist-entrepreneurs, given the path-shaping decisions they take pre-formation.

Technology-market matching is a vital capability for science-based businesses (Freeman, 1982; Maine and Garnsey, 2006; Schmookler, 1966). While early stage market selection is important for any innovating firm (Gruber et al., 2008), it takes on far more importance for science-based ventures commercializing technologies with broad applicability (Maine and Seegopaul, 2016; Maine et al., 2014a). Technology-market matching has predominantly occured after the formation of science-based ventures, and not in the labs of academic scientists (Maine and Garnsey, 2006; Maine et al., 2014a). Yet, given the long timelines from invention to innovation and the large sums of capital involved, early-stage entrepreneurial capability in technology-market matching could be enormously beneficial.

3. Methods

University spin-off emergence can be long and complex (Roberts, 1991), and case studies are particularly appropriate when the focus is on understanding the dynamics present within single settings (Eisenhardt, 1989). A single in-depth case can inform theory using evidence from a detailed study of an empirical exemplar (Garnsey et al., 2008). Pettigrew (1990) argues that it makes sense to select an “extreme” case when the phenomenon of interest is “transparently observable”. The study of an exemplar is appropriate and valuable to develop or expand theories, particularly in contexts with evolving, complex processes and little primary data elucidating them (Eisenhardt and Graebner, 2007; Yin, 2014). Science commercialization is such a context (Fini et al., 2018). The relationships uncovered through such in-depth, longitudinal, and multi-level analyses of single case studies (i.e. Galunic and Eisenhardt, 1996 & 2001; Murray, 2002) have proved invaluable in informing the metrics of subsequent quantitative studies.

The extended case method is a technique developed to link the macro and the micro levels through pre-existing theory (Burawoy, 2009). It is particularly useful when dealing with complex, multi-layered, and unstructured phenomena (Bjerregaard, 2011; Matthyssens and Vandenbempt, 2003). Researchers identify a case which is used to confront pre-existing theory, with the aim of using the anomalies from the case to identify the ways in which existing theory can be refined. This method emphasizes the importance of context, focusing on the specific characteristics of the single case that can illuminate the wider processes that can enable the focal organizations to survive and thrive. This study uses the extended case method to confront dynamic capabilities theory with the specific case of a star-scientist-entrepreneur who has co-founded over 30 science-based ventures.

Star-Scientist-Entrepreneurs are defined here as academic scientists with an above average level of productivity in generating scientific publications and patents and who have co-founded at least one science-based university spin-off (bubbles in Fig. 2). Interestingly, there is a skewed distribution, with the greatest impact (in terms of number of spin-offs founded, VC financing raised, number of IPOs, significant social issues addressed) coming from outliers (Fuller and Rothaermel, 2012; Nightingale and Coad, 2014). Thus, rather than studying a sample of SSEs, who may or may not have put any systematic thought into guiding spin-off emergence, the careful study of multiple spin-offs co-founded by an exemplar SSE (large bubble on top right of Fig. 2) can reveal entrepreneurial capabilities honed through the formation of multiple spin-offs over several decades.

The star-scientist-entrepreneur investigated in our study was identified based on insights from an earlier study (Maine et al., 2014b) and selected for further examination based on his extensive productivity in generating scientific papers, patents and ventures. Our multi-level, longitudinal analysis encompasses the SSE's capabilities, the backgrounds of his academic and business co-founders for each spin-off, temporal and strategic patterns revealed through patent-paper-venture matching, and venture success measured through financing raised and reaching an IPO. In studying the SSE, his lab, and his co-founded spin-offs over 4 decades, data on all of the papers and granted US patents with the star scientist as a co-author and co-inventor until 31st December 2014 are first gathered and then these patents are matched to the academic papers through a combination of extensive automated and manual matching. Papers which advanced a platform technology were identified, and the journal impact factors of publications were gathered from the Journal Citation Report 2012. Patents which were broad, blocking and relevant, were identified following the method outlined in section 3.2. Co-authored papers were identified from the Web of Science and also compared with the publication list on the lab website of the SSE (http://langer-lab.mit.edu/publications). After eliminating dual entries and errors, and accounting for any inconsistencies in the coverage of the Web of Science dataset, the total number of papers was 1476. All US patents issued between July 1979 and December 2014 with Robert S. Langer or Robert S. Langer Jr. as a co-inventor residing in Massachusetts were identified from the USPTO. In all, 363 US patents were identified and analysed through our patent-paper-matching technique (section 3.1).

Acknowledging the importance of context as required by the extended case method, the researchers conducted several interviews with the scientist-entrepreneur, the MIT IP Counsel, a scientific co-founder, and a co-founded venture CEO among others (Details in Appendix 2 and section 3.4). Extensive secondary data on each co-founded venture which included information on their patents, papers, initial leadership team, and scientific alumni from the scientist entrepreneur's lab, were collected from a variety of sources ranging from the US Patent Office, the MIT TLO, the SEC, Web of Science, Google Scholar, individual scientist CVs and webpages, university and firm webpages, and firm press releases, to published interviews of the scientist-entrepreneur and co-founded venture leadership team in periodicals and online sources (Details in Appendix 1). The scientist-entrepreneur was also invited to confirm patent-paper matches in a number of instances. In doing so, the researchers collaborated with the focal subject and confirmed their analysis through multiple follow-up interactions with the scientist-entrepreneur and the MIT TLO as suggested by the extended case method.

3.1. Patent-paper-venture matching

To enable the mapping of sensing and shaping capabilities to seizing capabilities in the pre-formation stage, the patent-paper matching technique (Murray and Stern, 2007) was extended to include ventures. Matching patents and papers to ventures allows for a nuanced understanding of the progression of science from research laboratory to science-based university spin-off. Patents were matched to papers by first creating a list of the top 10 matched papers for each patent. To do so, for each co-authored patent, the year of patent filing was identified, a list of inventors from each patent was compiled, and co-authored papers that had been published in the ± five year period from the patent filing date were identified. Next, the patent inventors were matched with the co-authors of the papers in this period. In many instances, multiple inventors were matched as co-authors on papers submitted and published within this period. The number of overlapping words

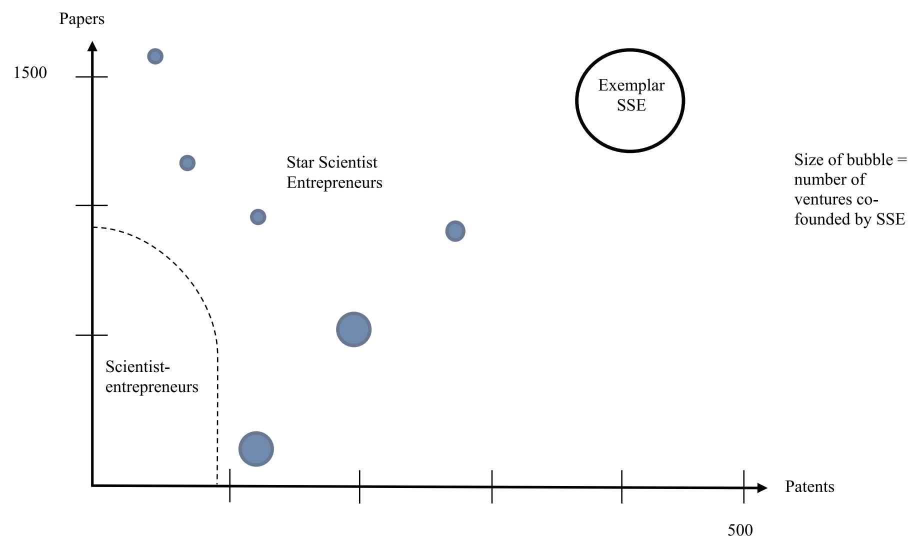

Fig. 2. Exemplar star-scientist-entrepreneur in context
(Schematic figure based on Thomas and Maine, 2019; Holley and Watson, 2017; Nightingale and Coad, 2014; Zucker and Darby, 1996).

between the titles and abstracts of the focal patent and the papers were also identified. Once the list of top 10 possible matched papers was generated through this technique, an overlap in the text and/or the figures in both sets of documents were manually verified, so that each patent could be accurately matched to the papers that inform it (Murray and Stern, 2007). The patent-paper matches thus identified are a combination of extensive automated and manual matching (Bubela et al., 2013) which, to the knowledge of the authors, has not previously been attempted on a dataset of this scale.

Once the patent-paper matches were complete, the core technology of each firm co-founded by the star-scientist-entrepreneur was identified. From descriptions on the company website, annual reports, press releases, SEC filings, published CEO interviews and firm media reports, the patent-paper sets were matched to the firms. In some instances firms had listed the papers and/or patents on which the firm's technology was based. This also helped in the matching exercise. The resultant patent-paper-venture matching enables the tracking of the commercialization of public science.

3.2. *Defining and measuring broad, blocking and relevant patents*

A patent is a property right granted by a government to an inventor, with the aim of protecting intellectual endeavours and supporting technological progress. A patent confers the right to *exclude* others from making, using, offering for sale, selling, or importing an invention into a particular jurisdiction for a specified period of time. Inventions or discoveries of a new and useful process, machine, manufacture, or composition of matter, or new and useful improvements in these categories, may be patented. The breadth of protection is determined through the patent claims, which define the scope of protection or the legal boundaries of the invention. Each patent can have two types of claims, independent and dependent. Independent claims stand alone and do not reference other claims within the patent. Dependent claims reference other claims, and can be considered as subsets of the claims on which they depend. The first claim in a patent is independent, defines the broadest scope of the patent protection (Huys et al., 2009) and is least restrictive (USPTO, 2015: MPEP §608.01(m)).

Patents are more valuable to science-based university spin-offs and to their investors when they are broad, blocking and relevant, as argued in Maine and Thomas (2017):

> “A broad patent is one which enables a wide range of applications (more value creation): filing a broad patent requires forethought of how widely a patent can be applied in the future. A blocking patent enables a spin-off to appropriate that value, as competitors have difficulty inventing around such a patent. A relevant patent is one which is deemed promising and useful, (for example, because it meets an unmet market need, has a large potential social impact, and/or is in an emerging area of scientific discovery), stimulating significant follow-on activity both by the firm and by others.” (Maine and Thomas, 2017)

Science-based spin-offs which emerge from university labs with broad, blocking and relevant patents are thus better resourced to enable the translation of breakthrough technologies.

Identifying broad, blocking and relevant patents, particularly in the US, is not straightforward. Unlike in Europe, where the blocking nature of a patent can be inferred by the X and Y classification in the search reports of forward citing patents (Torrisi et al., 2016), in the US no equivalent classification exists. Existing proxies for patent breadth, such as the number of IPC classes (Lerner, 1994) and the number of patent claims (Lanjouw and Schankerman, 2001), also have drawbacks (Maine and Thomas, 2017; Reitzig, 2004). To address this, the method described in Maine and Thomas (2017) was followed to identify broad, blocking and relevant patents in the US. First, the first 500 characters of the patent claims (the independent claim) were searched for the presence of the word “comprising,” which has been identified as an indicator of the broad nature of a patent (Radack, 1995). This indicator was then combined with data on patent forward citations, as these citations are indicative of the cumulative development of the technology by the scientist, his collaborators, and competitors. The criteria used to identify broad, blocking, relevant patents was those patents which have the word “comprising” in the first 500 characters of the patent claims *and* have more than 10 forward citations within 10 years from patent issue date or more than 5 forward patent citations within 5 years of patent issue date.

Our proxy for broad, blocking, relevant patents combines text from patent claims with forward patent citations, and enables large scale empirical studies. This approach responds to calls for using combinations of procedural and text based indicators of patent value (Reitzig, 2004). The argument has been made that forward citations are inconsistent with the blocking nature of a patent – because by definition a blocking patent cannot be cited, as it prevents other inventors from entering the space (Blind et al., 2009). However, other research

Table 2
University spin-off emergence from the star-scientist-entrepreneur's lab.

Technology-market matching (TMM)			Claiming and Protecting the Invention			Founding Team Composition			Strategic Timing
Spin-off§	Founded (Year)	TMM during project formulation (Y/N)	Elite Journal**	Platform Technology (Y/N)	Blocking Patent (Y/N) **$**	Academic Co-founder/s†*	Star Scientist's Formal Role/s at founding	Prior Experience of Business Co-founder/s	Time post grant of first blocking patent before firm formation (years)
Enzytech Inc.	1987	YES	**Nature (1976); JPS (1984); JPS (1987)**	YES	NO	Alexander Klibanov; Robert Langer		Biopharma	
Neomorphics	1988	YES	**JACS (1987); JPS (1988)**	YES	YES	Joseph Vacanti; Robert Langer		**VC** & Diagnostics	−3
Opta Food Ingredients	1991					Alexander Klibanov, Akiva Gross, Robert Langer		Food MNC	
Focal Inc.	1991					Jeffrey Hubbell; Henry Brem; Marvin Slepian; Robert Langer	BM; SAB	Medical Device MNC	
Acusphere Inc.	1993	YES	**Nature Biotechnology (1991); Science (1994)**	YES	YES	Robert Langer	BO; SAB	**VC**	1
EnzyMed Inc.	1993					Douglas Clark; John Dordick; Alexander Klibanov; Robert Langer	SAB	Biopharma & Medical Devices	
Reprogenesis Inc.	1993	YES	**Science (1993)**	YES	YES	Anthony Atala; Joseph Vacanti; Robert Langer		Serial Entrepreneur	2
Sontra Medical Inc.	1996	YES	**Science (1995)**	YES	YES	**Joseph Kost; Samir Mitragotri;** Robert Langer	BM; SAB	Serial Entrepreneur	8
Advanced Inhalation Research	1997	YES	**Science (1997)**	YES	YES	**David Edwards;** Robert Langer		**Langer Lab Alumni**	−2
MnemoScience Corporation GmbH	1998	YES	**Science (2002)**	YES	YES	**Andreas Lendlein;** Robert Langer		**Langer Lab Alumni**	−2
MicroCHIPS Inc.	1999	YES	**Nature (1999)**	YES	YES	**John Santini;** Michael Cima; Robert Langer	P; BO; BM	**Langer Lab Alumni**	1
TransForm Pharmaceuticals Inc.	1999				YES	Robert Langer	P; BO; BM	**VC** & Pharma MNC	
Combinent Biomedical Systems Inc.	2000				YES	William Crowley; Robert Langer	BO; EO; BM	**VC**	−10
Momenta Pharmaceuticals Inc.	2001	YES	**PNAS (1993)**; Science (1999); **PNAS (2003)**	YES	YES	**Ram Sasisekharan; Ganesh V. Kaundinya;** Robert Langer	BO; BM	**VC** & Pharma	3
Pulmatrix Inc.	2003	YES	**Science (1997)**; **PNAS (2001)**	YES	YES	**David Edwards;** Alexander Klibanov; Robert Langer	BO; SAB	**VC** & Pharma MNC	4
Pervasis Therapeutics	2003	YES	**Nature (1992)**; PNAS (2000)	YES	YES	**Elazer Edelman;** Helen M. Nugent; Joseph Vacanti; Robert Langer	BO; BM	Medical Device	6
InVivo Therapeutics	2005	YES	**PNAS (2002)**	YES	YES	Yang Teng; **Rajiv Saigal**; Robert Langer	SAB	Engineering MNC	8
Living Proof	2005	NO	**JACS (2000)**	YES	NO	**Daniel Anderson;** Robert Langer	BO; BM	**VC & Langer Lab Alumni**	
Arsenal Medical	2005	NO	**Nature Biotechnology (2002)**	YES	YES	Jeffrey Carbeck, Milan Mrksich; George Whitesides; Robert Langer	BO; BM	Chemical MNC	−5
Bind Therapeutics	2006	YES	**Science (1994); PNAS (2006)**	YES	YES	**Omid Farokhzad;** Robert Langer	BO; BM; SAB	**VC** & Pharma	10
Semprus Biosciences	2006	YES	Nature (2006)	YES		**Christopher Loose;** Gregory Stephanopoulos; Robert Langer	BO; BM	**VC**	
T2 Biosystems	2006					Ralph Weissleder; Michael Cima; Tyler Jacks; Lee Josephson; Robert Langer	BM	**VC**	
Selecta Biosciences	2007	YES	**Science (1994);** NEJM (2000); **PNAS (2008)**	YES	YES	Ulrich von Andrian, **Omid Farokhzad**; Robert Langer	BM; SAB	Pharma	11
Taris Biomedical	2008		JCR (2010)			Michael Cima; Robert Langer	BM	Pharma MNC	

(*continued on next page*)

Table 2 (*continued*)

Technology-market matching (TMM)			Claiming and Protecting the Invention			Founding Team Composition			Strategic Timing
Seventh Sense Biosystems	2008	YES	**PNAS (1993); Nature Biotechnology (2008)**	YES	YES	**Samir Mitragotri;** R. Rox Anderson; **Joerg Lahann;** Robert Langer	BO; BM; SAB	**VC**	12
Kala Pharmaceuticals	2009		PNAS (2007)	YES	YES	**Justin Hanes;** Robert Langer	BM	**VC** & Pharma	
Moderna Therapeutics	2010		Cell Stem Cell (2010)	YES		Derrick Rossi; Kenneth Chien; Robert Langer	BM; SAB	Biotech MNC	
Blend Therapeutics	2011	YES	**JCR(2001); PNAS (2008)**	YES	YES	**Omid Farokhzad;** Stephen Lippard; Robert Langer	BM	Pharma MNC	10
480 Biomedical	2011	NO	**Nature Biotechnology (2002)**	YES	YES	George Whitesides; Robert Langer	BM	Biotech	1
Gecko Biomedical	2013	YES	**Nature Biotechnology (2002); PNAS (2008); STM (2014)**	YES	YES	**Jeffrey Karp;** Jacques Marescaux; Patrick Houvet; Robert Langer	SAB	Biopharma	3

*Academic co-founder as mentioned on patents/papers/company website/documents/press releases/SEC filings.
§ Firm founded from Langer Lab technology in bold.
**Langer co-authored papers in bold. A blank cell indicates no elite journal paper associated with the emergence of that venture. Platform technologies are identified from the journal paper.
$ YES indicates one or more broad, blocking and relevant patents with Langer as a co-inventor. A blank cell indicates no Langer co-invented patent associated with the spin-off.
† Langer Lab Alumni in bold.
P: Promoter; BO: Beneficial Owner; BM: Member, Board of Directors; SAB: Scientific Advisor; EO: Executive Officer.

suggests that self-citations are a greater indicator of market value than external forward citations (Hall et al., 2005). Maine and Thomas (2017) argue that the star scientist's collaborators build on his blocking patents, extending the technology in differing directions, resulting in high citations.

3.3. Identifying papers based on platform technologies

Content analysis was employed on the star scientist's co-authored papers to determine platform technologies (Hsieh and Shannon, 2005). The top 200 frequently occurring words in the titles and abstracts of all these papers were identified. Three of the authors then independently assessed this list and eliminated commonly used words in English and in the biomedical domain. In the few cases where there was a difference in perception, the authors discussed and resolved their differences. Co-occurring words such as “tissue engineering” and “controlled release polymers” were combined as key phrases and included in the list. The refined list consisted of words such as nanoparticles, aptamers, and polymers, which are highly indicative of platform technologies as they are broadly applicable across multiple domains. Using this selective, validated list, papers were identified which had used these words in the titles and abstracts and thus classified as describing platform technologies in the biomedical domain. The list generated by this automated and manual verification exercise is available on request.

3.4. Entrepreneurial capabilities to endow the university spin-off for success

The patterns revealed by the patent-paper-venture matching, the identification of broad, blocking patents, and the identification of platform technologies were compared and contrasted, with particular attention paid to paper characteristics, patent characteristics, the selection of markets, co-authors, co-inventors, co-founders, and timing of spin-off formation. A process model of four key entrepreneurial capabilities which lead to well-endowed university spin-offs was iteratively developed. These capabilities were then further explored at the level of the university spin-off and their impact on success assessed.

Ten interviews were conducted and three additional video interviews with key individuals were also used to inform and refine the process model (Appendix 2). Consistent with the extended case study method, following initial interviews with the star-scientist-entrepreneur and initial patent-paper-venture matching, the analysis was iteratively refined with direct involvement of the SSE in categorizing patents and in confirming co-inventor and co-founder involvement. Three interviews were conducted with the MIT TLO IP counsel who leads the patent portfolio of the SSE. A scientific co-founder, a business co-founder, a venture capitalist who was also CEO of a Langer lab spin-off, and an IP counsel of a co-founded spin-off were also interviewed. Interviews with these varied stakeholders in the innovation ecosystem informed and validated analysis of the entrepreneurial capabilities of the focal SSE.

Further data was gathered on all 30 spin-offs to demonstrate the four entrepreneurial capabilities identified through our patent-paper-venture matching and through our interviews and archival data. For the 30 spin-offs co-founded by the SSE, technology-market matching was observed and validated at the project formulation stage, as well as at the platform technology and the firm-level. Claiming and protecting the invention was demonstrated for all 30 spin-offs by observing the presence or absence of elite publications, blocking patents, and platform technologies in the emergence of each venture. Strategic timing was measured as the time from the issuing of the first blocking patent associated with the spin-off to the time of firm founding.

Attracting and mentoring the founding team was observed through the founding team composition, including documenting the involvement of collaborating labs, academic co-founders, and his lab alumni. The tenure of the initial CEO – sometimes a founder and sometimes recruited up to 5 years after the firm was founded – was documented, and their prior education was coded as PhD scientist or non-scientist.

Table 3
Endowing science-based university spin-offs for success.

Firm	Founded	Initial CEO Prior Business Experience & Education	SSE's Role in Attracting and Mentoring the Founding Team	Raised + IPO + Acquisition[a] (Million US$)	Million US$ Dollars Raised/ Year	Technology Development Status[a]	10 Year Survival Status[b]
Advanced Inhalation Research	1997	Phd Scientist. No relevant business experience.	Mentoring Scientist-Entrepreneurs; Attracting VCs	115.00	57.50	Technology in use	**A**
Living Proof	2005	Cosmetics MNC - SVP (Marketing). Non-scientist.	Mentoring Scientist-Entrepreneurs; Attracting VCs	355.00	32.27	Technology in use	**S**
Momenta Pharmaceuticals	2001	Biopharma SVP (Corp. Dev.). Non-scientist.	Mentoring Scientist-Entrepreneurs; Attracting VCs	74.80	24.93	Products on market and in clinical trials	**S**
Selecta Biosciences	2007	Biopharma CEO. PhD Scientist.	Mentoring Scientist-Entrepreneurs; Attracting VCs	265.68	24.15	In clinical trials	**S**
Acusphere Inc.	1993	Biopharma CEO. VC. Non-scientist.	Attracting VCs	147.50	14.75	Product not approved	**S**
BIND Therapeutics	2006	Biopharma CEO. Non-scientist.	Mentoring Scientist-Entrepreneurs; Attracting VCs	144.00	14.40	Technology assets acquired by incumbent partner	**S**
Blend Therapeutics	2011	Biopharma CEO. Non-scientist.	Mentoring Scientist-Entrepreneurs; Attracting VCs	104.29	14.90	In clinical trials	Has survived for 7 years.
Semprus Biosciences	2006	VC. Non-scientist.	Mentoring Scientist-Entrepreneurs; Identifying & nurturing business talent	60.26	10.04	Technology development discontinued by acquirer.	**A**
Gecko Biomedical	2013	Biopharma (Marketing & Sales). Non-scientist.	Mentoring Scientist-Entrepreneurs	43.70	8.74	CE Mark approval in Europe	Has survived for 5 years.
Enzytech Inc.	1987	Biopharma CEO. Non-scientist.		41.50	8.30	Technology in use	**A**
Seventh Sense Biosystems	2008	VC. PhD Scientist.	Mentoring Scientist-Entrepreneurs; Attracting VCs	74.73	7.47	FDA approval for device	**S**
Neomorphics	1988	Med-tech. VC. Non-scientist.		27.00	6.75	Technology in use	**A**
480 Biomedical	2011	Biopharma EVP (Law). Non-scientist.	Attracting VCs	45.00	6.43	Product in clinical testing	Has survived for 7 years.
Pulmatrix Inc.	2003	VC. Non-scientist.	Mentoring Scientist-Entrepreneurs; Attracting VCs	74.35	4.96	In clinical trials	**S**
Arsenal Medical	2005	Medical Devices. PhD Scientist.	Attracting VCs	47.00	3.62	FDA approval for clinical study	**S**
Pervasis Therapeutics	2003	Biopharma VP (Marketing & Sales). Non-scientist.	Mentoring Scientist-Entrepreneurs. Attracting VCs.	42.80	3.57	Development halted after Phase 2	**A**
MicroCHIPS Inc.	1999	Serial Entrepreneur. Non-scientist.	Mentoring Scientist-Entrepreneurs; Attracting VCs	58.00	3.05	In clinical development	**S**
Sontra Medical Inc.	1996	Serial Entrepreneur. Non-scientist.	Mentoring Scientist-Entrepreneurs; Attracting VCs	32.90	2.99	Technology licensed out	**S**
Reprogenesis Inc.	1993	Serial Entrepreneur. Non-scientist.		17.00	2.43	SSE-related programs suspended in 2002	**S**
Invivo Therapeutics	2005	No relevant business experience. Non-scientist.	Mentoring Scientist-Entrepreneurs Identifying & nurturing business talent	31.10	2.39	No revenues.	**S**
MnemoScience Corp. GmbH	1998	No relevant business experience. Langer lab alumni.	Mentoring Scientist-Entrepreneurs	unclear		–	**S**

[a] Calculated from SEC filings, company press releases, annual reports, news articles and Thayer (2016).
[b] **S** = Has survived for at least 10 years. **A** = Acquired within 10 years.

The prior business experience of the founding CEO was coded as biopharma executive, biopharma, medtech, VC, serial entrepreneur, and cosmetics MNC executive. The SSE's formal roles at founding, as documented in SEC filings, were coded as board member, scientific advisory board member, beneficial owner and/or promoter. Informal roles carried out by the SSE in attracting and mentoring the founding team were observed and coded as one or more of: mentoring scientist-entrepreneurs, identifying and nurturing business talent, attracting experienced CEOs, and attracting VCs. Mentoring scientist-entrepreneurs may happen both pre- and post-formation. It can occur in the star scientist's lab or it may occur when the star scientist continues to mentor former lab alumni through his membership in the scientific advisory boards of co-founded university spin-offs. Identifying and nurturing business talent occurs when the eventual CEO of a venture was identified and mentored by the SSE prior to firm formation. Attracting VCs is observed when a VC is a co-founder along with the SSE and in the case of documentation of a VC investing (sometimes in multiple ventures) because of the SSE's reputation.

Science-based university spin-offs endowed with valuable IP, skilled people, and technology-market orientation enjoy enhanced chances of success. This measure of “well-endowed university spin-off” is proxied with ten-year survival status and with total financing raised/year since founding. The total amount of financing raised by each university spin-off was gathered from SEC filings, press releases, and other secondary sources, and includes seed and venture capital financing raised, money raised through an IPO, and money received upon the acquisition of the firm. This measure includes all non-government finance raised from firm founding until firm exit or until February 2018, and thus may understate the total financing received by the spin-offs. To control for the wide range of age of the firms, the success metric of millions of US$ raised per year was calculated for each of the spin-offs which emerged from the SSE's lab. This measure aims to be a proxy for well-endowed university spin-offs. The impact of founding team characteristics and the SSE's role in attracting and mentoring the founding team are assessed.

4. Findings

The science-based university spin-offs co-founded by the exemplar star-scientist-entrepreneur are well-endowed compared to an average science-based spin-off (Table 2, Table 3). His stats are compelling on every dimension (for comparison in the biomedical sector, see Holley and Watson, 2017). First, as a prolific academic, he has published over 1400 papers, and is the most highly cited chemical engineer in history (>300,000 citations). With over 1000 patents issued or pending worldwide, including over 360 issued US patents, he exceeds the patenting output of all but the most established biopharmaceutical firms. Technologies developed in his lab have improved the lives of millions of people. And as the co-founder of 30 well-endowed science-based university spin-offs, he has refined commercialization processes which help translate his laboratory inventions to ventures with a higher likelihood for success.

The focal SSE did not begin his career as a star scientist, nor was he identifiable as such for over a decade. When he graduated with a PhD in Chemical Engineering from MIT in 1974, at the height of the oil crisis, he turned down four lucrative job offers from oil companies, preferring to work as an engineer in the clinical research laboratory of Dr. Judah Folkman at the Harvard Medical School. His interdisciplinary research was fruitful, but not recognized by much of the establishment, and was met with scepticism from leading researchers, granting agencies and the US Patent Office. His first 9 NIH grants were rejected, and his first 5 patent filings failed the “non-obviousness test”. He was granted his first patent only after presenting the patent office with signed affidavits from established scientific leaders in his field attesting to the highly unconventional nature of his work.

From this inauspicious start, spin-offs from the lab of this star scientist have raised over US$2 billion cumulatively. These spin-offs have achieved success by several measures including meeting the 10-year survival threshold, raising multiple rounds of financing, and, for some of the more mature ventures, getting products to market (Table 3). All ventures spun out of the lab of the SSE meet or are in the process of meeting the 10-year survival threshold, if acquisitions are included as survival (Table 3). In contrast, most science-based university spin-offs are likely to fail within the first decade of founding (Dimov and De Clerq, 2006; Timmons, 1990). As to financing, all but two of the ventures spun out of the lab of the SSE raised at least US$27 million in financing (Table 3). Zhang (2009, Table 6) finds that, of those university spin-offs which raise venture capital, average total VC money raised is US$23.55 million, giving a comparison level for our data. This provides further evidence that spin-offs co-founded by the star scientist entrepreneur are well-endowed pre-formation.

The evidence of entrepreneurial capabilities deployed by the SSE is analysed with a focus on the capacity to sense and shape opportunities and to seize opportunities *pre-formation*. One pre-formation entrepreneurial capability central to sensing and shaping opportunities was observed and validated through further interviews. Three pre-formation entrepreneurial capabilities involved in seizing opportunities were revealed through patent-paper-venture matching, further data analysis, and additional interviews.

The four entrepreneurial capabilities are depicted in a process model (Fig. 3), which begins with technology-market matching at the project formulation stage in the research lab. The process of the emergence of the university spin-off was observed to proceed sequentially onwards through claiming and protecting the invention (influenced by the university TLO and the USPTO), to attracting and mentoring the founding team (influenced by VCs, academic collaborators and experienced entrepreneurs), and finally to the founding of science-based university spin-offs (with strategic timing influenced by the scientist, his academic collaborators and VCs). The cycle resumes as new lab members are attracted to the star scientist's lab and directed towards solving unmet market needs, often leveraging existing platform technologies. These four entrepreneurial capabilities leading to well-resourced science-based university spin-off emergence are described next, along with the evidence which supports them.

4.1. Sensing and shaping opportunities: technology-market matching

The star-scientist entrepreneur sensed and shaped opportunities through technology-market matching and this capability was passed on to his graduate students and through them to his co-founded ventures. Strong technology-market matching capability was demonstrated within the research lab in formulating research projects targeting unmet market needs (Table 2), in co-founding ventures based on technologies outside his lab (Table 2), and in co-founding multiple spin-offs from the same platform technology (Fig. 4). The star scientist has built an unusual lab culture around identifying and prioritizing research ideas. He purposefully steers his lab members and academic collaborators in the selection and development of research projects that address significant unmet market needs. As depicted in Table 2, we observed pre-formation technology-market matching at the project formulation stage in 18 out of 21 spin-offs from the lab of the SSE.

The focal SSE practiced *pre-formation* technology-market matching in both directions: leading from the market, and leading from the technology through formation of multiple ventures from a single platform technology. Leading from the market is less common for scientist-entrepreneurs but can be clearly demonstrated in the genesis of the star scientist's co-founded ventures Applied Inhalation Research (AIR) and MicroCHIPS. In the case of AIR, when applied mathematician David Edwards came to him to get advice, the star scientist steered him towards a known problem which would utilize both Edwards' mathematical modelling expertise and the star scientist's most renowned platform technology of controlled release polymers. This market-focused research sought to design therapeutic particles which could be inhaled

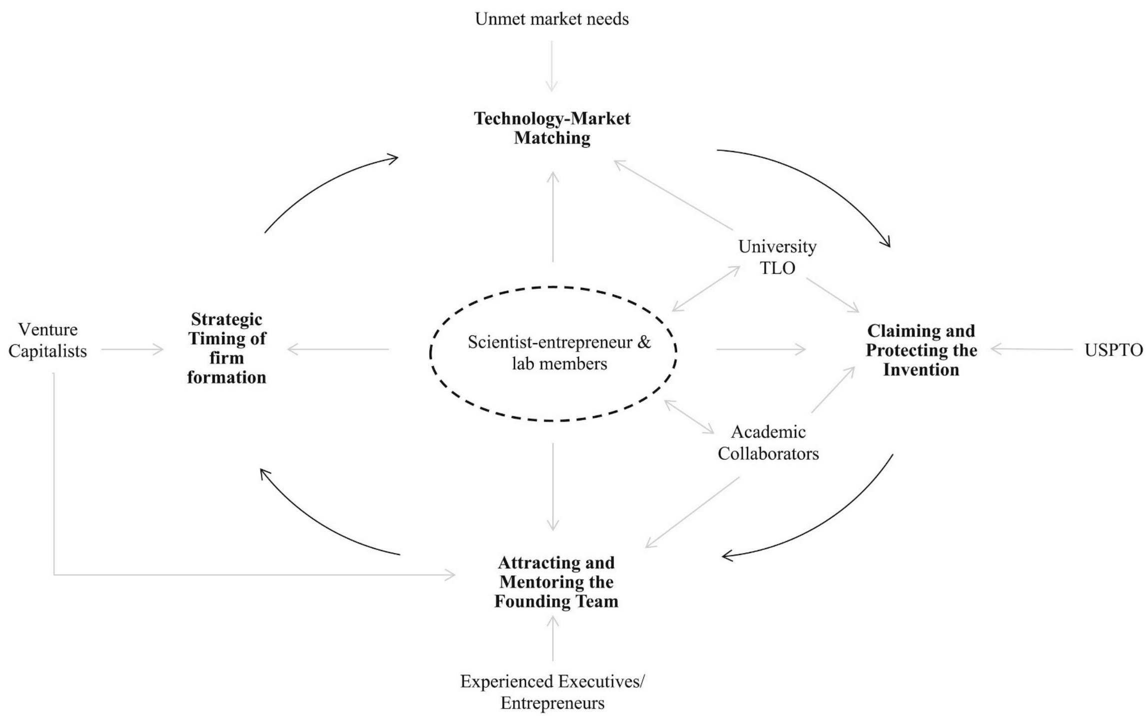

Fig. 3. A process model of entrepreneurial capabilities leading to well-endowed university spin-off emergence.

deeply and dispersed widely throughout the lungs. Edwards and the star scientist went on to develop large porous particles for pulmonary drug delivery, filing a broad, blocking patent in 1996 and publishing the key research in Science in 1997, and co-founding AIR that same year (Table 2). In another instance, the star scientist was inspired by conventional microchip fabrication and envisaged another solution to a health problem, that of people forgetting to take medications and contraceptives at the prescribed times. As he had no previous experience with microchip fabrication technology, the star scientist discussed his ideas for a programmable, implanted biomedical device which would enable the controlled release of therapeutics over years or even decades, with an MIT colleague in Materials Engineering, Prof. Michael Cima. This matching of technology and market in the star scientist's mind led to an exploratory research collaboration and the eventual co-founding of MicroCHIPS (Table 2). Co-founder Michael Cima credits the star scientist with being "gifted at 'connecting technologies to true medical needs.'" (Schaffer, 2015).

The SSE's capability in technology-market matching was also observed in the ventures he co-founded where the technology did not come from his lab. In these instances, scientists from other labs and institutions approached him because of his known entrepreneurial capabilities. Derrick Rossi, a researcher at Boston Children's hospital and co-founder of Moderna Therapeutics, approached him with a stem cell invention, and was redirected to commercialize a breakthrough platform technology:

> Rossi's first breakthrough was to create a disguise for the mRNA so that it could slip into the cell unnoticed. As he explained to Langer, he did this by modifying two of the mRNA's nucleotides, or building blocks. Once they breached the cells' defense mechanism, the mRNA reprogrammed the cells into IPS cells. That was the feat that got Rossi so much acclaim. But what most struck Langer as he listened to Rossi was the first part: the technique that Rossi had developed to modify the mRNA. "This is a much bigger discovery than something that affects stem cell behavior," Langer told Rossi, already imagining the potential. "You could apply it to make anything."
>
> (Elton, 2013)

The formation of multiple ventures from a single platform technology is another form of technology-market matching, in this case leading from the technology, although the process is still iterative. As depicted in Fig. 4, the 30 spin-offs co-founded by this star scientist stem from 8 platform technologies. Most notably, he has co-founded 10 spin-offs over 25 years which draw on his platform technology of controlled release polymers. This technology is so broad that one firm has virtually no chance of tackling the entire breadth of value creation, and multiple ventures are formed even from sub-platforms. For example, following the development of controlled release nanoparticles (Gref et al., 1994), the star scientist and his post-doctoral fellow, Omid Farokhzad, developed stealth nanoparticles which could bind to targeted sites to treat cancer. This led to the formation of BIND Therapeutics, Selecta Biosciences, and Blend Therapeutics over the following years (Fig. 4), matching the controlled release targeted nanoparticle platform technology to the treatment of malaria, life-threatening allergies, smoking cessation, type 1 diabetes, inflammation, and pain. With the technology matched to several markets, greater value is created, learning occurs, and more opportunities for success are available. The SSE along with the MIT TLO coordinate this technology-market matching pre-formation by licensing patents by field of use, leaving room for future spin-offs (Appendix 2**, interviews 5 and 15,** Fig. 4**).**

4.2. Seizing opportunities

Once an opportunity is sensed and shaped, additional capabilities are required to seize that opportunity (Teece, 2007). We observed this seizing of opportunities through three entrepreneurial capabilities demonstrated by the star-scientist-entrepreneur pre-formation (Fig. 1, Fig. 3). Notably these pre-formation entrepreneurial capabilities imprint upon the nascent firm through the mentoring of lab members who go on to leadership roles in the emerging science-based spin-off.

4.2.1. Claiming and protecting the invention

A second entrepreneurial capability demonstrated was through claiming and protecting lab inventions in order to create and capture value. The SSE and his academic co-founders repeatedly invented a

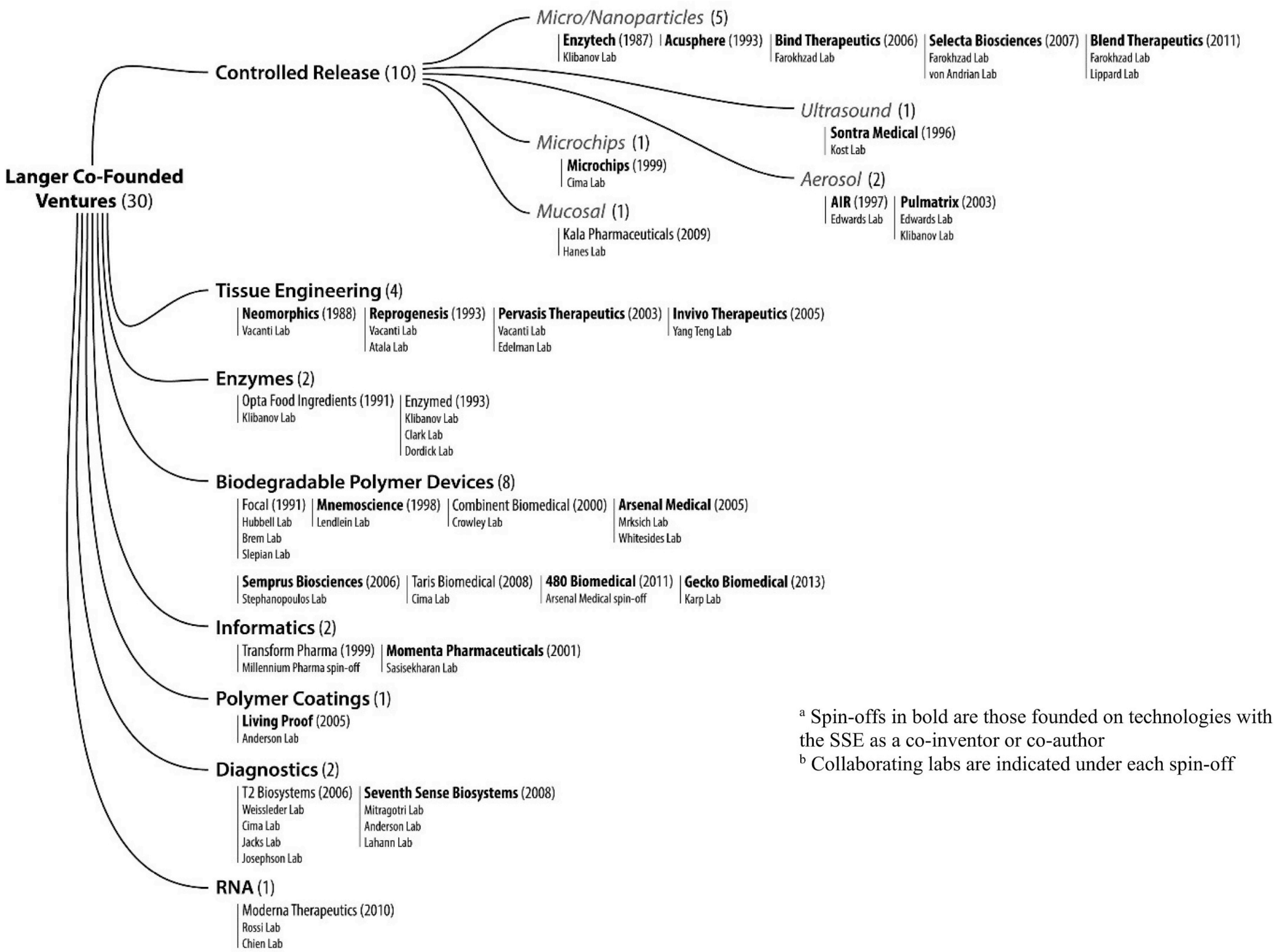

Fig. 4. Technology-Market Matching: SSE co-founded spin-offs based on platform technologies[a,b].

platform technology, published the results in an elite journal, and obtained at least one broad, blocking, and relevant patent. Such patents send a strong signal to potential investors (Maine and Thomas, 2017). This strategy was consistent in spin-offs formed from 1987 to 2013, demonstrated by 18 of 21 spin-offs from the lab of the star scientist (Table 2). This method of claiming and protecting scientific inventions enhances the probability of raising external financing for the spin-off.

Through patent-paper-venture matching, the prevalence and importance of broad, blocking, relevant patents on a platform technology is revealed (Table 2). Surprisingly, the timing of filing such patents is also distinctive in the approach of this star scientist (Table 2, far right column). The conventional wisdom for biomedical firms is to patent narrowly first and patent more broadly later in commercialization (Hegde et al., 2009). In contrast, the star scientist, his lab members, collaborating labs, and the MIT TLO, file broad patents as early as possible and in such a way as to give his collaborators protected room to take the technology in different directions through patent continuations-in-part (CIPs) sharing the same priority date as their parent document. The broad, blocking patents are filed early (Table 2), and broad protection is also generated through multiple patents on alternative scientific mechanisms.

It was clear from primary interviews (Appendix 2, **interviews 5 and 7**), as well as previous studies (Hsu and Bernstein, 1997; Nelsen, 2004; Shane and Stuart, 2002), that the MIT TLO plays a critical role throughout the patenting and licensing process for all MIT scientists, by selecting the invention disclosures to take forward into patent application and prosecution. In cases where the inventors are from multiple organizations, the MIT TLO often plays the role of the lead organization, coordinating negotiations with licensees and carefully licensing out pieces of the intellectual property by fields of use, with clauses indicating that the licence has to be returned in case commercialization milestones are not met within a specified timeframe (Appendix 2**, interview 5**). By ensuring that the technologies developed in the star scientist's lab and across MIT are protected by patents before public dissemination, the TLO is able to satisfy both the need for sharing new knowledge in scientific journals while at the same time maintaining strong property rights to incentivize commercialization.

Unusually, we see evidence of the SSE and the MIT TLO coordinating the manner in which claiming and protecting the IP is done to enable broader technology-market matching from platform technologies. In several instances, the star scientist's patents have been licensed by field of use and even by type of therapeutic payload to allow multiple opportunities for value creation. This strategic management of IP is particularly evident with the star scientist's platform technologies of controlled release polymers and biodegradable polymer devices (Fig. 4). Such field of use licensing is practiced both by the MIT TLO and by the spin-offs themselves, once they have in-licensed and built their own IP portfolio.

4.2.2. *Attracting and mentoring the founding team*

The star-scientist-entrepreneur demonstrated another entrepreneurial capability in attracting and mentoring the founding team.

He limited operational involvement in his spin-offs, primarily acting in a scientific advisory role and as a Board Member (Table 2). This created a greater need for scientific leadership within the spin-off, given the need to refine inventions from the SSE's lab into replicable, viable products. As shown in Table 2, in 15 of the 21 spin-offs from his lab, a lab alumnus is a co-founder (the SSE co-founded 5 more spin-offs with faculty at other Boston institutions and was the sole academic founder of Acusphere). These lab co-founders, along with other lab alumni and earlier lab spin-offs, co-developed the platform technology underlying the spin-off and are exceptionally dedicated to the cause (Langer, 2013). In most instances, these lab co-founders take on a scientific leadership role, and are paired with experienced managers taking on the role of CEO, although, interestingly, there is sometimes a lag between firm founding and the hiring of the first CEO. Thus the university spin-off benefits from tight linkages to the SSE's lab through lab alumni in scientific roles permitting easier flow of tacit knowledge.

Past the SSE's formal role at founding (such as being on the board of directors and/or the Scientific Advisory Board), three ways in which he attracted and mentored the founding team were observed and were coded as mentoring scientist-entrepreneurs, identifying and nurturing business talent, and attracting VCs (Table 3). Notably, direct evidence of the star scientist attracting experienced CEOs was not observed. In the most successful ventures, evidence of mentoring scientist-entrepreneurs and attracting VCs was found (Table 3). This capability was identified more frequently in the latter half of his career (Table 3).

4.2.2.1. Mentoring scientist-entrepreneurs. The mentoring of scientist-entrepreneurs can happen in the university lab and also – in the case of repeat ventures – in the spin-off when the star-scientist-entrepreneur provides mentoring through the scientific advisory board. As identified in Table 3, evidence of such mentoring was found in 15 of 21 ventures spun out of the lab of the focal SSE. Lab alumni who co-founded a spin-off with the SSE had been mentored both as a scientist and with an entrepreneurial mindset *pre-formation*. In the same way that the SSE was mentored in solving significant problems in the Folkman lab (Cooke, 2001), he mentored lab members in his own lab. A pattern began in 1996 with Sontra Medical, the first of these ventures which commercialized the research of a student supervised in the lab of the SSE. In the case of repeat ventures with the same alumni, mentoring continued to occur through the scientific advisory board. Out of the 6 ventures for which this informal role was not observed, 4 were co-founded with experienced scientist-entrepreneurs and the remaining 2 were at the beginning of the star scientist's entrepreneurial career.

4.2.2.2. Identifying and nurturing business talent. A less frequent but unusual role observed was that of the star-scientist-entrepreneur identifying and nurturing business talent. Clear evidence of this was found in 2 ventures (Table 3). In the case of Semprus Biosciences, the SSE met the eventual CEO David Lucchino years before the founding, recommended that he study for his MBA at MIT, and offered to help match him with one of the technologies being developed in his lab. Lucchino was a co-founder of Semprus, and served as President and CEO from founding through to successful acquisition 6 years later (Table 3). In the case of INVIVO, eventual CEO Frank Reynolds, also studying for his MBA at MIT, was attracted to the SSE's research on spinal cord injury because of his personal experience with this type of injury. The SSE supported him in the development of the commercialization strategy for his treatment for spinal cord injury, which was the topic of Reynolds' MBA thesis. Reynolds subsequently co-founded INVIVO, serving as CEO from founding in 2005 until 2013.

4.2.2.3. Attracting VCs. Another part of the star-scientist-entrepreneur's capabilities in attracting and mentoring the founding team lies in his ability to repeatedly attract VCs. Since co-founding AIR with VC Terrance McGuire, the SSE has developed deep relationships with venture capitalists (two of whom are alumni from his lab). A VC was a co-founder in 6 of the 21 ventures co-founded by the SSE from his lab. In 2 other cases, evidence was found that a VC was attracted to invest because of the reputation or network of the SSE. No evidence was found of the SSE directly attracting experienced CEOs: however there was some evidence of an indirect role through the networks of the VCs he attracted.

Venture capitalists often suggest managerial talent including initial CEOs, drawing on their extensive networks. The reputation and credibility of the SSE's view of the potential impact of the technology is key to convincing such business talent to take the risk of joining the founding team. Stephane Bancel, CEO of Moderna, part of the network of the founding VC, was attracted to the venture by the potential of the technology and the reputation of the SSE, explaining “I was willing to take a career risk by working on something that might not work, but it would have to be something that, if it worked, would change the world” (Elton, 2013). Alternatively, venture capitalists may join the founding team themselves as placeholder CEOs until a suitable CEO is found, as observed in Living Proof (Table 3), or later joining as CEO when pursuing an IPO, as observed in BIND.

The business co-founders (and the initial CEO) chosen brought experience as a serial entrepreneur, a venture capitalist, or as a senior executive in a biotech, pharmaceutical or chemical multinational corporation. Lab alumni rarely took on business leadership roles, more typically co-founding and/or joining in scientific leadership roles. A VC who served as CEO in one of the spin-offs co-founded by the star scientist made the case that the leadership of university spin-offs was as much or more important to their success as the technology:

> [a science-based university spin-off] “want[s] foundational patents that can define game changing technology” … [and] … “you want great science, some patent protection and a great team around it.” …. a “great team can be successful with a not so great technology” [but you can ruin the commercialization of a great technology with a poor team]. (Appendix 2**, interview 4**)

Spin-offs whose initial CEO had executive experience at a larger biopharma company were more likely to be successful (Table 3). There are two notable exceptions: in the case of Living Proof – a spin-off with no clinical trial hurdles and a competitive commercialization environment, the executive experience of the initial CEO comes from a cosmetics multinational corporation; in the case of AIR – it was acquired after only 2 years, and focused on scientific development during those first years. Thus, the university spin-off benefits from both the networks and experience of attracted venture capitalists and the initial CEOs, who facilitate alliance partnerships and investment.

4.2.3. Strategic timing

The patent-paper-venture matching methodology enabled the identification of the entrepreneurial capability of strategic timing, which contributes to the emergence of well-endowed university spin-offs. The star-scientist-entrepreneur and his collaborators identify critical unmet needs and formulate projects in an attempt to solve them. For projects which lead to breakthrough solutions, they patent, publish, and continue to refine these ideas (sometimes in stealth mode) until they are ready for commercialization through spin-off formation. The SSE guides technology-market matching during project formulation and mentors lab members in understanding, evaluating, and mitigating the gap between successful experiments in the research lab and commercial viability. Pre-formation, technology-market matching begins unusually early – at the project formulation stage (Table 2). Next, the SSE repeatedly files broad, blocking, relevant patents at the earliest opportunity. These are coordinated in timing and context with elite publications (Table 2). In contrast, the SSE co-founds the venture far later than might be expected (Table 2). Thus, the spin-offs from the lab of the SSE often have a prolonged gestation period within the university. During this gestation time, further technical goals are set and achieved, with additional journal publications and follow-on patent protection.

As a tangible example, in the case of Bind Therapeutics, the unmet market need was targeted drug delivery through the bloodstream and the controlled release of that drug. Ruxandra Gref, Yoshiharu Minamitake, and Maria Peracchia, Langer lab post-doctoral fellows, succeeded in inventing a solution and published this research in Science in 1994. The broad, blocking, relevant patent was filed even before the paper was submitted. Many scientists entrepreneurs would have launched a venture at that time. However, the technology was not considered by Langer to be viable yet, because it was too far from meeting the clinical needs of patients in the identified market opportunity – the therapeutic nanoparticles circulated in the bloodstream for less than an hour and needed to circulate for several hours and to release their payload accurately – and developing those aspects of the technology would take longer than a venture capital fund's investment window (Maine and Thomas, 2017). During the gestation period within MIT, advances were made in the limiting factors preventing viability. Aspiring scientist-entrepreneur Omir Farokhzhad joined the Langer Lab and extended the research, making a breakthrough in developing targeting to specific tumour sites, and further advancing the technology within his own lab when he started a faculty position at Harvard. Together, Farokhzhad and Langer founded both Bind Therapeutics and Selecta Therapeutics, from the same underlying technology, when they assessed the remaining development time and perceived value to be a good fit with venture capital investors.

Timing his publishing and patenting and, in particular, spin-off formation strategically, the SSE was able to build a strong case for multiple rounds of spin-off funding. Early focus on an unmet market need guided the development of the breakthrough research. Early timing of the initial elite paper and broad, blocking relevant patent were essential to prevent either scientific or commercial pre-empting of the innovation idea. But a conscious choice was made to *delay* venture formation until the technology was assessed to be viable, until scientific leadership of the venture was mentored, and until venture capitalist timelines and perception of value was met. Venture capitalist and co-founder Terry McGuire endorses this strategy but notes how unusual it is for scientist-entrepreneurs to delay venture formation (Arnaud, 2012). Yet, given the typical VC investment window of 3–5 years, ventures with a longer time to commercial viability post-formation, will be less likely to raise VC financing (Maine and Thomas, 2017; Pisano, 2010).

Our broader observations suggest that, since 2001, founding of the SSE's lab spin-offs have been purposively delayed until the technology is closer to commercial viability. Gestation times are presented for all of the spin-offs formed from technologies co-developed in the focal star scientist's lab and with him as a co-inventor (Table 2). The length of time from granting of the first broad, blocking, relevant patent on the platform technology to the founding of the corresponding spin-off (gestation time) has increased over his career. The average length of time to founding in the earlier half of the spin-offs formed out of the star scientist's lab was 0.2 years: this timing has grown to an average of 6.2 years in the latter half (Table 2). Thus, stategic timing is observed in the coordination and sequencing of the other three pre-formation entrepreneurial capabilities and is most notable in the timing of firm formation (Table 2, Fig. 3).

5. Discussion

Most science-based university spin-offs emerge through long, complex pathways (Roberts, 1991). Some entrepreneurship scholars suggest that these spin-offs are less efficient at developing inventions than incumbents and make predictable mistakes: “For instance, they may hire the wrong people, develop the product for the wrong market, or try to develop it for too many markets and succeed at none, or simply run out of money.” (Dalay and Fosfuri, 2019, pp. 236; Arora et al., 2018). Linking science-based university spin-offs to the patent-paper pairs informing them reveals how early decisions taken by the star scientist entrepreneur (and his academic collaborators, with the support of the TLO), along with their coordination and sequencing, have laid a strong foundation for the emergence of these spin-offs pre-formation. The role of the SSE in four key entrepreneurial capabilities, which endow these science-based university spin-offs for success is depicted in Fig. 3 and discussed in this section.

5.1. Implications for theory

Teece (2007) has identified three key dynamic capabilities which impact firm performance: sensing and shaping opportunities, seizing opportunities, and transforming opportunities. While these capabilities are at the firm-level, there are growing calls for focusing on the “entrepreneurial function embedded in dynamic capabilities” Protogerou et al. (2012) p. 641. This is particularly relevant as the pre-formation stage of venture formation is seen as a neglected issue in the spin-off literature (Druilhe and Garnsey, 2004) and in entrepreneurship theory (Phan, 2004; Rasmussen, 2011). In focusing on entrepreneurial capabilities pre-formation, this study follows the emerging trend of focusing on individual-level skills and capabilities (Augier and Teece, 2009; Helfat and Peteraf, 2015) to further enrich the dynamic capabilities framework. Our study also responds to calls for more process-oriented studies to extend dynamic capabilities theory (Schilke et al., 2018).

At the firm-level, our study confirms dynamic capabilities of sensing and shaping capabilities, and seizing opportunities. The sensing and shaping capability is observed through technology-market matching at the firm-level (Fig. 4). The seizing opportunities dynamic capability is also observed at the firm-level through claiming and protecting the invention, attracting and mentoring the founding team, and strategic timing (Table 2). These firm-level capabilities enable the well-endowed science-based spin-offs to continue to outperform (Table 3).

Extending dynamic capabilities theory, we employ the patent-paper-venture matching technique developed in this paper to elucidate four entrepreneurial capabilities which the star-scientist-entrepreneur uses to better endow co-founded spin-offs *pre-formation* (Fig. 1). Whereas all spin-offs shown in Fig. 4 are co-founded by the SSE, those shown in bold font also have the SSE as a co-inventor or co-author, indicating his direct involvement from guiding the science from concept through potential applications and on to its commercialization through application specific ventures. This individual-level entrepreneurial capability termed technology-market matching (Table 2, Fig. 4) is an essential component of the sensing and shaping dynamic capability at the firm-level (Fig. 1).

The firm-level dynamic capability of seizing opportunities can be linked to the individual-level entrepreneurial capabilities of claiming and protecting the invention, attracting and mentoring the founding team, and strategic timing (Fig. 1). The entrepreneurial capability of claiming and protecting the invention at the individual level can be observed through the role of the SSE as a co-inventor on broad, blocking and relevant patents (Table 2). The entrepreneurial capability of attracting and mentoring the founding team by the SSE can be observed in Table 3 and through founding team members who are Langer lab alumni (Table 2). The individual level entrepreneurial capability of strategic timing can be observed through Table 2. Technology-market matching happenes very early on during project formulation. After technology market matching, successful breakthrough research is protected through broad, blocking, relevant patents which are then paired with elite publications. In constrast, venture formation is frequently delayed.

5.1.1. Sensing and shaping opportunities: technology-market matching

As Teece (2007, p. 1323) notes, “opportunity creation and/or discovery by individuals require both access to information and the ability to recognize, sense, and shape developments.” For science-based ventures, the entrepreneurial capability central to sensing and shaping opportunities – and linked to venture success – is technology-market matching (Gruber et al., 2008; Maine and Garnsey, 2006; Maine et al., 2014a). This entrepreneurial capability has rarely been observed *pre-formation* in a research laboratory. A notable exception is Rasmussen's study of university spin-offs where he notes the early shaping of research projects according to perceived market needs (Rasmussen, 2011, pp. 457). In the star-scientist-entrepreneur's research lab, we observed this capability practiced in the project formulation stage – both leading with the market opportunity and leading with the technology opportunity.

In the first approach to technology-market matching, large unmet needs trigger the search for *new* technologies to solve these problems. Star scientists can do this at the project formulation stage if they have an extensive awareness of multiple scientific domains and the ability to bring together an interdisciplinary team of other faculty members, postdoctoral fellows or graduate students. Reputation, trust, and past commercialization experience might underpin the ability of a star scientist to form such interdisciplinary teams. In this way the human capital and social capital of the star scientist and the human capital embodied in his network of collaborators (Murray, 2004), help in selecting promising avenues of research and in forming interdisciplinary project teams which can then target large unmet needs.

The second approach to technology-market matching is the ability to match *existing* technologies to viable market applications. Although sometime derided as "technology-driven," effective technology-market matching can happen from either direction (Maine and Garnsey, 2006). In fact, a star scientist may choose to use her in-depth domain expertise to carve out multiple university spin-offs from the same or similar platform technologies, each targeting a different unmet market need (Fig. 4). In this manner, the SSE is able to leverage the learning from one set of experiments and use it to form another spin-off targeted at a different market. This approach also serves to diversify the risk of failure among multiple university spin-offs: the success of one can benefit other related spin-offs, but the failure of one spin-off may not mean that the other spin-offs based on similar technology will fail. This risk diversification argument is consistent with Shane's (2004, pp.123–124) arguments for general purpose technology (GPT) commercialization by university spin-offs. However, whereas Shane (2004) anticipated this risk diversification to yield benefit to a single venture, the funding environment of science-based ventures seldom allows a single venture to focus on the full breadth of opportunities afforded by the platform technology. The additional benefit of multiple spin-offs from one platform, coordinated by the SSE and the TLO, is observed in this study.

5.1.2. Seizing opportunities

In introducing his second category of dynamic capability – seizing opportunities – Teece (2007, p. 1326) notes "once a new (technological or market) opportunity is sensed, it must be addressed through new products, processes, or services. This almost always requires investments in development and commercialization activity." Teece (2007) also elucidates the potential competitive advantage of locking up assets and of timing commercialization decisions. For a science-based university spin-off, the individual-level entrepreneurial capabilities *pre-formation* central to seizing opportunities are claiming and protecting the invention, attracting and mentoring a founding team to commercialize the invention, and strategic timing. Each entrepreneurial capability is discussed below in the context of related literature.

5.1.2.1. Claiming and protecting the invention. Patenting and publishing are central to the commercialization of breakthrough scientific inventions, constituting the currency of the venture (Hsu and Ziedonis, 2008; Maine and Thomas, 2017; Pisano, 2010). Consistent with Murray (2010) and with Murray and Stern (2007), we find that patents and papers may be based on the same underlying scientific knowledge, and that a primary match between a patent and a paper allows for longitudinal observation of attributes of the commercialization of academic research. The extension of the Murray and Stern (2007) methodology from patent-paper matching to patent-paper-venture matching allowed a complete longitudinal observation of the commercialization of public science, and revealed patterns underlying the observed entrepreneurial capabilities. This methodology also enabled the multi-level analysis advocated by Fini et al. (2018, pp. 8) when they observe that "an interesting feature of science commercialization is that many of the relevant impacts occur at other levels of analysis".

The star-scientist-entrepreneur investigated in this study played a central role in claiming and protecting his inventions through publishing the results of his research in elite scientific journals while also protecting it with one or more broad, blocking patents prior to spin-off founding (Table 2, Fig. 3). In doing so, the star scientist and TLO create currency for the university spin-off in their subsequent quest to raise financing (Hsu and Ziedonis, 2008; Maine and Thomas, 2017). Further, broad, blocking patents on platform technologies enable different spin-offs to simultaneously develop the technology for specific market applications, as one spin-off may not be able to commercialize all applications of a platform technology. This coordination enables broader value creation from platform technologies (Arora et al., 2001; Gambardella and McGahan, 2010). Such practices reduce the holdup problem, particularly problematic with large incumbent firms, which can lose interest in in-licensed technologies (Langer, 2013). Supporting the arguments of Al-Aali and Teece (2013), this case evidence demonstrates how the strategic management of IP can influence venture success, and suggests strategies which may be followed by other scientist-entrepreneurs and their university TLOs.

5.1.2.2. Attracting and mentoring the founding team. The evidence summarized in Table 3 suggests that the pre-formation entrepreneurial capability of the star-scientist-entrepreneur in attracting and mentoring the founding team impacts university spin-off success. This finding is consistent with founder imprinting (Beckman and Burton, 2008), but – critically – this is imprinting *pre-formation*. In line with the perspective of Mathias et al. (2015) that "certain sources of imprint have an *enduring* effect on how entrepreneurs think about themselves, *their opportunities*, and their *ventures,*" graduate school can be considered a formative stage in the life of a scientist, and the imprinting from an SSE during this sensitive stage can manifest itself in the decision of the lab alumni to undertake science commercialization through science-based university spin-off formation. More broadly, the SSE influences the founding team of the university spin-off (and thus the human capital endowment of the firm) through mentoring scientist-entrepreneurs, identifying and nurturing business talent, attracting VCs, and through their networks, experienced CEOs.

There is substantial evidence of the SSE mentoring lab members, both in their scientific approach and in their entrepreneurial role (Table 3). In line with founder imprinting effects (Beckman and Burton, 2008), we argue that the graduate students and postdoctoral fellows who are part of the team inventing the underlying technology can embody the characteristics of the star scientist founder. We propose that founder imprinting may not only occur between founder and firm *post-formation*, but can also occur between the SSE and his or her lab members *pre-formation*. Thus, lab alumni who go on to be scientist-entrepreneurs may imprint the values and characteristics of the SSE on their spin-off, whether co-founded with the SSE or not.

Mentoring lab members to become co-founders in a scientific role brings four advantages to university spin-offs: One, a direct link between the lab and the spin-off is created, facilitating tacit knowledge flow. Two, the SSE is freed to explore additional avenues to extend the platform technology within the academic research lab, which may directly or indirectly benefit the spin-off. Three, the level of passion and commitment for the commercialization of this technology will be much higher than with a licensor scientist, especially if the underlying technology has been based on the thesis/project of the lab member. Four, the entrepreneurial mindset and practices of the SSE will have been imprinted on the lab alumni pre-formation.

Our findings also concur with and elucidate findings by Eesley et al. (2014), who argue that the impact of founding team diversity is contingent on technology innovativeness. Consistent with their study, we find that science-based university spin-offs with purely scientific founding teams, where no CEO is hired for several years after firm formation, do not appear to be penalized while raising financing (Table 3). The most commonly observed pattern seen in our sample, however, is the SSE pairing his lab alumni with experienced business co-founders, generally identified through the networks of VC investors. Notably, spin-offs were more successful at raising financing when their initial CEOs had executive experience at a biopharma company (Table 3), suggesting that such managerial experience and social capital enable success in this sector. Such executives are not typically within the networks of academic scientists.

Thus, the role of the SSE in attracting VCs and, through their networks, experienced business co-founders, also contributes to the success of the venture. Venture capitalists provide much needed capital resources to science-based university spin-offs (Maine and Thomas, 2017; Shane and Stuart, 2002). They also leverage their network in the search for professionals with appropriate management experience who can lead the fledging university spin-off (Hellmann and Puri, 2002). Beyond their financial capital and social capital, association with a reputed venture capitalist is in itself a signalling mechanism to other potential investors (Hsu, 2006). Such an association with a venture capitalist can help the university spin-off raise multiple rounds of financing, which is the most significant predictor of an IPO (Shane and Stuart, 2002).

5.1.2.3. Strategic timing. During the uncertainty-filled pre-formation stage, significant efforts are needed to attract high quality human capital and sufficient ongoing funding. The timing of key decisions in the early stages of venture emergence is attracting growing attention. Scholars have noted that nascent entrepreneurs take important decisions during this period, and that the coordination and sequencing of such decisions can impact venture viability (Dimov, 2010; Hopp and Greene, 2018; Rasmussen, 2011). Related research on the importance of timing to commercialization has looked at this problem from the view of firm entry and exit strategies (Arora et al., 2018; Suarez et al., 2015), the impact of timing patents on future licensing (Kim et al., 2016), and signalling the quality of the intellectual property to potential investors (Hsu and Ziedonis, 2008; Maine and Thomas, 2017). This study contributes to the timing literature by identifying the pre-formation coordination, sequencing, and timing of technology-market matching, elite publications and broad, blocking, relevant patents, and firm formation, demonstrating how a star scientist endows science-based university spin-offs.

Teece (2007, pp. 1326) argues that well positioned firms can afford to wait to exploit opportunities until the timing is most advantageous. We demonstrate the same is true in the case of nascent science-based ventures. The early timing of technology-market matching and of publications and patents, coupled with delayed spin-off formation by the star scientist and his collaborators, can give a positive ex ante signal to better align venture timelines and expectations with those of venture capital investors. This timing is important as few science-based spin-offs are able to raise venture capital or reach an IPO (Fini et al., 2018; Maine and Thomas, 2017) and yet science-based spin-off ventures require vast amounts of risk capital over extended time periods to commercialize their inventions (Maine and Seegopaul, 2016; Pisano, 2010). Teece (2007, pp. 1326) argues for the importance of "getting the timing right" and that "the capacity to make high-quality, unbiased but interrelated investment decisions in the context of network externalities, innovation, and change …", is the dynamic capability of seizing opportunities. We argue such an entrepreneurial capability is also relevant *pre-formation* (Fig. 1), in that the coordination, sequencing, and timing of commercialization decisions made by the scientist entrepreneur enable opportunities to be seized.

The relative timing of patenting to firm formation allows insight into this dynamic capability around strategic timing. Table 2 depicts the gestation period (timing in years from grant of first blocking patent until firm formation) of each venture. This period is notably long as the SSE times patents and key papers as early as possible, and yet delays the formation of the venture. Post patenting, the assessment of *when* a science-based university spin-off is sufficiently endowed for the biomedical commercialization challenge involves dynamic assessment of technology and commercial viability (Arnaud, 2012; Gruber and Tal, 2017; Maine et al., 2005; Teece, 2012), the readiness of a scientific-entrepreneur to lead further technological development within the firm (Clarysse and Moray, 2004), and the fit of the remaining developmental timeline with venture capitalists' institutional logic and window for investment (Maine and Seegopaul, 2016; Maine and Thomas, 2017; Pahnke et al., 2015). During the longer gestation times, the SSE further develops the technology towards commercial viability, mentors scientific leadership for the eventual venture, and helps attract VCs. These are all aspects of the pre-formation entrepreneurial capability of strategic timing. For those ventures spun out of the lab of the SSE which had longer gestation times, we observed evidence that the technology was not initially considered to be viable in the chosen market opportunity, and that, during the gestation time, the SSE mentored scientist-entrepreneurs and was involved in attracting VCs (Tables 2 and 3), as well as further developing the technology towards commercial viability. Such strategy has systematically led to multiple rounds of financing from venture capitalists and the public market (Table 3). These levels of financing are far higher than typical VC financing for university spin-offs (Zhang, 2009, Table 6).

Much basic research and certainly generic platform technologies allow for a broad range of applications over time (Maine and Garnsey, 2006). As projects that draw on this platform technology are formulated, iterative technology-market matching done at the project formulation stage allows the star scientist and lab members additional time to design experiments to establish commercial viability prior to firm formation. As depicted in Fig. 4, 10 ventures were spun out of the platform technology of controlled release polymers over nearly 40 years: noteably, for 9 of these 10 spin-offs, technology-market matching occurred in the project formulation stage (Table 2).

The strategic importance of early technology-market matching and of delaying venture formation is likely to have increased during the past two decades. Innovation scholars argue that managing and rewarding science commercialization has become increasingly difficult during this period of time (Arora et al., 2019; Arora et al., 2018; Pisano, 2010). Our data is consistent with the increasing difficulty of taking a breakthrough technology to market, with the gestation period of science-based university spin-off ventures lengthening from an average of 0.2 years for the first 15 ventures co-founded by the star scientist entrepreneur to an average of 6.2 years for the latter 15 ventures co-founded by the star scientist entrepreneur.

Beyond deciding when a venture is commercially viable, the importance of coordination and sequencing in the timing of key commercialization decisions is a contribution to the literature. Although each commercialization decision may be recognized as important individually, our study reveals the importance of the *coordination* and *sequencing* of these key decisions in leading to well-endowed university spin-offs pre-formation. Repeatedly, we observed technology-market matching during the project formulation stage, the broad, blocking, relevant patents linked to elite publication and the delayed firm formation. Such coordination, sequencing, and timing of decisions by the SSE (with his collaborators and the TLO), mostly in stealth mode, helps prepare the nascent venture in the pre-formation and early post-formation stages of venture emergence. The holistic nature of this extended case method study, and the nuanced empirical evidence anchored in time by the patent-paper-venture matching method represent a significant contribution to the strategic timing literature, as well as to the broader literatures on academic entrepreneurship and dynamic capabilities.

5.2. Implications for practice

Four potentially replicable practices for scientist-entrepreneurs are recommended. First, scientist-entrepreneurs will increase their likelihood of value creation by developing proficiency in technology-market matching to formulate projects which address critical unmet needs and to capture broader value. Second, focusing on platform technologies, publishing in elite journals, and filing early, broad, blocking patents can increase a science-based spin-off's likelihood of securing financing, with the caveat that such patents are expensive to file and maintain. Third, by mentoring lab members to develop solutions for significant unmet market needs, attracting venture capitalists, and by identifying and nurturing business talent, academic entrepreneurs can endow science-based university spin-offs for success. Fourth, incubating a nascent spin-off *until* the breakthrough technology has demonstrated commercial viability and the scientific leadership is mentored gives the university spin-off a greater chance of meeting venture capital investor expectations. Taken together, these practices can help in translating scientific inventions from lab to market.

Investors might also benefit from the insights provided by our study. Our measure of broad, blocking, relevant patents might be a useful metric for them to utilize in identifying high potential ventures ex-ante. Investors – particularly those with domain-specific expertise – may also choose to invest in long term relationships with scientist-entrepreneurs, helping them develop technology-market matching capabilities and introducing them to their networks of potential venture CEOs.

5.3. Implications for policy

There are several implications of this research for university leadership and innovation policymakers. The need for strategic leadership in the role played by universities in our knowledge-based economy has never been greater (Fini et al., 2018; Leih and Teece, 2016). Creating an entrepreneurial culture and facilitating interdisciplinary collaboration, even when identified as a priority, require significant change (Leih and Teece, 2016; Mathias et al., 2015; Sharp, 2014). At MIT, both have been purposefully nurtured over the past decades (Roberts et al., 2015; Sharp, 2014).

The importance of strategic management of intellectual property to science-based university spin-offs is demonstrated. All too often, claiming, protecting and commercializing IP is unintentionally constrained by university TLOs and national innovation policies (Bubela and Caulfield, 2010; Hall et al., 2014; Huang-Saad et al., 2016). Success metrics would ideally align the incentives of university TLOs with long term objectives for the university as well as with regional and national systems of innovation (Bubela and Caulfield, 2010; Christini, 2012; Langford et al., 2006). For example, technology licensing offices, if better resourced, could follow MIT in deciding to file patents on invention disclosures with potential impact (Nelsen, 2004, Appendix 2, **interview 5**) rather than rationing their resources based on short term revenue or cost recovery considerations. Entrepreneurial education for potential scientist-entrepreneurs can lead to better utilization of TLO resources by reducing basic mistakes and by making faculty/TLO interactions more productive (Bienkowska et al., 2016; Council of Canadian Academies, 2018; Huang-Saad et al., 2016).

There are also implications from our findings for national and regional innovation policymakers. Consistent with Fini et al. (2018), this study suggests innovation policies which support "bottom up" initiatives to enable the emergence of higher quality university spin-offs are needed. We show that the entrepreneurial capabilities of a star-scientist-entrepreneur can enable well endowed (in other words, high quality) university spin-offs. Yet policies focused on importing star-scientist-entrepreneurs are both impractical and insufficient. Rather than importing star scientists, policymakers can create the conditions to nurture their emergence through innovation policies aimed at developing and supporting *pre-formation* entrepreneurial capabilities.

The dynamic capability of science-based ventures to rapidly respond to opportunities or crises such as the COVID-19 pandemic, originates pre-formation in the purposeful building of the four key entrepreneurial capabilities described in this study. Thus, the firm-level dynamic capability of technology-market matching at the innovative vaccine development firm Moderna Therapeutics originated in the entrepreneurial capabilities practised and imprinted pre-formation. Entrepreneurship programs aimed at scientists and engineers can develop entrepreneurial capabilities in technology-market matching, claiming and protecting IP, attracting and mentoring the founding team, and strategic timing. The US NSF training program I-Corps has demonstrated some success in educating scientist-entrepreneurs in later stage technology-market matching, and also broadening their entrepreneurial networks (Huang-Saad et al., 2016). However, Harms et al. (2015) argues that existing programs are ill-suited to sectors with high technology uncertainty and long gestation times. Additional or alternative educational programs, focused on building pre-formation entrepreneurial capabilities in university scientists, could unlock substantial additional value from university inventions. Policies which lower barriers to claiming and protecting IP and to strategic timing by scientist-entrepreneurs – such as by better resourcing TLOs, making patenting an eligible cost by granting agencies, and not requiring venture formation by faculty in order to be eligible for early commercialization grants – when combined with committed university leadership, will support the emergence of well-endowed science-based university spin-offs.

5.4. Limitations

This study has two main limitations. First, by concentrating on the career of an unusually prolific biomedical star-scientist-entrepreneur at MIT, the generalizability of the results may be questioned. Clearly, entrepreneurial outcomes at elite universities located in leading technology clusters are not representative of the average university or region (Nightingale and Coad, 2014; Siegel and Wright, 2015). Nevertheless, we contend that such universities are where the phenomenon of science-based university spin-off emergence is most prevalent. Stuart and Ding (2006) find that elite universities form the most science-based spin-offs, with scientists at the top 20 US universities being 3 times more likely to become a scientist-entrepreneur, and that scientists involved in the founding of a university spin-off published at a rate of 1.7 times that of their matched "pure" scientist. There is also evidence of an increasing prevalence of serial scientist-entrepreneurs (Lawson and Sterzi, 2014; Stuart and Ding, 2006). The nuanced evidence provided in this study about the role of this exemplar scientist-entrepreneur in university spin-off formation can inform and enhance commercialization activities by academic-entrepreneurs at a broad range of institutions. For example, technology-market matching at the project formulation stage is a learned capability which can be developed by academic scientists in any region.

Second, the entrepreneurial capability of claiming and protecting IP may not be easily replicable in less munificent environments. Some universities may not be able to provide funds to support extensive patenting activities. Government grants may also not support patenting. While acknowledging this limitation, we contend that limited funds at university TLOs mean that even more care needs to be taken to ensure that the fewer patents being filed are broad and blocking in nature. Thus even if the inventor decides to license their technology to incumbents, having broad, blocking, patent protection (along with elite journal publications) can increase the chances that their inventions will reach society. A caveat here is that securing a broad, blocking, relevant patent is not always under the control of the scientist or the TLO, and can be characterized as a protracted give-and-take affair with the patent office.

6. Conclusions

Utilizing the extended case method, existing dynamic capabilities theory is confronted and extended with evidence as to how an exemplar scientist-entrepreneur senses, shapes, and seizes opportunities to endow university spin-offs pre-formation. Responding to calls for process-oriented, individual-level studies to extend dynamic capabilities theory (Protogerou et al., 2012, pp. 641; Schilke et al., 2018), this study contributes to the academic entrepreneurship literature by extending dynamic capabilities theory to the individual-level during the pre-formation stage of science-based university spin-offs. Methods were developed to identify biomedical platform technologies and match the inventions (embodied in 363 granted US patents and 1476 papers) of a biomedical star-scientist-entrepreneur with the 30 university spin-offs he co-founded over 40 years of his career, allowing for a longitudinal examination of the progression of science from research laboratory to science-based university spin-off.

A process model was developed, depicting the key role played by the SSE in four pre-formation entrepreneurial capabilities which endow these science-based university spin-offs for success: technology-market matching, claiming and protecting the invention, attracting and mentoring the founding team, and strategic timing. This paper demonstrates how these entrepreneurial capabilities can be developed and deployed by scientist-entrepreneurs. We propose that such entrepreneurial capabilities can also be taught more broadly to university scientists. Our study suggests that innovation policies should place greater emphasis on supporting scientist-entrepreneurs in the pre-formation stage of university spin-off emergence. The recommendations drawn from this research can guide academic scientists, investors, university leadership, and policy makers in fostering the commercialization of scientific inventions through university spin-offs.

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Appendix 1. List of archival documents

Code	Date Range	Document Type	Number of Documents /Page Length
d1	1976–2014	USPTO Granted Patents (Star Scientist as co-inventor)	363 patents
d2	1976–2014	Journal Articles (Star Scientist as co-author)	1170 papers
d3	1976–2014	Conference Papers (Star Scientist as co-author)	306 papers
d4	1974–2014	Star Scientist's Patent Portfolio (MIT TLO)	188 pages
d5	1995–2014	SEC filings of Star Scientist's co-founded spin-offs	6460 pages
d6	1998–2015	Archived webpages	123 pages
d7	1988–2016	Archived News Articles	449 pages
d8	1984–2015	Additional documents (FDA & analyst reports, theses, etc.)	1893 pages
d9	Oct. 22, 2009	Star Scientist's Royal Academy of Engineering lecture	31 pages
d10	Feb. 18, 2013	Star Scientist's AAAS Symposium manuscript	65 pages
d11	Jun. 10, 2013	Nature Biotechnology Bioentrepreneur Article	3 pages

Appendix 2. List of interviews and duration

Code	Date	Role and Affiliation	Description	Duration/Page Length
i1	Apr. 5, 2011	Star Scientist Entrepreneur, MIT	Face to Face	29:06 min transcribed
i2	Feb. 18, 2013	Star Scientist Entrepreneur, MIT	Q&A	5 pages transcribed
i3	Jan. 22, 2014	MIT TLO, lead on Star Scientist Entrepreneur's Patent Portfolio	Phone	60 min, 6 pages of notes
i4	May 13, 2014	Business Co-Founder & CEO, Star Scientist Entrepreneur's Spin-off	Face to Face	20 min
i5	Aug. 24, 2014	MIT TLO, lead on Star Scientist Entrepreneur's Patent Portfolio	Face to face	54 min, 27 pages transcribed
i6	Aug. 24, 2014	Venture Capitalist & CEO, Star Scientist Entrepreneur's Spin-off	Face to face	60 min, 8 pages of notes
i7	Aug. 24, 2014	IP Counsel, Star Scientist Entrepreneur's Spin-off	Face to face	60 min, 8 pages of notes
i8	Oct. 24, 2014	IP Counsel, Star Scientist Entrepreneur's Spin-off	Phone	20 min Q&A
i9	Jan. 9, 2015	MIT TLO, lead on Star Scientist Entrepreneur's Patent Portfolio	Phone	30 min
i10	Mar. 3, 2015	Star Scientist Entrepreneur, MIT	Email	8 emails Q&A
i11	Mar. 13–17, 2015	Star Scientist Entrepreneur, MIT	Email	7 emails Q&A
i12	Oct. 26, 2015	Star Scientist Entrepreneur, MIT, QE Prize lecture	Video lecture	25:04 min
i13	Mar. 17, 2016	Star Scientist Entrepreneur, MIT	Video interview	8:29 min
i14	June 1, 2016	Star Scientist Entrepreneur and Venture Capitalist Co-Founder	Video interview	23:12 min
i15	Jan. 19, 2017	Star Scientist Entrepreneur's Lab Alumni and Academic Co-Founder	Phone	60 min

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