Invention to Innovation: A Framework and The Roles of Uncertainty and Open Innovation in an Emerging Personalized Medicine Ecosystem

by

Andrew Park

MBA, Simon Fraser University, 2012

Thesis Submitted in Partial Fulfillment of the
Requirements for the Degree of
Doctor of Philosophy

in the
Segal Graduate School
Beedie School of Business

SIMON FRASER UNIVERSITY
Fall 2021

Declaration of Committee

Name:	**Andrew Park**
Degree:	**Doctor of Philosophy**
Title:	**Invention to Innovation: A Framework and The Roles of Uncertainty and Open Innovation in an Emerging Personalized Medicine Ecosystem**
Committee:	**Chair: Christina Atanasova** Professor, Business
	Elicia Maine Supervisor Professor, Business
	Sarah Lubik Committee Member Lecturer, Business
	Jan Kietzmann Committee Member Associate Professor, Business University of Victoria
	Leyland Pitt Examiner Professor, Business
	Catherine Beaudry External Examiner Professor, Mathematical and Industrial Engineering Polytechique Montréal

Abstract

In this dissertation, I explore the antecedents, processes and outcomes of the translation of scientific invention to innovation, which is of particular interest to scholars and policy makers who wish to understand how publicly funded university research can be harnessed to increase national productivity. While there has been an increasing amount of research on the roles that innovation intermediaries and mechanisms play in science innovation, there have been few attempts at characterizing the inputs, mediators and outputs of this process. Innovation management and policy research is far more developed around technology innovation than science innovation. Few empirical studies have been conducted at the ecosystem level in emerging science-based contexts. Firms in such contexts exhibit markedly different characteristics compared to large software incumbents, including higher technical and market uncertainty. In three essays I explore the following research questions: "what factors influence the translation of scientific invention to innovation?", "do uncertainty, partnerships and patenting have an influence on innovation performance outcomes?" and "why and under what conditions do the Open Innovation mechanisms of selective revealing, strategic timing and strategic partnering affect value capture by personalized medicine firms?". The investigation of these questions aims to inform scientist-entrepreneurs, scholars, policy makers and university leadership on how to more effectively translate breakthrough invention to improved economic, health and social outcomes. This dissertation contributes to the Technology and Innovation Management literature in three ways. In the first essay, the results of a bibliographic review are synthesized into a novel theoretical framework on science innovation. In the second essay, the relationship between uncertainty, patenting and innovation performance outcomes is explored, using a novel and custom-built dataset on British Columbia personalized medicine firms. The results show that uncertainty, partnerships and patenting play a role in innovation performance outcomes, which have implications for both practitioners and policy makers. In the third essay, I heed the call from the Open Innovation research community to more deeply explore the boundary conditions of Open Innovation. A new model on Open Innovation is presented, which is empirically supported by two key findings: the Open Innovation mechanisms of Strategic Partnerships, Selective Revealing and Strategic Timing appear to play important roles in value capture, but this relationship is moderated by technical uncertainty.

Keywords: science innovation; industry emergence; selective revealing; personalized medicine; open innovation

Acknowledgements

This work was supported by Discovery Foundation through its 2020 Technology Education Program and The Social Sciences and Humanities Research Council (SSHRC) Grant No. 895-2018-1006.

Table of Contents

Introduction

In this dissertation, the antecedents, processes and outcomes of the translation of breakthrough invention to innovation are explored, specifically within the context of science-based businesses; this investigation is aim at improving our understanding of how breakthrough scientific inventions can be translated to global economic, health and social impacts. A novel conceptual framework on science innovation is presented, and the factors leading to successful science innovation are empirically examined, using firms within the emerging personalized medicine innovation ecosystem as the level of analysis. In three essays, I explore the following research questions: “what factors influence the translation of scientific invention to innovation?”, “does the level of technical uncertainty of personalized medicine firms have an influence on innovation performance outcomes?” and “why and under what conditions do the Open Innovation mechanisms of selective revealing, strategic timing and strategic partnering affect value capture by personalized medicine firms?”.

In the first essay, the first research question is investigated by studying the role universities play as inputs and mediators in the conversion of invention to innovation. This process is further elucidated through the development of a novel framework on science innovation. Innovation intermediaries, such as universities, play a central role in successful science innovation, which leads to societal and economic benefits through increased regional and national productivity (Thomas et al., 2020; Bolzani et al., 2020). They stimulate economic growth by facilitating applied research and supporting the founding of science-based spin-off ventures (Barirani, Beaudry & Agard; 2017; Roberts, Murray & Kim, 2015). In addition, star scientists within these universities who become entrepreneurs through the founding of spin-off ventures play important roles in both the development of new inventions and their successful commercialization (Zucker & Darby, 1998; Thomas et al., 2020; Nightingale & Coad, 2014).

Despite the increasing evidence of the importance of universities to science innovation and a steady increase in government investments in university science, Arora et al. (2019) note that total factor productivity (total production divided by the weighted average of inputs) growth is lower today than it was before 1970. Other innovation scholars also observe this trend, noting that an increase in government research spending has not resulted in the equivalent improvements in economic and societal challenges in hard technology sectors such as biotechnology and clean technology (National Academies of Sciences, Engineering and Medicine, 2020). Through the completion of a detailed bibliographic review of science innovation, which helps identify and categorize the salient inputs, outputs and mediators of the invention to innovation process, and by drawing on evidence in the form of current debates and examples of practice from the 2020 R&D Management Symposium, I synthesize a novel theoretical framework on science innovation. I outline the antecedents and outputs of science innovation as well as the factors that influence the relationship between invention and innovation.

In the second essay, an empirical study is conducted to elucidate this science innovation process through the delineation and examination of influencing and controlling factors in the science commercialization process, and the resultant value capture within an emerging personalized medicine innovation ecosystem. Specifically, I attempt to answer the question, “does the level of technical uncertainty of personalized medicine firms have an influence on innovation performance outcomes?”. Whereas firm formation, patenting and ecosystems research has been conducted in the long-established biotechnology industry (LifeSciences BC, 2015; Schiffauerova & Beaudry, 2011; Holbrook, 2003), little is known about the factors impacting value capture and the successful translation of invention to innovation in a highly uncertain, emerging hard technology field such as personalized medicine. Important determinants of innovation outcomes include technical uncertainty (Pisano, 2010), strategic partnerships (Niosi, 2003; Baum & Silverman, 2004) and strategic timing of patents (Maine & Thomas, 2017; Hsu & Ziedonis, 2008), however, these relationships have not been widely studied, particularly in our novel and emerging context.

This gap is relevant and important because identifying the determinants of value capture for highly technical ventures such as personalized medicine firms through an innovation management framework can inform both innovation policy and firm strategy. In particular, effective management by policy makers of the burgeoning personalized medicine ecosystem, and the therapeutics, diagnostics, medical device and digital health subsectors within it, could lead to profound improvements in social economic outcomes (Cullis, 2015; Vicente, Ballensiefen, Jonsson, 2020). During the global pandemic of COVID-19, British Columbia personalized medicine firms, such as AbCellera, were central to vaccine and therapeutics solutions. The emergence of a regional personalized medicine innovation ecosystem can lead to improved health outcomes, more technology-based jobs, and heightened interest from researchers and industry practitioners globally (Gavan, Thompson & Payne, 2018). Thus, this study aims to identify the firms that currently underpin the burgeoning British Columbia personalized medicine innovation ecosystem and analyze the relationship between uncertainty and innovation performance among these firms.

In the third essay, the conclusions regarding the importance of uncertainty, partnerships and patenting in the science innovation process and within the personalized medicine innovation ecosystem are further explored, using an Open Innovation lens. Open Innovation is a key strategy employed by science-based businesses, such as biotechnology, nanotechnology and pharmaceutical ventures, which operate under prolonged and high degrees of uncertainty. Given the timelines, complexity, and commercialization costs involved, attracting investors and alliance partners with complementary assets is vital to science-based businesses (Maine & Garnsey, 2006; Pisano, 2010). Despite their importance to the commercialization success of science-based ventures, few empirical studies exist that investigate the role of alliance partners in Open Innovation (e.g., Zobel, Balsmeier & Chesbrough, 2016).

Alliance partners of science-based firms are typically large incumbents with complementary technical capabilities, in such areas as clinical trials and manufacturing, and/or commercial resources, such as established distribution and marketing channels. However, openness and value capture are not consistently correlated across firms and the relationship may be radically different across different industries. These boundary conditions of the effects of Open Innovation remain underexplored, limiting the extensibility of previous Open Innovation research. Moreover, most Open Innovation research has focused on specific case studies or a limited set of firms; few empirical studies have been conducted at the industry or ecosystem level. Furthermore, numerous scholars (Dahlander & Gann, 2010; Armellini, Kaminski & Beaudry, 2014) have noted the need for contexts outside the American software industry, to assess the external validity of current Open Innovation research. Since this call, some new contexts have been studied in Open Innovation research (Zobel, Balsmeier & Chesbrough, 2016; Armellini, Kaminski & Beaudry, 2014; Bianchi et al., 2011), but the seminal papers are still based on studies of large, multinational software firms.

To elucidate these understudied boundary conditions, I investigate the research question, “why and under what conditions do Open Innovation mechanisms affect value capture by personalized medicine firms?”. This empirical study sheds light on the relationship between openness and value capture and makes several contributions to the Open Innovation literature. First, a theory explicating why Open Innovation affects firm value capture, and how this relationship is moderated by uncertainty, is proposed. Second, the study is conducted on the emerging personalized medicine sector that is radically transforming medicine and clinical practice (Cullis, 2015). In so doing, I use a novel context outside the American software domain (the dominant context in Open Innovation research). Third, the study findings have important implications for practitioners and policy makers. If Open Innovation mechanisms are critical to the commercialization success of emerging science-based firms, then loosening constraints on patenting or subsequent licensing of those patents should be a consideration for innovation researchers and policymakers.

By exploring the three research questions that comprise this dissertation, three key contributions are made to the innovation management field. First, several new frameworks and research models aimed at elucidating the determinants and processes of the effective translation of invention to innovation are developed, including a comprehensive input/output framework on science innovation, which reveals notable mediators such as innovation policy, firm entrepreneurial strategy and innovation policy. Along with this overarching, multi-level science innovation framework, I present an additional firm-level framework, showing that Open Innovation strategies are positively associated with value capture, defined as the appropriation of payments by consumers (Priem, 2007), and moderated by the level of technical uncertainty.

Second, the empirical investigations in this dissertation are centered on a highly novel, previously under-researched hard technology sector, personalized medicine. To enable this, the first (to the best of my knowledge) personalized medicine-specific database capturing invention-based inputs and innovation performance outcomes is created; this dataset has the potential to be expanded across Canada and other international jurisdictions in future studies aimed at testing the external validity of the arguments in this dissertation. The continued study of this emerging personalized medicine innovation ecosystem is critical to understanding what drives innovation performance in high potential and science-based business facing significant technical uncertainty and could be of potential interest to innovation policy makers given its high potential in improving health and social outcomes and creating knowledge economy jobs.

Lastly, based on the findings, each of the three essays offers implications for stakeholders in science-based innovation ecosystems. These implications as a whole suggest ways to explore the effectiveness of government funded university research. Each stakeholder (scientist entrepreneurs, university leadership, scholars, innovation policy makers) plays a specific role in the overall process of the translation of invention to innovation. The three papers that comprise this dissertation have relevant findings for a subset, or all of these stakeholders and targeted recommendations are developed in each discussion section.

References

Armellini, F., Kaminski, P. C., and Beaudry, C. 2014. The open innovation journey in emerging economies: an analysis of the Brazilian aerospace industry. Journal of Aerospace Technology and Management, 6(4), 462-474.

Arora, A., Belenzon, S., Patacconi, A., & Suh, J. (2019). Why the US innovation ecosystem is slowing down. Harvard Business Review.

Barirani, A., Beaudry, C., & Agard, B. (2017). Can universities profit from general purpose inventions? The case of Canadian nanotechnology patents. *Technological Forecasting and Social Change*, *120*, 271-283.

Baum, J. A., & Silverman, B. S. (2004). Picking winners or building them? Alliance, intellectual, and human capital as selection criteria in venture financing and performance of biotechnology startups. *Journal of Business Venturing*, *19*(3), 411-436.

Bianchi, M., Cavaliere, A., Chiaroni, D., Frattini, F., & Chiesa, V. (2011). Organisational modes for Open Innovation in the bio-pharmaceutical industry: An exploratory analysis. *Technovation*, *31*(1), 22-33.

Bolzani, D., Munari, F., Rasmussen, E., & Toschi, L. (2020). Technology Transfer Offices as providers of science and technology entrepreneurship education. The Journal of Technology Transfer, 1-31.

Cullis, P. 2015. The personalized medicine revolution: how diagnosing and treating disease are about to change forever. Greystone Books.

Dahlander, L., Gann, D.M., 2010. How open is innovation? Research Policy, 39 (6),699–709.

Gavan, S. P., Thompson, A. J., & Payne, K. (2018). The economic case for precision medicine. *Expert review of precision medicine and drug development*, *3*(1), 1-9.

Holbrook, J.A. 2003. The Vancouver biotechnology cluster. Centre for Policy Research on Science and Technology, Simon Fraser University.

Hsu, D. H., & Ziedonis, R. H. (2008, August). Patents as quality signals for entrepreneurial ventures. In *Academy of Management Proceedings* (Vol. 2008, No. 1, pp. 1-6). Briarcliff Manor, NY 10510: Academy of Management.

LifeSciences British Columbia & PricewaterhouseCoopers. 2015. The life sciences sector in BC: economic impact now and in the future. LifeSciences British Columbia. Retrieved from http://lifesciencesbc.ca/wp-content/uploads/2015/06/LifeSciences-BC-Sector-Report-2015.pdf

Maine, E., and Garnsey, E. (2006). Commercializing generic technology: The case of advanced materials ventures. Research Policy, 35(3), 375-393.

Maine, E., & Thomas, V. J. (2017). Raising financing through strategic timing. *Nature Nanotechnology*, *12*(2), 93-98.

National Academies of Sciences, Engineering, and Medicine. (2020). Review of the SBIR and STTR Programs at the Department of Energy. National Academies Press.

Nightingale, P., & Coad, A. (2014). Muppets and gazelles: political and methodological biases in entrepreneurship research. Industrial and Corporate Change, 23(1), 113-143.

Niosi, J. (2003). Alliances are not enough explaining rapid growth in biotechnology firms. *Research Policy*, 32(5), 737-750.

Pisano, G. P. 2010. The evolution of science-based business: innovating how we innovate. *Industrial and Corporate Change*, 19(2), 465-482.

Priem, R. L. (2007). A consumer perspective on value creation. *Academy of Management Review*, 32(1), 219-235.

Roberts, E. B., Murray, F., & Kim, J. D. (2015). Entrepreneurship and Innovation at MIT: Continuing global growth and impact.

Schiffauerova, A., & Beaudry, C. (2011). Star scientists and their positions in the Canadian biotechnology network. *Economics of Innovation and New Technology*, *20*(4), 343-366.

Thomas, V. J., Bliemel, M., Shippam, C., & Maine, E. (2020). Endowing university spin-offs pre-formation: Entrepreneurial capabilities for scientist-entrepreneurs. Technovation, 96-97, 102153.

Vicente, A. M., Ballensiefen, W., & Jönsson, J. I. (2020). How personalised medicine will transform healthcare by 2030: the ICPerMed vision. *Journal of translational medicine*, *18*(1), 1-4.

Zobel, A. K., Balsmeier, B., & Chesbrough, H. (2016). Does patenting help or hinder open innovation? Evidence from new entrants in the solar industry. *Industrial and Corporate Change*, 25(2), 307-331.

Zucker, L. G., & Darby, M. R. (1998). Entrepreneurs, star scientists, and biotechnology. NBER Reporter Online(Fall 1998), 7-10.

Essay 1:

Invention to Innovation: Creating the Conditions for Impact from University Science

Park, A.[1], Maine, E. [1], Fini, R. [2], Rasmussen, E. [3], Di Minin, A. [4], Dooley, L. [5], Mortara, L. [6], Lubik, S.[1], & Zhou, Y[7].

[1]Beedie School of Business, Simon Fraser University, Canada

[2]University of Bologna, Italy

[3]Nord University Business School, Norway

[4]Scuola Superiore Sant'Anna, Italy

[5]University College Cork, Ireland

[6]University of Cambridge, UK

[7]School of Public Poilcy and Management, Tsinghua University, China

Abstract

Universities play a central role in producing breakthrough inventions and translating them to societal and economic benefits. Scholars and policy makers have devoted significant efforts to understand how university research can be more effectively harnessed to increase regional and national productivity, and to address global challenges related to climate, health and sustainability development goals. This paper aims to critically analyze the growing literature on science-based innovation, present the current state of understanding of the field and provide practical recommendations for scholars, policymakers, scientist-entrepreneurs and university leadership. In addition, we conduct a bibliometric analysis of nearly 2,000 articles from leading technology innovation management journals to develop a novel framework of the determinants and outcomes of science-based innovation. We support this framework with examples of practice from the 2020 R&D Management Symposium, including analyses of science-based innovation in quantum computing, artificial intelligence, clean technology and personalized medicine. Our framework reveals that understanding the process of translating university science to economic and societal impacts requires looking beyond traditional metrics and factors such as university spin-off rates or individual firm strategies. It requires a nuanced exploration of the direct roles of important stakeholders in the university context. We conclude by recommending strategies and policies for the

commercialization of breakthrough inventions from universities and for the growth of science-based innovation ecosystems.

Keywords: science innovation; scientist-entrepreneur; entrepreneurial strategy; innovation intermediaries; innovation policy

Introduction

Universities are both important sources and enablers of the translation of breakthrough invention to innovation, which delivers societal and economic benefits (Dill, 1990; Bonnaccorsi & Piccaluga, 1994; Thomas et al., 2020; Bolzani et al., 2020). Consequently, governments across the globe support university research activity through targeted public funding. The benefits from university scientific research stimulate economic growth by spurring applied research, attracting foreign talent and encouraging the founding of impactful science-based spin-off ventures (Roberts, Murray & Kim, 2015), which contribute to the development of regional technology clusters (Zucker & Darby, 1998; Maine et al., 2014; Maine, Shapiro & Vining, 2010). Moreover, academic scientists within the university context play important roles in both the development of new inventions and their successful commercialization, leading to benefits for society (Zucker & Darby, 1998; Thomas et al., 2020; Nightingale & Coad, 2014). While recognizing the potential synergistic benefit of public funding supporting university research in addressing economic and societal challenges, innovation scholars note the declining effectiveness of the process of translating science-based invention to science-based innovation (Arora et al., 2019; Arora et al., 2020; Guzman & Stern, 2020) and pose the question, “how can the process be managed more effectively?”

Against the backdrop of this question, we seek to elucidate the role universities play in the translation of science-based invention to science-based innovation and realising societal benefits. We define science-based innovation as the commercial exploitation (i.e., development of new or improved products and services) of a patented invention or unpatented scientific expertise derived from university-based research (Perkmann et al., 2013; Shane, 2004; Fini et al., 2018).

This paper contributes in three ways. First, we provide the first bibliographic review of the growing science-based innovation literature (1,963 papers) in

Technology and Innovation Management (TIM) journals. This reveals patterns in past research activity and identifies issues requiring attention from future innovation research. Second, by synthesizing the learning from the bibliographic review, we propose a processual “science innovation” framework for translating science-based invention to science-based innovation. This framework highlights the salient inputs and outputs of science-based innovation, together with the interrelated process mediators that influence commercial outcomes and enhance societal impact. To illuminate the cohesiveness of this framework, we leverage recent presentations and research submissions of accepted articles from the 2020 R&D Management Symposium, which are rooted in the science entrepreneurship, innovation policy and innovation ecosystem domains. Third, based on reflections from the research, we propose recommendations to enhance the translation of science-based innovation within a university context and to improve the effectiveness of public-funded research in addressing economic and societal challenges. These recommendations are not only relevant to policymakers who wish to better understand what mechanisms and factors enhance the commercialization of university science, but also to the research community in identifying areas for future study within the field.

Literature Review

This section presents current research on science-based innovation and identifies several factors that have led to the disconnect between government university-research investments and desired economic and societal outcomes. A case is made for a systematic review of the literature within TIM journals, using bibliometric studies, to deepen our understanding of the science-based innovation process within the university context.

Review of Emerging Literature on Translation of Invention to Innovation

The Disconnect Between Research Funding and Innovation

Innovation management researchers observe that an increase in government research funding has not resulted in commensurate improvements to the economic and societal challenges governments wish to solve, particularly in hard technology sectors such as biotechnology, nanotechnology, quantum computing, artificial intelligence and advanced materials (National Academies of Sciences, Engineering and Medicine, 2020). Some scholars point to a shift in the commercialization paths of breakthrough inventions, with corporate research labs playing a lesser role, and these research labs focusing on physical technological innovation and not on broader societal or economic benefits (Arora, 2020; Nelson & Nelson, 2002). Other scholars examining the enablers of science-based innovation have suggested a “Triple Helix”, or “Quadruple Helix” approach combining the skillsets of industry, university, government and end-users in translating breakthrough invention into impactful innovation (Etzkowitz, 2003; Etzkowitz & Leydesdorff, 2000; Meyer, 2003; Hernandez-Trasobares & Murillo-Luna, 2020; Miller et al., 2016; Miller, McAdam & McAdam, 2018; Cunningham, Menter & O’Kane, 2018; McAdam & Debackere, 2018).

Arora et al. (2019) expand on the lessening role of corporate research labs, pointing to an increasing division between research and invention produced by universities, and the profit driven commercialization efforts by corporations as one of the causes of a slowdown in national productivity. This slowdown has occurred despite a steady increase in government investment in science, numbers of PhDs trained, and scientific articles published. Similarly, Guzman & Stern (2020) note that the likelihood of U.S. startups to reach their potential has declined since the 1990s and that the U.S. entrepreneurial ecosystem is not conducive to startup growth. It is argued that division between corporate and university research has resulted in university research becoming increasingly driven either solely by curiosity or by incremental reward metrics, rather than by a mission to solve specific economic problems (Arora et al., 2020; Whitesides, 2013).

Arora (2020) also notes an increasing tendency for large corporations to source inventions externally through acquisitions instead of nurturing them through internal R&D initiatives. Arora calls for increased academic research on how corporations can better manage research collaborations and for more federal support of industry-based scientific research and universities for seeding breakthrough inventions. Other scholars (Surana, Doblinger & Anadon, 2020; Budd, 2020; Yaghmaie & Maine, 2020; Song et al., 2020) also call for innovation and economic policy incentives to bridge the gap between invention and innovation in hard-tech solutions for climate change. Within the science-based innovation literature there is a growing number of scholars focusing on the university as the initiator of breakthrough innovation (O’Shea, 2007; Bolzani et al, 2020;

Fini et al, 2020; Thomas et al, 2020), while also highlighting the challenges in translating these inventions into innovations of benefit to wider society.

Addressing the Disconnect

Recent innovation research suggests several avenues to bridge this gap: align university Intellectual Property and Technology Transfer Office policies with the commercialization ambitions of star-scientists, create entrepreneurship education initiatives to produce sound early-stage entrepreneurial decisions by scientist-entrepreneurs (Thomas et al., 2020; Fini et al., 2019; Etzkowitz & Zhou, 2019; Etzkowitz & Zhou, 2018;) and encourage deeper collaboration between scientist-entrepreneurs and regional and national policymakers. As an example, Eesley & Miller (2017) note that Stanford enjoys a disproportionate number of alumni who have built or led high impact companies, spanning the biotechnology, information technology and financial services industries. They attribute this success in part to Stanford's deep culture of providing curricula specifically tailored to developing entrepreneurs, which include formal mentorships and deep engagement with alumni-entrepreneurs. Leih & Teece (2016) similarly suggest that Stanford's rapid global rise in research and commercial impact since the 1950s is aided by its purposeful activities in fostering university-industry interactions.

Universities who don't have the same resources or rich pedigree of alumni-entrepreneurs can also take specific steps to increase value capture from its scientific discoveries. Rasmussen & Borch (2010) identify several key resources a university should acquire to improve its innovative capacity, including networks with industry and investors, government grants, and supportive infrastructure for scientist-entrepreneurs through a well-structured Technology Transfer Office. Maine (2020) supports this latter point, arguing that Canadian innovation can be improved through university support of high impact research from scientist-entrepreneurs. While there are multiple development vehicles by which the translation of science-based invention to innovation can occur, the most commonly practiced are those of open science, licensing, venture creation and joint venture (Lundqvist and Williams, 2005; Philpott et al, 2011; Perkmann et al., 2013). Research also suggests that university initiatives supporting academic entrepreneurship do indeed have a positive effect on the creation of academic spin-offs, particularly in the STEMM fields (Fini, Grimaldi & Meoli, 2020). Finally, to increase the innovative capacity and vibrancy of a regional ecosystem, Stern (2020) argues that there must be a synergy between innovative capacity and entrepreneurial capacity, where both have shared requirements in human capital, funding, infrastructure and culture. These elements contribute to the commercial capacity of an ecosystem, which must be adequately developed for technology entrepreneurs to have the best chance at value creation and capture (Gans & Stern, 2003). These are examples of how research related to science-based innovation has drawn considerable recent attention from innovation scholars.

Despite the importance of the area, a systematic review of the development of the field of science-based innovation has not yet been conducted. In particularly, we were not able to identify any meta-analyses or bibliographic studies that collate and present the current knowledge structure of the domain. Such a systematic review would enrich our understanding of the patterns that have arisen in the field and allow us to identify under-researched areas and directions for future research.

Review of Science-Based Innovation Bibliometric Studies

Several bibliometric studies have been published in the TIM journals that comprise our analysis (e.g., Meyer-Brotz et al., 2018; Casper & Murray, 2005; Noyons, Luwel & Moed, 1998; Zhang et al., 2019; Marzi et al., 2018), however, they are focused either more broadly on the general TIM field (Huang et al., 2019) and not specifically on science-based innovation, or on topics unrelated to science-based innovation (Chao, Yan & Jen, 2007) or are narrow in journal scope, such as a specific bibliometric review on Research-Technology Management (Shum et al., 2019). In contrast to these studies, our analysis uses a textual and citation-based bibliographic approach to review the evolution of science-based innovation research in TIM journals. Our analysis offers the following advantages over previous studies: 1) it spans several decades and thus illustrates the development of the field over a long time period, 2) it focuses specifically on our topic of interest (science-based innovation), allowing us to synthesize the results of our bibliographic analyses into a novel “science innovation” framework and 3) it incorporates a larger number of papers than previous bibliometric studies, to enable a comprehensive view of the domain.

Methodology

This section presents the methods used to conduct our bibliographic analysis of the science-based innovation literature, including the selection of TIM journals, search terms, data sources and the choice of visualization software. Our objective is to determine the known inputs, outputs, and influencers in the science-based innovation process, which lead to our novel “science innovation” framework. This framework serves to improve our understanding of how breakthrough science-based invention from universities is converted to innovative products and services and improved societal and economic outcomes.

To identify key influencers of the science-based innovation process, we look to the 2020 R&D Management Symposium, where the symposium organizers developed three streams of discussion, with each stream representing a key mediator in the invention to innovation process. Furthermore, we draw on research from the symposium to provide recent examples of practice and debate to support our framework.

Search Terms, Data Source and Web of Science

The unit of analysis for our study is articles published in leading TIM journals, and the abstract, references, number of citations, and authors of each article. We chose these journals based on a meta-analysis conducted by Huang et al. (2019). In their study, the authors compared five extant papers which ranked the top TIM journals based on numbers of publications, citations and impact factors (Hall, 2016; Lee, 2015; Linton, 2006; Thongpapanl, 2012; Yang & Tao, 2012). The authors identified all journals that appeared at least twice in all five studies, which resulted in the 13 journals that comprise our study: *Journal of Product Innovation Management, Research Policy, Research-Technology Management, R&D Management, IEEE Transactions on Engineering Management, Technological Forecasting and Social Change, International Journal of Technology Management, Technovation, Technology Analysis & Strategic Management, Journal of Engineering and Technology Management, Journal of Technology Transfer, Industrial and Corporate Change and Industry and Innovation*.

The source of data was the Web of Science database. It is a scientific citation indexing service that enables a researcher to conduct a comprehensive citation search for a single journal or many journals. We extracted the full bibliographic records of science-based innovation papers in our selected journals through a Boolean logic search query. Specifically, we queried an intersection of the following search terms: “innovation” and “science”. By searching for all papers related to the co-occurrence of innovation and science search terms, we examine a broad but defining spectrum of specific topics in the TIM domain, capturing a breadth of innovation papers but avoiding science papers unrelated to innovation or commercialization.

We included only articles (not editorials, book reviews, notices etc.) for the period 1971-2020 and collected bibliometric information from 11,166 articles related to “innovation”, which includes author names, author affiliations, countries, journals, titles, abstracts, keywords, publication years and cited references. Among these, 1,963 papers were related to “science”.

Data Analysis, Visualization and Theme Mapping

Data Analysis and Visualization using VOSViewer

To analyze the articles, we employed a bibliographic approach. This allows us to analyze, map and visualize different networks in the data, a task that is increasingly considered important by bibliometricians, as it reveals how a research topic has evolved over time, under- and over-researched subtopics and potential avenues for future research based on these under-researched subtopics (Milojević, 2014; van Eck & Waltman, 2014; Zhao & Strotmann, 2015; Brown, Park & Pitt, 2020; Park et al., 2020; Feng et al., 2020). We utilized the VOSViewer software tool to conduct our bibliographic analyses. Further details on how this tool was used for our bibliographic analysis and the insights derived from it can be seen in Appendix B.

Theme Mapping from the 2020 R&D Management Symposium

To facilitate the development of our framework, we map our bibliographic analysis across three key themes drawn from three parallel research streams from the 2020 R&D Management Symposium: Innovation Policy, Entrepreneurial Strategy and Innovation Intermediaries. This virtual symposium was organized to explore the translation of science-based invention to science-based innovation and was attended by relevant exemplars in the innovation management community. These three themes, which represent mediators in the invention to innovation process, were developed by the symposium organizers (thought leaders in this field) and also comprised the streams within the symposium's call for papers. For the Innovation Policy theme, several of these researchers have produced influential papers related to the creation of government innovation policy that either help or hinder science innovation and ecosystem growth (Fini, Grimaldi & Meoli, 2020; Marco, Martelli & Di Minin, 2020). For the Entrepreneurial Strategy theme, scholars have written articles on the decisions that entrepreneurs and their firms make that have key path dependent effects on the growth of their ventures (Cesaroni, Di Minin & Piccaluga, 2005; Ahn et al., 2016; Maine, Soh & Dos Santos, 2015). Finally, for Innovation Intermediaries theme, several researchers have explored the role innovation intermediaries such as incubators and technology transfer offices play in converting lab-based inventions to economic and societal benefits (Rasmussen, Mosey & Wright, 2014; Clausen & Rasmussen, 2011; Mortara & Parisot, 2016).

In creating a structured "science innovation" framework, we organize our bibliographic analysis by these themes. We subsequently draw on the papers and presentations from the symposium to show support for our framework through the illustration of current debates and examples of practice. All three themes provide contexts through which we can improve our understanding of the role universities play in the science-based invention to science-based innovation process. The papers and keynote presentations from the symposium provide a comprehensive and contemporary view of the field and what practices and strategies are being explored to optimize the science-based invention to science-based innovation process.

Results

This section presents the results of the bibliographic analysis, focusing on the evolution of the science-based innovation research field and the key themes within it that contribute to the development of our "science innovation" framework. A more generalized bibliographic analysis of the science-based innovation field, including overall trends, themes, authors, papers, authorship, and citation networks is presented in Appendix B.

Bibliographic Analysis of the Science-Based Innovation Literature

Evolution of Science-Based Innovation Research

In our bibliographic analysis, we examine research activity, key themes and authors. Figure 1a shows that the publication volume of papers related to the translation of breakthrough university invention to innovation and hard technology has been growing steadily. We organize and quantify the papers in our dataset into the three themes of the 2020 R&D Management Symposium: Innovation Policy, Innovation Intermediaries and Entrepreneurial Strategy; Figure 1b shows the growth of these themes over time. We normalize the relative proportion of papers in each of the three themes as a percentage of the total number of papers in our sample in each decade, to control for the overall growth in the number of publications. We see rapid growth in the Entrepreneurial Strategy segment, with more modest growth in Innovation Policy and Innovation Intermediaries.

We find that papers in our dataset do not necessarily focus on a single theme, rather they can draw from two or more themes, signalling the conceptual connectivity and linkage between these three themes, which we examine further in the Discussion. To show examples of this connectivity, we list influential papers (i.e., the top ten most cited papers in our dataset) that examine the effects of more than one of the three themes in Table 1.

We note that our dataset includes nearly 2,000 papers written by over 3,600 authors, highlighting the scale of the domain. Our bibliographic analysis, which is the first conducted on the science-based innovation field, identifies the intellectual roots of topic area, its evolution and the current state of research. The earlier, seminal papers in this field, as seen in the list of top cited papers in Table 2, which include Etzkowitz and his colleagues' work on Triple Helix university-industry-government relations, illustrates the importance of the role each of these stakeholders plays in translating science-based invention to innovation. However, as seen from the growing influence of the Entrepreneurial Strategy theme, much more attention has been given recently to the *process* of invention to innovation, particularly with respect to what firms, intermediaries and policymakers can do to influence the outcome of science-based innovation. Examples of recent process-focused research include Stern (August, 2020), who focuses on entrepreneurial ecosystem acceleration and Rasmuseen, Benneworth &

Gulbrandsen (2020), who suggest avenues for universities to change their incentive structures to encourage more science-based entrepreneurship.

Keywords of Science-Based Innovation Research

We observe several prominent keywords within our dataset, specifically related to inputs and outputs of the empirical and conceptual papers within it. Commonly observed keywords that are coupled with the terms “input” or “explanatory variable” include “scientist”, “entrepreneur”, “founder”, “technology”, “invention”, “funding” and “university”. Commonly observed keywords that are coupled with the terms “output” or “dependent variable” or “outcome” include “revenue”, “GDP”, “firms”, “products”, “patents”, “productivity” and “sustainability”. We synthesize these keywords to develop the input, process and output variables of our “science innovation” framework, which we discuss in the following section. A broader and generalized bibliographic analysis of the papers within our dataset, including citation, publication and network visualizations of authors, journals and co-citations is presented in Appendix B.

Discussion

In this section, we present a conceptual framework for the process of translating science invention to innovation through a distillation of our bibliographic analysis of the research in TIM journals. Moreover, we identify examples of key papers from our bibliographic analysis to validate and illuminate the framework in terms of its inputs, outputs and process mediators. To further support our framework, we draw upon the papers and presentations from the 2020 R&D Management Symposium to reflect on the emerging state of the art. A summary of this framework and its link to key bibliographic papers and symposium insights is presented in Table 3. We conclude this section by providing recommendations for innovation policymakers, university leadership and scientist-entrepreneurs regarding how the translation from science-based invention to science-based innovation can be facilitated.

A Framework for Science Innovation

Synthesizing our analysis of the research field, we note several salient inputs for a framework of the “science innovation” process. Drawing on past research across the field, this framework views the process in terms of its inputs, translation and eventual outcomes achieved. Process phases are interdependent, and universities need to manage both the individual development and synthesis between these phases, to optimise economic and societal benefit from the public funds invested in science research. The insights gained from the literature provide the basis for the conceptual framework presented in Figure 2, outlining the various inputs, outputs and influencers of the “science innovation” process. Key papers from our bibliographic analysis that validate the inclusion of each of these inputs, outputs and process components (mediators) are listed in Table 3. The framework highlights that the translation of scientific invention to innovation is not linear given the complexity, risk and uncertainty that surrounds the process. Invention-specific contextual factors such as market knowledge, project champions, entrepreneurial capabilities and organizational culture change have an iterative influence on subsequent cycles of the translational process, as the university, entrepreneur and/or policymaker learns from past experience and enhances its overall translation capability.

The initial phase of the process relates to *inputs* of university scientific research activity and encompasses the marriage between the depth of technological resources applied, the calibre of the scientists progressing research, the university capabilities to support research and the availability of funding streams to maintain ongoing research advancement. There is a strong interrelationship between these inputs (as with all phases) and development of these inputs impacts translation success and is discussed in previous literature (Fini et al., 2018; Aschooff & Sofka, 2009; De Fuentes & Dutrenit, 2012). Equally, the latter phase of the process relates to beneficial *outputs* resulting from the translation process and encompasses scientific advancements in the field, economic development generated through exploitation and the subsequent resultant societal impact. Key challenges related to translating from scientific invention to innovation includes establishing cause and effect, together with the prioritisation of more immediate and tangible outcome benefits over more ambiguous societal benefits. While benefits across these three outcomes are not mutually exclusive, there is a strong association with the translation vehicle adopted (e.g., open science, licencing, venture creation, joint venture) in the process and the value appropriation across the vehicles. The importance of managing this phase of the process has been acknowledged and is discussed in past research (Bhave, 1994; Rasmussen, Mosey & Wright, 2011; Chan & Lau, 2005).

The ‘heart’ of our framework is the translation process itself, which is a poorly understood phase of university scientific research activity. Drawing on insight from the systematic review of past literature, we view this phase of the process as achieving transformation through integration of three process mediators, namely Innovation Policy, Innovation Intermediaries and Entrepreneurial Strategy. The first of these mediators, Innovation Policy, encompasses the governmental ambitions and objectives associated with public research funding input and the emerging societal grand challenges that require response. While addressed in research to date (Nemet, 2009; Hyytinen & Toivanen, 2005), key questions remain unanswered, including how to optimise the public funding of technology and developing business models to ensure a ‘fair share’ appropriation of value by society, rather than allowing the private industry to disproportionately benefit, relative to the exploration risks taken on and the balance of public-private funding in university research activity. The second mediator of the transformation, Innovation Intermediaries, relates to the supports, internal and external to the university, that can be leveraged to affect translation of scientific invention to innovation. The least explored in past research, questions related to this mediator include the role of these intermediaries, the timing and phase of their engagement in the process and the fit of specific intermediaries within the different translation vehicles selected as part of the entrepreneurial strategy. This mediator encompasses where the fields of innovation management and regional ecosystem development intersect and represents an opportunity for significant research development in the coming years. The final mediator in the transformation phase of the framework is that of Entrepreneurial Strategy and is an area currently attracting significant research attention (Zott, Amit & Massa, 2011; Acs, Audretsch & Lehmann, 2013; Dattee, Alexy & Audio, 2018). It encompasses the alignment of tensions between technology and market requirements and the decision choices taken by the university and entrepreneur, both in selecting the vehicle for translation and development of the scientific invention itself. The impact on outcome is not only influenced by the selected strategy but also by the synergistic alignment with the other mediators of Innovation Policy and Innovation Intermediaries.

Effective interlinkage across the three process mediators can nurture enhanced university capability in translating scientific invention from research activity to scientific innovation and can allow government investment in university research to better address economic and societal needs. The process is an evolving learning system where, over time and acquired experience, process capabilities and synergies can be optimised to deliver the desired outputs (Menzel & Fornahl, 2010; Maine, Soh & Dos Santos, 2015; Huenteler, Schmidt & Ossenbrink, 2016). While this is the ultimate objective in addressing the identified research gap, it is important to emphasize that, similar to any innovation system, a degree of failure is inevitable, given the complexity and uncertainty involved. Without such failure and the subsequent learning from same, discovery research will tend towards incremental as opposed to frontier breakthroughs and science inventions will lack the necessary novelty to deliver required outcomes. Thus, the framework maintains the university potential in continuing to produce breakthrough scientific inventions and translating them for economic and societal benefit.

Illustration of the Science Innovation Framework

To support and illustrate examples of our novel “science innovation” framework, we draw on the 2020 R&D Management Symposium, which explores the science-based invention to science-based innovation process through three core themes: Innovation Policy, Entrepreneurial Strategy and Innovation Intermediaries. The presentations and discussions at the 2020 R&D Management Symposium elucidate the roles of academics, industry leaders and policymakers in creating the conditions for breakthrough university research to contribute to innovation ecosystems, specifically through the formation and growth of science-based ventures. Each of these players in the innovation ecosystem has a critical role to play in creating the conditions for impact in regional and national ecosystems.

We highlight here the key contribution of this framework: our model implies that understanding the process of translating university science to innovative products and services that have societal and economic impact requires looking beyond simple success metrics such as the number of spin-off ventures. Rather, we need to understand the way the inputs and outputs of the invention to innovation process are influenced by stakeholders such as policymakers, scientist-entrepreneurs and university leadership. The potential of university science to be transformed into economic and social value creation is enormous, however, the science-based invention to science-based innovation process is highly uncertain. Through our framework, we note that these stakeholders, who shape or enact science-based innovation in universities, play a direct role in helping both nascent ventures and incumbent firms identify technological competencies, translate these competencies into products and services and make meaningful contributions to the societies in which they operate. In this sub-section, we present the core symposium findings organized by the three key themes as examples of current debates and practice to support our “science innovation” framework and its contribution to the innovation management field. A summary of key symposium insights that support our framework are listed in Table 3. Additional examples from the 2020 R&D Management Symposium that support our “science innovation” framework are presented in Appendix C.

Innovation Policy Theme

In the Innovation Policy stream, speakers and presenters explored the question of how innovation policy can improve knowledge economy jobs. Stern (2020) presented MIT’s REAP program, where the university partners with communities around the world to strengthen their entrepreneurial ecosystems. MIT offers training to representatives in these communities to align the activities of the region’s universities, governments, corporate sector, entrepreneurs and financiers in an effort to drive the community’s entrepreneurial impact. In contrast to Stern’s (2020) regional analysis, which comprises several different types of stakeholders, Dalziel et al. (2020) examined the Artificial Intelligence sector at the level of the scientist-entrepreneur; they argue that individual scientist-entrepreneurs have been critical to the growth of the Canadian AI ecosystem and that academics and governments may be underestimating the importance of knowledge transfer through social ties.

Innovation Intermediaries Theme

In the Innovation Intermediaries stream, researchers discussed the roles of innovation intermediaries in creating the conditions for breakthrough innovations in science-based ventures. For example, Rasmussen (2020) presented his findings on universities as innovation intermediaries and detailed the critical role they play in facilitating spin-off venture formation based on scientific research. He notes that it is particularly important to conduct research on mid-range universities as most universities are not located in ecosystems with a rich history of technology-based entrepreneurial activity (Clarysse et al., 2005; Rasmussen & Borch, 2010). He suggests that these mid-range universities can improve their spin-off formation rates over time by developing three main capabilities: creating new paths of action, balancing academic and commercial interests and integrating new resources (Rasmussen & Borch, 2010).

Entrepreneurial Strategy Theme

In the Entrepreneurial Strategy stream, scholars explored strategies firms can use to enable value creation and capture within their innovation ecosystems. For the last two decades, universities have played an increasingly important role in creating opportunities for emerging industries through breakthrough invention (Arora 2019, Maine & Seegopaul, 2016; Rasmussen & Borch, 2010). However, university spin-offs do not enjoy the same funding resources as corporate research labs (Arora, 2019; Pisano, 2010). Thomas et al. (2020) argue that scientist-entrepreneurs will increase their chances of value creation of their spin-off firms by learning how to optimally match their technologies to specific markets, securing financing by filing early, broad blocking patents, attracting and mentoring lab members and business partners and incubating their ventures until commercial viability. These capabilities can be effectively nurtured through formalized entrepreneurial programs at universities (Maine, 2020; Eesley & Miller, 2017, Leih & Teece, 2016; Lubik, Treen, & Gemino, 2020). This example illustrates the mediating effect of Entrepreneurial Strategy in the translation of invention to innovation.

Recommendations and Future Research

This section provides a call for future research related to our “science innovation” framework and lists several recommendations to innovation policymakers, university leadership and science-entrepreneurs to more effectively translate science-based invention to science-based innovation. A summary of the key recommendations for each of these three stakeholders is presented in Table 4.

Future Research

In this paper we present a novel framework on “science innovation”, identifying three interrelated mediators at the heart of the translation process. This framework provides structure for development of the field and illuminates areas for future research, that will further validate and strengthen the model and enhance university effectiveness in translating public-funded scientific invention to innovative outputs. We note that the outputs: economic development, scientific research and societal impacts can be defined using various outcome variables and can even operate at different levels. Scholars have noted the need for the innovation management field to explore societal outcomes such as sustainability more deeply (Bocken et al., 2019; Ritala, 2019; Fini et al., 2018), and our framework aims to serve as a conceptual starting point. In order to test our framework empirically, we call for scholars within the innovation management field to study the causal relationships between the inputs, mediators and outputs we offer in our model, with specified variables for each. The strength of the linkages between the inputs, process mediators and outputs of our framework may be heterogenous across the three mediator types and the levels at which the variables operate. Moreover, the interplay among the mediators between the science-based invention and science-based innovation process should be further examined. For example, each mediator may amplify the effects of the other mediators, and collectively, may have a pronounced effect on the development of an emergent innovation ecosystem.

Recommendations for Innovation Policymakers

To create more economic and social value from university inventions, we recommend innovation policymakers support science-based innovation and the growth of the knowledge-based economy by expanding on the learnings derived from the Innovation Policy theme in the 2020 R&D Management Symposium. For example, innovation policymakers can invest in specialized entrepreneurial training for scientists and support the commercial development and de-risking of breakthrough university inventions before firm formation. Governments can provide funding for specific skills training to enable cross collaboration between entrepreneurs and scientists and to empower scientists to become entrepreneurs through awareness and education programs such as Invention to Innovation (Mitacs, Beedie, Simon Fraser University) and Quebec Science Entrepreneurship (District 3 Innovation Centre, Concordia University). For the de-risking of breakthrough university inventions, policymakers can fund commercialization post-doctoral fellows and access for scientist entrepreneurs to university and government process scale up facilities (e.g., Cyclotron Road, Berkeley National Laboratory).

Additionally, policymakers can play an important role in resolving the information asymmetry between emergent ventures who require capital to grow and venture capitalists who are unable to determine whether the venture is going to succeed. Policymakers can bridge this gap by encouraging universities to aid their spin-off ventures by signaling the high quality of the ventures to outside investors through research assessments, research evaluations and strategic IP (Rasmussen, Benneworth & Gulbrandsen, 2020; Thomas et al., 2020; Hsu & Ziedonis, 2008).

Recommendations for University Leadership

Alignment of incentives and capabilities at the level of individual scientists, research universities and regional and national systems of innovation is essential. Universities can work collaboratively with policymakers by paying specific attention to improving their capabilities around creating new paths to spin-off formation, balancing academic and commercial interests and integrating new resources, such as translational government grants and seed-funding. For example, universities who wish to improve their success rates in establishing spin-offs can start by creating a well-defined policy on intellectual property rights and by funding, but clearly separating, academic and commercial activities within a research lab to avoid conflicts of interest and ambiguities around goals for each activity (Rasmussen & Borch, 2010). Most importantly, university leaders should create institutional frameworks to allow its faculty and employees to benefit from entrepreneurship and to build their social linkages with internal and external intermediaries to support their translation efforts. For example, faculty members can be rewarded for entrepreneurship activities by allowing those activities to partially fulfill core academic, teaching and service obligations, which factor into tenure and promotion decisions (Rasmussen, Benneworth & Gulbrandsen, 2020).

Recommendations for Scientist-Entrepreneurs

Most academic scientists are motivated by making a positive impact with their scientific inventions. However, their extensive scientific training and experience seldom prepares them to make the strategic entrepreneurial decisions in the research lab and in innovation intermediaries which would give them the best chance to realize that ambition. Scientists are too often derided for technology push by innovation intermediaries, such as university accelerators. Whereas an early incorporation of unmet market needs is crucially important, the opportunity creation potential inherent in breakthrough invention is too frequently suppressed, alienating scientists from the entrepreneurial process.

With the long timelines from invention to innovation of breakthrough science, the decisions an academic scientist makes in the research lab of what experiments to run, technology attributes to explore and IP to protect have long lasting consequences for future science-based spinoffs. Many university scientists assume that a business co-founder will make all the business decisions, however, successful science-based ventures frequently can trace their success to entrepreneurial decisions made in the research lab prior to firm-formation (Thomas et al., 2020). This was evidenced by the remarkable response of scientists and science-based ventures to the COVID-19 pandemic, which revealed the need for science-based ventures which had already been formed and had been commercializing university research, and thus which had both the technology platform capabilities and the adaptation capabilities to pivot quickly and effectively. The path dependent nature of decisions scientists make in their research labs is a critical factor in the translation of science-based invention to science-based innovation. Furthermore, scientists who become entrepreneurs use their new skills to engage in novel exploratory work that enhances their research impact (Fini, Perkmann & Ross, 2021). Thus, academic scientists who develop entrepreneurial capabilities for themselves and their lab members increase the likelihood of creating impact from their scientific inventions.

Conclusion

Utilizing a bibliometric review, we characterize and explore the emergence of the science-based innovation literature. We identify the inputs, outputs, and influencers of the translation of invention to innovation and provide a conceptual framework for the science-based innovation process. Our framework reveals that understanding the process of translating university science to economic and societal impacts requires looking beyond traditional metrics and factors such as university spin-off rates or individual firm strategies. It requires a nuanced exploration of the direct roles of important stakeholders in the university context, including policymakers, scientist-entrepreneurs, and university leadership. Our analysis has generated novel insights into the nature of science-based innovation literature but also indicates areas that warrant future research.

Based on our review, we also provide recommendations that can guide policymakers, academic scientists, and university leadership to better translate breakthrough inventions at universities to innovation. An important function of universities is to educate and train researchers; however, the graduate researchers produced by modern universities are woefully underutilized in the science-based innovation ecosystem. Innovation policymakers can fund educational and commercialization programs which align the incentives of scientists, universities and the regional and national innovation ecosystem. Furthermore, they can facilitate funding of university spin-off ventures by encouraging universities to signal the high quality of their spin-offs to venture capitalists through research assessments, research evaluations and strategic IP.

In addition, universities, and scientists themselves can improve this situation. Universities can prepare scientists with innovation and entrepreneurship training and support them with entrepreneurship mentoring and prototype development. They can also encourage entrepreneurship activity by giving professors partial fulfillment of academic, teaching and service requirements upon engagement and successful completion of those activities. Scientist-entrepreneurs can proactively develop their entrepreneurial capabilities by seeking out training programs at universities: science entrepreneurship programs will enhance their chances of successfully commercializing their inventions by nurturing their skills in prioritizing markets for their technologies, strategically managing their IP and incubating their ventures until commercial viability. Such changes will better harness breakthrough inventions at universities to both address global challenges and stimulate economic growth.

References

Acs, Z. J., Audretsch, D. B., & Lehmann, E. E. (2013). The knowledge spillover theory of entrepreneurship. *Small Business Economics*, *41*(4), 757-774.

Acs, Z. J., Anselin, L., & Varga, A. (2002). Patents and innovation counts as measures of regional production of new knowledge. Research Policy, 31(7), 1069-1085.

Ahn, J., & Kim, T. (August, 2020). Happily ever after? – The longitudinal impact of government R&D subsidy on innovative small firms. R&D Management Symposium, Virtual.

Ahn, J. M., Ju, Y., Moon, T. H., Minshall, T., Probert, D., Sohn, S. Y., & Mortara, L. (2016). Beyond absorptive capacity in open innovation process: the relationships between openness, capacities and firm performance. *Technology Analysis & Strategic Management*, *28*(9), 1009-1028.

Arora, A., Belenzon, S., Patacconi, A., & Suh, J. (2020). The changing structure of American innovation: Some cautionary remarks for economic growth. Innovation Policy and the Economy, 20(1), 39-93.

Arora, A. (August, 2020). Changing role of corporate research labs and universities. Keynote session at the R&D Management Symposium, Virtual.

Arora, A., Belenzon, S., Patacconi, A., & Suh, J. (2019). Why the US innovation ecosystem is slowing down. Harvard Business Review.

Aschhoff, B., & Sofka, W. (2009). Innovation on demand—Can public procurement drive market success of innovations?. *Research Policy*, *38*(8), 1235-1247.

Asheim, B. T., & Coenen, L. (2005). Knowledge bases and regional innovation systems: Comparing Nordic clusters. *Research Policy*, *34*(8), 1173-1190.

Bhave, M. P. (1994). A process model of entrepreneurial venture creation. *Journal of Business Venturing*, *9*(3), 223-242.

Bocken, N., Ritala, P., Albareda, L., & Verburg, R. (2019). Introduction: innovation for sustainability. In *Innovation for Sustainability* (pp. 1-16). Palgrave Macmillan, Cham.

Bonaccorsi, A., & Piccaluga, A. (1994). A theoretical framework for the evaluation of university-industry relationships. R&D Management, 24(3), 229-247.

Bolzani, D., Munari, F., Rasmussen, E., & Toschi, L. (2020). Technology Transfer Offices as providers of science and technology entrepreneurship education. The Journal of Technology Transfer, 1-31.

Brown, T., Park, A., & Pitt, L. (2020). A 60-Year Bibliographic Review of the Journal of Advertising Research. *Journal of Advertising Research*.

Budd, T. (August, 2020). Advances in integrating technological innovation for analysing deep decarbonization policies of emissions-intensive and trade-exposed (EITE) industries. R&D Management Symposium, Virtual.

Casper, S., & Murray, F. (2005). Careers and clusters: analyzing the career network dynamic of biotechnology clusters. *Journal of Engineering and Technology Management*, *22*(1-2), 51-74.

Cesaroni, F., Minin, A. D., & Piccaluga, A. (2005). Exploration and exploitation strategies in industrial R&D. *Creativity and Innovation Management*, *14*(3), 222-232.

Chan, K. F., & Lau, T. (2005). Assessing technology incubator programs in the science park: the good, the bad and the ugly. *Technovation*, *25*(10), 1215-1228.

Chao, C. C., Yang, J. M., & Jen, W. Y. (2007). Determining technology trends and forecasts of RFID by a historical review and bibliometric analysis from 1991 to 2005. *Technovation*, *27*(5), 268-279.

Clarysse, B., Wright, M., Lockett, A., Van de Velde, E., & Vohora, A. (2005). Spinning out new ventures: a typology of incubation strategies from European research institutions. Journal of Business venturing, 20(2), 183-216.

Clausen, T., & Rasmussen, E. (2011). Open innovation policy through intermediaries: the industry incubator programme in Norway. *Technology Analysis & Strategic Management*, *23*(1), 75-85.

Cooke, P., Uranga, M. G., & Etxebarria, G. (1998). Regional systems of innovation: an evolutionary perspective. Environment and Planning A, 30(9), 1563-1584.

Cunningham, J. A., Menter, M., & O'Kane, C. (2018). Value creation in the quadruple helix: A micro level conceptual model of principal investigators as value creators. R&D Management, 48(1), 136-147.

Dalziel, M., Zhao, X., Watkins, A., & Shapira, P. (August, 2020). Godfathers and Dissemination: Knowledge Spillovers and Ecosystems in Artificial Intelligence. R&D Management Symposium, Virtual.

Dattée, B., Alexy, O., & Autio, E. (2018). Maneuvering in poor visibility: How firms play the ecosystem game when uncertainty is high. *Academy of Management Journal*, *61*(2), 466-498.

De Fuentes, C., & Dutrénit, G. (2012). Best channels of academia–industry interaction for long-term benefit. *Research Policy*, *41*(9), 1666-1682.

De Marco, C. E., Martelli, I., & Di Minin, A. (2020). European SMEs' engagement in open innovation When the important thing is to win and not just to participate, what should innovation policy do?. *Technological Forecasting and Social Change*, *152*, 119843.

D'Este, P., & Patel, P. (2007). University–industry linkages in the UK: What are the factors underlying the variety of interactions with industry?. *Research Policy*, *36*(9), 1295-1313.

Dill, D. D. (1990). University/industry research collaborations: An analysis of interorganizational relationships. R&D Management, 20(2), 123-129.

Eesley, C. E., & Miller, W. F. (2017). Impact: Stanford university's economic impact via innovation and entrepreneurship. Available at SSRN 2227460.

Etzkowitz, H. (2003). Innovation in innovation: The triple helix of university-industry-government relations. Social Science Information, 42(3), 293-337.

Etzkowitz, H., & Zhou, A. (2019). Triple Helix : a universal innovation model ?. In Handbook on Science and Public Policy. Edward Elgar Publishing.

Etzkowitz, H., & Leydesdorff, L. (2000). The dynamics of innovation: from National Systems and "Mode 2" to a Triple Helix of university–industry–government relations. *Research Policy*, 29(2), 109-123.

Etzkowitz, H., Webster, A., Gebhardt, C., & Terra, B. R. C. (2000). The future of the university and the university of the future: evolution of ivory tower to entrepreneurial paradigm. Research Policy, 29(2), 313-330.

Etzkowitz, H., & Zhou, C. (2018). Innovation incommensurability and the science park. *R&D Management*, 48(1), 73-87.

Feng, C. M., Park, A., Pitt, L., Kietzmann, J., & Northey, G. (2020). Artificial intelligence in marketing: A bibliographic perspective. *Australasian Marketing Journal*, j-ausmj.

Fini, R., Grimaldi, R., & Meoli, A. (2020). The Effectiveness of University Regulations to Foster Science-Based Entrepreneurship. Research Policy.

Fini, R., Perkmann, M., & Ross, J. M. (2021). Attention to exploration: The effect of academic entrepreneurship on the production of scientific knowledge. *Organization Science*, Forthcoming.

Fini, R., Rasmussen, E., Siegel, D., & Wiklund, J. (2018). Rethinking the commercialization of public science: From entrepreneurial outcomes to societal impacts. *Academy of Management Perspectives*, 32(1), 4-20.

Fini, R., Rasmussen, E., Wiklund, J., & Wright, M. (2019). Theories from the lab: How research on science commercialization can contribute to management studies. Journal of Management Studies, 56(5), 865-894.

Furman, J. L., Porter, M. E., & Stern, S. (2002). The determinants of national innovative capacity. Research Policy, 31(6), 899-933.

Gallouj, F., & Weinstein, O. (1997). Innovation in services. Research Policy, 26(4-5), 537-556.

Gans, J., Kearney, M., Scott, Er., & Stern, S. (August, 2020). Choosing Technology: An Entrepreneurial Strategy Approach. R&D Management Symposium, Virtual.

Gans, J. S., & Stern, S. (2003). The product market and the market for "ideas": commercialization strategies for technology entrepreneurs. *Research Policy*, 32(2), 333-350.

Guzman, J., & Stern, S. (2020). The State of American Entrepreneurship: New Estimates of the Quantity and Quality of Entrepreneurship for 32 US States, 1988–2014. American Economic Journal: Economic Policy, 12(4), 212-43.

Hall, J. (2016). The 2015 impact factors and emerging recognition of technology and innovation management journals. *Journal of Engineering and Technology Management,* 41, v-vi.

Hernández-Trasobares, A., & Murillo-Luna, J. L. (2020). The effect of triple helix cooperation on business innovation: The case of Spain. *Technological Forecasting and Social Change*, 161, 120296.

Howells, J. (2006). Intermediation and the role of intermediaries in innovation. Research Policy, 35(5), 715-728.

Hsu, D. H., & Ziedonis, R. H. (2008, August). Patents as quality signals for entrepreneurial ventures. In *Academy of Management Proceedings* (Vol. 2008, No. 1, pp. 1-6). Briarcliff Manor, NY 10510: Academy of Management.

Huang, Y., Ding, X. H., Liu, R., He, Y., & Wu, S. (2019). Reviewing the domain of technology and innovation management: A visualizing bibliometric analysis. SAGE Open, 9(2), 2158244019854644.

Huenteler, J., Schmidt, T. S., Ossenbrink, J., & Hoffmann, V. H. (2016). Technology life-cycles in the energy sector—Technological characteristics and the role of deployment for innovation. *Technological Forecasting and Social Change*, *104*, 102-121.

Hyytinen, A., & Toivanen, O. (2005). Do financial constraints hold back innovation and growth?: Evidence on the role of public policy. *Research Policy*, *34*(9), 1385-1403.

Jensen, M. B., Johnson, B., Lorenz, E., Lundvall, B. Å., & Lundvall, B. A. (2007). Forms of knowledge and modes of innovation. *The learning economy and the economics of hope*, *155*.

Klevorick, A. K., Levin, R. C., Nelson, R. R., & Winter, S. G. (1995). On the sources and significance of interindustry differences in technological opportunities. *Research Policy*, *24*(2), 185-205.

Lakhani, K. R., & Von Hippel, E. (2004). How open source software works: “free” user-to-user assistance. In Produktentwicklung mit virtuellen Communities (pp. 303-339). Gabler Verlag.

Laursen, K., & Salter, A. (2004). Searching high and low: what types of firms use universities as a source of innovation?. *Research Policy*, *33*(8), 1201-1215.

Lee, H. (2015). Uncovering the multidisciplinary nature of technology management: Journal citation network analysis. *Scientometrics*, 102, 51-75.

Leih, S., & Teece, D. (2016). Campus leadership and the entrepreneurial university: A dynamic capabilities perspective. Academy of Management Perspectives, 30(2), 182-210.

Linton, J. (2006). Ranking of technology and innovation management journals. *Technovation*, 26, 285-287.

Lubik, S., Treen, E, & Gemino, A. (August, 2020). Measuring the Impact of Entrepreneurial Programming: Entrepreneurial Mindset Scale Development. R&D Management Symposium, Virtual.

Lundqvist, M., & Williams, K. (2005). Adding licensing and venture creation to a university mission of open exchange. In Triple Helix conference 2005, May, Torino, Italy.

Maine, E. (August, 2020). Innovation capabilities for scientist-entrepreneurs. Keynote session at the R&D Management Symposium, Virtual.

Maine, E., Shapiro, D. M., & Vining, A. R. (2010). The role of clustering in the growth of new technology-based firms. Small Business Economics, 34(2), 127-146.

Maine, E., & Seegopaul, P. (2016). Accelerating advanced-materials commercialization. Nature Materials, 15(5), 487-491.

Maine, E., Soh, P. H., & Dos Santos, N. (2015). The role of entrepreneurial decision-making in opportunity creation and recognition. *Technovation*, 39, 53-72.

Maine, E., Thomas, V., Bliemel, M., Murira, A., & Utterback, J. (2014). The emergence of the nanobiotechnology industry. Nature nanotechnology, 9(1), 2.

Malerba, F. (2002). Sectoral systems of innovation and production. Research Policy, 31(2), 247-264.

Marzi, G., Caputo, A., Garces, E., & Dabić, M. (2018). A three decade mixed-method bibliometric investigation of the IEEE transactions on engineering management. IEEE Transactions on Engineering Management.

McAdam, M., & Debackere, K. (2018). Beyond 'triple helix'toward 'quadruple helix'models in regional innovation systems: Implications for theory and practice. R&D Management, 48(1), 3-6.

McQuarrie, E., Simon, C., Simmons, S., & Maine, E. (August, 2020). The Emerging Commercial Landscape of Quantum Computing. R&D Management Symposium, Virtual.

Menzel, M. P., & Fornahl, D. (2010). Cluster life cycles—dimensions and rationales of cluster evolution. *Industrial and corporate change*, *19*(1), 205-238.

Meyer-Brötz, F., Stelzer, B., Schiebel, E., & Brecht, L. (2018). Mapping the technology and innovation management literature using hybrid bibliometric networks. *International Journal of Technology Management*, *77*(4), 235-286.

Meyer, M. (2003). Academic entrepreneurs or entrepreneurial academics? Research–based ventures and public support mechanisms. R&D Management, 33(2), 107-115.

Miller, K., McAdam, R., & McAdam, M. (2018). A systematic literature review of university technology transfer from a quadruple helix perspective: toward a research agenda. R&D Management, 48(1), 7-24.

Miller, K., McAdam, R., Moffett, S., Alexander, A., & Puthusserry, P. (2016). Knowledge transfer in university quadruple helix ecosystems: an absorptive capacity perspective. R&D Management, 46(2), 383-399.

Milojević, S. (2014). Network analysis and indicators. In Measuring Scholarly Impact (pp. 57-82). Springer, Cham.

Mortara, L., & Parisot, N. G. (2016). Through entrepreneurs' eyes: the Fab-spaces constellation. *International Journal of Production Research*, *54*(23), 7158-7180.

National Academies of Sciences, Engineering, and Medicine. (2020). Review of the SBIR and STTR Programs at the Department of Energy. National Academies Press.

Nemet, G. F. (2009). Demand-pull, technology-push, and government-led incentives for non-incremental technical change. *Research policy*, *38*(5), 700-709.

Nightingale, P., & Coad, A. (2014). Muppets and gazelles: political and methodological biases in entrepreneurship research. Industrial and Corporate Change, 23(1), 113-143.

Nelson, R. R., & Nelson, K. (2002). Technology, institutions, and innovation systems. Research policy, 31(2), 265-272.

Noyons, E. C. M., Luwel, M., & Moed, H. F. (1998). Assessment of Flemish R&D in the field of information technology: A bibliometric evaluation based on publication and patent data, combined with OECD research input statistics. *Research Policy*, *27*(3), 285-300.

O'Shea, R. P., Allen, T. J., Morse, K. P., O'Gorman, C., & Roche, F. (2007). Delineating the anatomy of an entrepreneurial university: the Massachusetts Institute of Technology experience. R&D Management, 37(1), 1-16.

Park, A., Montecchi, M., Feng, C., Plangger, K. A, & Pitt, L.F. (2020). Understanding Fake News: A Bibliographic Perspective. *Defense Strategic Communications*, *8*(Autumn), 141-172.

Park, A., & Maine, E. (August, 2020). To Reveal or Not to Reveal? Open Innovation Mechanisms Within an Emerging Personalized Medicine Innovation Ecosystem. R&D Management Symposium, Virtual.

Perkmann, M., Tartari, V., McKelvey, M., Autio, E., Broström, A., D'este, P., … & Sobrero, M. (2013). Academic engagement and commercialisation: A review of the literature on university–industry relations. *Research Policy*, 42(2), 423-442.

Pisano, G. P. (2010). The evolution of science-based business: innovating how we innovate. Industrial and corporate change, 19(2), 465-482.

Philpott, K., Dooley, L., O'Reilly, C., & Lupton, G. (2011). The entrepreneurial university: Examining the underlying academic tensions. Technovation, 31(4), 161-170.

Rasmussen, E., Mosey, S., & Wright, M. (2011). The evolution of entrepreneurial competencies: A longitudinal study of university spin‐off venture emergence. *Journal of Management Studies*, *48*(6), 1314-1345.

Rasmussen, E. (August, 2020). Innovation capabilities for universities. Keynote session at the R&D Management Symposium, Virtual.

Rasmussen, E., Benneworth, P., & Gulbrandsen, M. (2020). Motivating universities to support spin-off firms: Stakeholders and start-up incubation ecosystems. In *Research Handbook on Start-Up Incubation Ecosystems*. Edward Elgar Publishing.

Rasmussen, E., & Borch, O. J. (2010). University capabilities in facilitating entrepreneurship: A longitudinal study of spin-off ventures at mid-range universities. *Research Policy*, 39(5), 602-612.

Ritala, P. (2019). Innovation for Sustainability: Sceptical, Pragmatic, and Idealist Perspectives on the Role of Business as a Driver for Change. In *Innovation for Sustainability* (pp. 21-34). Palgrave Macmillan, Cham.

Roberts, E. B., Murray, F., & Kim, J. D. (2015). Entrepreneurship and Innovation at MIT: Continuing global growth and impact.

Rothaermel, F. T., Agung, S. D., & Jiang, L. (2007). University entrepreneurship: a taxonomy of the literature. *Industrial and Corporate Change*, *16*(4), 691-791.

Shane, S. A. (2004). *Academic entrepreneurship: University spinoffs and wealth creation*. Edward Elgar Publishing.

Shum, V., Park, A., Maine, E., & Pitt, L. F. (2019). A bibliometric study of research-technology management, 1998–2017: An analysis of 20 years of RTM articles offers a perspective on trends and evolutions in the journal's content and in the field of innovation management. *Research-Technology Management*, *62*(1), 34-43.

Song, Y., Zhang, J., Song, Y., Fan, X., Zhu, Y., & Zhang, C. (2020). Can industry-university-research collaborative innovation efficiency reduce carbon emissions?. *Technological Forecasting and Social Change*, 157, 120094.

Stern, S. (August, 2020). Accelerating Entrepreneurial Ecosystems: Lessons from the MIT Regional Entrepreneurship Acceleration Program. R&D Management Symposium, Virtual.

Stilgoe, J., Owen, R., & Macnaghten, P. (2013). Developing a framework for responsible innovation. *Research Policy*, 42(9), 1568-1580.

Surana, K., Doblinger, C., & Anadon, L. D. (2020). Collaboration Between Start-Ups and Federal Agencies: A Surprising Solution for Energy Innovation. Information Technology and Innovation Foundation.

Thomas, V. J., Bliemel, M., Shippam, C., & Maine, E. (2020). Endowing university spin-offs pre-formation : Entrepreneurial capabilities for scientist-entrepreneurs. *Technovation*, 96-97, 102153.

Thongpapanl, N. (2012). The changing landscape of technology and innovation management: An updated ranking of journals in the field. *Technovation*, 32, 257-271.

Van Eck, N. & Waltman, L. (2009). Software survey: VOSviewer, a computer program for bibliometric mapping. *Scientometrics*, *84*(2), 523-538.

Van Eck, N. J. & Waltman, L. (2014). Visualizing bibliometric networks. In *Measuring Scholarly Impact* (pp. 285-320). Springer, Cham.

Whitesides, G. M. (2013). Cool, or simple and cheap? Why not both?. Lab on a Chip, 13(1), 11-13.

Yang, P., & Tao, L. (2012). Perspective: Ranking of the world's top innovation management scholars and universities. *Journal of Product Innovation Management*, 29, 319-331.

Yaghmaie, P., & Maine, E. (2020). BC's Regional Innovation Ecosystem: Innovation policies to enhance the Knowledge-based Economy of BC. R&D Management Symposium, Virtual.

Zhao, D., & Strotmann, A. (2015). Analysis and visualization of citation networks. *Synthesis Lectures on Information Concepts, Retrieval, and Services*, *7*(1), 1-207.

Zhou, Y., Pan, M., & Xu, G. (2020). Tie strength or structural configurations? The network effect of innovation diffusion of emerging technologies from network evolution perspective. R&D Management Symposium, Virtual.

Zott, C., Amit, R., & Massa, L. (2011). The business model: recent developments and future research. *Journal of Management*, *37*(4), 1019-1042.

Zucker, L. G., & Darby, M. R. (1998). Entrepreneurs, star scientists, and biotechnology. NBER Reporter Online (Fall 1998), 7-10.

Additional Details on Bibliographic Methods

To produce network visualizations, we used the software VOS (Visualization of Similarities) Viewer (van Eck & Waltman, 2009) to analyze and quantify bibliometric data and construct and to view bibliographic network maps for visual interpretation. We quantify the number of papers published based on the following two subqueries from our dataset of 1,963 science-based innovation articles: (university) and (biotech* OR nanotech* OR fusion OR “quantum computing” OR “artificial intelligence” OR “machine learning” OR “advanced materials” OR chemi*). The latter subquery represents papers related to hard technology. The results are then grouped by date range. These subqueries are performed to elucidate and visualize the growth in research activity related to the impact of universities and academic entrepreneurship on science-based innovation as well as the research activity of papers rooted in hard technology contexts.

Supplementary Bibliographic Analysis

The Authors, their Co-Authors, and their Papers

The dataset includes 1,963 papers written by 3,619 separate authors. The ten most-published authors are shown in Table C1 along with their total number of citations and mean citations per paper. The most prolific authors for the search terms studied in the TIM journals are Porter, Youtie, Shapira, Guo and Meissner. The ten most-cited authors are shown in Table C1 along with their total number of papers published and mean citations per paper. The most cited authors are Etzkowitz, Leydesdorff, von Hippel, Stern and Nelson. It is worth noting that no authors appear on both lists, suggesting a weak link between number of published papers and number of citations.

Table C2 shows the top ten most cited papers, indicating the intellectual roots of the TIM field. It is evident that Etzkowitz and his Triple Helix model of university, industry and government collaboration to facilitate science-based innovation is heavily influential in the domain, with two of his papers being cited nearly 4000 times. Malerba’s (2002) and Cooke, Uranga & Etxebarria’s (1998) papers on sectoral systems of innovation and regional systems of innovation respectively, have also garnered over 1000 citations each and figure prominently in the field.

In Figure C1, a VOSViewer map of co-authorship of the papers in our dataset is shown. It is apparent that many scholars work in teams and networks of between 2 and 3 authors on these issues, although the map also shows that several scholars have published papers with no other co-authors. There are several notable networks of authors, with Etzkowitz, Von Hippel, Stern and Perkmann at the centers of each. The size of the circles attached to the name reflects the number of papers published by a particular author in our dataset and the colors denote individual co-authorship networks (there is no significance to the specific colors). This indicates that there remains significant opportunity for expanded co-authorship and interdisciplinary research in the innovation management field, which could strengthen the conclusions and framework developed in this paper through novel conceptual and empirical approaches. We expand on this opportunity for follow-on research in Section 5.

Co-Citations with Other Journals

The network of the overall most cited journals in our dataset is shown in Figure C2. Several networks of journals dominate the co-citation space. *Research Policy* lies at the center of the co-citation map and links other prominent journal networks both in and outside the TIM field, including *Strategic Management Journal*, *Technological Forecasting and Social Change*, *Technovation* and *American Economic Review*. *Strategic Management Journal*, *Administrative Sciences Quarterly* and *Harvard Business Review* dominate the green network in the figure, which is comprised mostly of other traditional management journals. These results illustrate that the science-based innovation literature draws on a wide variety of papers outside the traditional TIM field. The presence of some journals outside the management field altogether such as *Scientometrics* indicates the nascent interdisciplinary nature of science-based innovation research.

Additional Examples to Support Our Science Innovation Framework from the 2020 R&D Management Symposium

Innovation Policy Theme

At the government level, authors have explored the role of governments (Yaghmaie & Maine, 2020; Arora, 2020; Stern, 2020) in fostering the growth of these emerging technology innovation ecosystems and found that the government research funding can produce dramatically different results in innovative output depending on the strategic management of those funds. Similarly, a study of government R&D subsidies on small, technology-driven firms in Korea shows mixed results in their effectiveness (Ahn & Kim, 2020) suggesting that blind deployment of resources may not be enough to foster the creation of knowledge economy jobs. These examples highlight the role policymakers play in influencing the translation of science-based invention to science-based innovation.

Innovation Intermediaries Theme

A panel discussion comprised of presentations from Lubik (Invention to Innovation, Simon Fraser University), Apiou (Longfellow Model, Massachusetts General Hospital Research Institute), and Somerville (District 3 Innovation Centre, Concordia University), explored the theme of capability development in academic settings such as universities and medical centers in further detail. A common thread in these presentations was observed, namely that all three ecosystems suffer from a disconnect between scientific research and value capture in the commercial setting. The panelists noted various strategies their innovation intermediaries have employed to bridge this gap, ranging from enhancing the entrepreneurial mindset of individual scientists (Invention to Innovation, District 3) (Lubik, Treen & Gemino, 2020) to tightening the link between academia and industry through industry-supported initiatives, such as project competitions (Longfellow Model). These case studies highlight the critical role intermediaries play in the invention to innovation process.

Entrepreneurial Strategy Theme

The choices an entrepreneur and a firm should make during the firm’s maturation and their resultant effects on value capture remain nuanced. Gans et al. (2020) argue that traditional research on the Technology S-curve is oversimplified; they suggest that the curve itself can be reshaped by entrepreneurial decisions and an entrepreneur may decide to stay in either exploration or exploitation mode longer than is typically suggested by management literature.

Tables

Table 1. Ten most cited papers spanning two or more science innovation themes

Paper	Citations
Etzkowitz, H., & Leydesdorff, L. (2000). The dynamics of innovation: from National Systems and "Mode 2" to a Triple Helix of university–industry–government relations. *Research Policy*, *29*(2), 109-123.	2773
Etzkowitz, H., Webster, A., Gebhardt, C., & Terra, B. R. C. (2000). The future of the university and the university of the future: evolution of ivory tower to entrepreneurial paradigm. *Research Policy*, *29*(2), 313-330.	1052
Malerba, F. (2002). Sectoral systems of innovation and production. *Research Policy*, *31*(2), 247-264.	1021
Acs, Z. J., Anselin, L., & Varga, A. (2002). Patents and innovation counts as measures of regional production of new knowledge. *Research Policy*, *31*(7), 1069-1085.	749
Jensen, M. B., Johnson, B., Lorenz, E., Lundvall, B. Å., & Lundvall, B. A. (2007). Forms of knowledge and modes of innovation. *The learning economy and the economics of hope*, *155*.	745
Rothaermel, F. T., Agung, S. D., & Jiang, L. (2007). University entrepreneurship: a taxonomy of the literature. *Industrial and Corporate Change*, *16*(4), 691-791.	725
D'Este, P., & Patel, P. (2007). University–industry linkages in the UK: What are the factors underlying the variety of interactions with industry?. *Research Policy*, *36*(9), 1295-1313.	697
Asheim, B. T., & Coenen, L. (2005). Knowledge bases and regional innovation systems: Comparing Nordic clusters. *Research Policy*, *34*(8), 1173-1190.	695

Paper	Citations
Klevorick, A. K., Levin, R. C., Nelson, R. R., & Winter, S. G. (1995). On the sources and significance of interindustry differences in technological opportunities. *Research Policy*, *24*(2), 185-205.	649
Laursen, K., & Salter, A. (2004). Searching high and low: what types of firms use universities as a source of innovation?. *Research Policy*, *33*(8), 1201-1215.	539

Table 2. Ten most cited papers

Paper	Citations
Etzkowitz, H., & Leydesdorff, L. (2000). The dynamics of innovation: from National Systems and “Mode 2” to a Triple Helix of university–industry–government relations. Research Policy, 29(2), 109-123.	2773
Etzkowitz, H., Webster, A., Gebhardt, C., & Terra, B. R. C. (2000). The future of the university and the university of the future: evolution of ivory tower to entrepreneurial paradigm. Research Policy, 29(2), 313-330.	1052
Malerba, F. (2002). Sectoral systems of innovation and production. Research Policy, 31(2), 247-264.	1021
Cooke, P., Uranga, M. G., & Etxebarria, G. (1998). Regional systems of innovation: an evolutionary perspective. Environment and Planning A, 30(9), 1563-1584.	1019
Furman, J. L., Porter, M. E., & Stern, S. (2002). The determinants of national innovative capacity. Research Policy, 31(6), 899-933.	889
Howells, J. (2006). Intermediation and the role of intermediaries in innovation. Research Policy, 35(5), 715-728.	834

Paper	Citations
Gallouj, F., & Weinstein, O. (1997). Innovation in services. Research Policy, 26(4-5), 537-556.	783
Lakhani, K. R., & Von Hippel, E. (2004). How open source software works:“free” user-to-user assistance. In Produktentwicklung mit virtuellen Communities (pp. 303-339). Gabler Verlag.	753
Acs, Z. J., Anselin, L., & Varga, A. (2002). Patents and innovation counts as measures of regional production of new knowledge. Research Policy, 31(7), 1069-1085.	749
Stilgoe, J., Owen, R., & Macnaghten, P. (2013). Developing a framework for responsible innovation. Research policy, 42(9), 1568-1580.	745

Table 3. Links Between Framework, Key Bibliographic Papers and Symposium Insights

Framework Element	Key Bibliographic Papers	Symposium Insights
Inputs	Furman, Porter & Stern, 2002 Arora, 2019	Yaghmaie, & Maine, 2020 McQuarrie et al., 2020
Process- Innovation Policy	Arora, 2020 McAdam & Debackere, 2018	Stern, 2020 Dalziel, 2020
Process- Innovation Intermediaries	Etzkowitz & Zhou, 2018 D'Este & Patel, 2007	Rasmussen, 2020 Lubik, Treen & Gemino, 2020
Process- Entrepreneurial Strategy	Gans & Stern, 2003 Lauren & Salter, 2004	Arora, 2020 Gans et al., 2020
Outputs	Fini et al., 2018 Eesley & Miller, 2017	Park & Maine, 2020 Budd, 2020

Table 4. Key Recommendations for Invention to Innovation Stakeholders

Stakeholder	Key Recommendations
Scholars	• Explore the interplay between Innovation Policy, Entrepreneurial Strategy and Innovation Intermediaries • Study the causal relationships between inputs, mediators and outputs, with specifically defined variables • Further examine the selection and adaptation loop between science-based innovation and science-based invention
Innovation Policymakers	• Support universities to signal the quality of their spin-off ventures through research assessments, research evaluations and strategic IP • Invest in specialized entrepreneurial training for scientists
University Leadership	• Create frameworks to allow faculty and departments to benefit from entrepreneurship, e.g., allow entrepreneurship activities to serve as partial fulfillment of academic, teaching and service obligations • Create a well-defined policy on intellectual property rights that align incentives of researchers, the university and the innovation ecosystem • Separate academic and commercial activities within a research lab to avoid conflicts of interest and ambiguities around goals of each activity
Scientist-Entrepreneurs	• Recognize the path dependent nature of decisions made in the research lab • Exemplar market prioritization and IP strategy enable quick pivots of a venture to match emerging market needs • Develop entrepreneurial capabilities for principal investigators and their lab members

Table C1. Ten most published authors, number of papers and mean citations per paper

Author	Papers	Citations	Mean Citations
Porter, A	18	471	26.2
Youtie,J	13	438	33.7
Shapira, P	12	334	27.8
Guo, Y	10	319	31.9
Meissner, D	10	103	10.3
Watanabe, C	10	257	25.7
Franzoni, C	9	286	31.8
Grupp, H	8	403	50.4
Robinson, Douglas	8	281	35.1
Van Rijnsoever, F	8	354	44.3

Table C2. Ten most cited authors, number of citations and mean citations per paper

Author	Papers	Citations	Mean Citations
Etzkowitz, H	4	4584	1146.0
Leydesdorff, L	3	2947	982.3
Von Hippel, E	5	1798	359.6
Stern, S	2	1440	720.0
Nelson, R	4	1436	359.0
Veugelers, R	3	1355	451.7
Cooke, P	3	1299	433.0
Webster, A	4	1197	299.3
Lakhani, K	2	1174	587.0

Figures

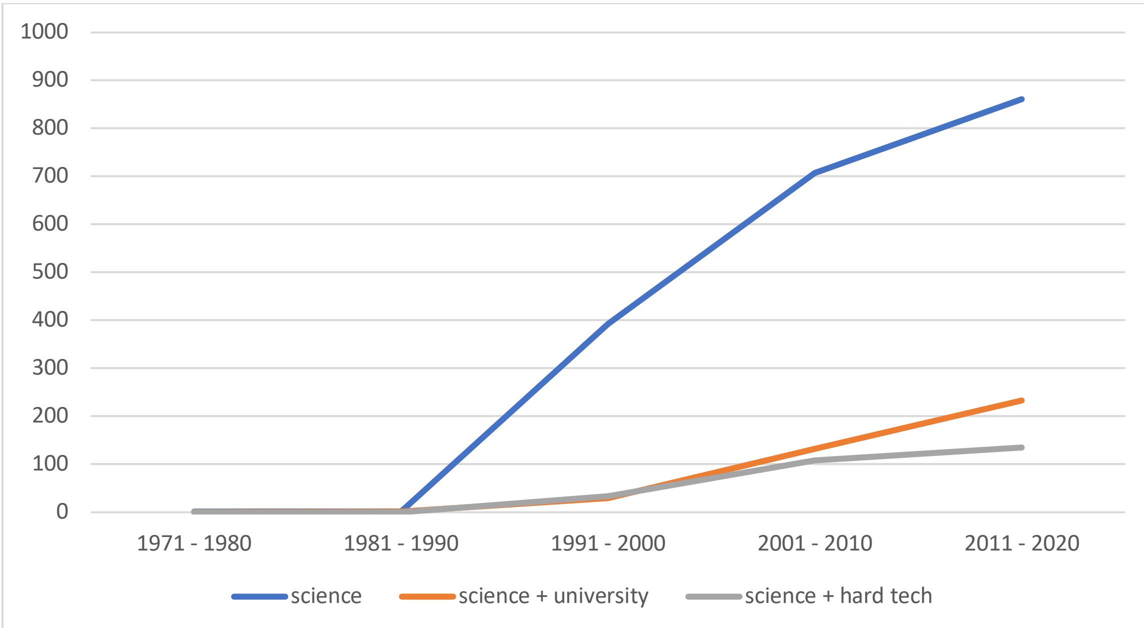

Figure 1a. **Trends in publications on innovation and science within TIM journals**

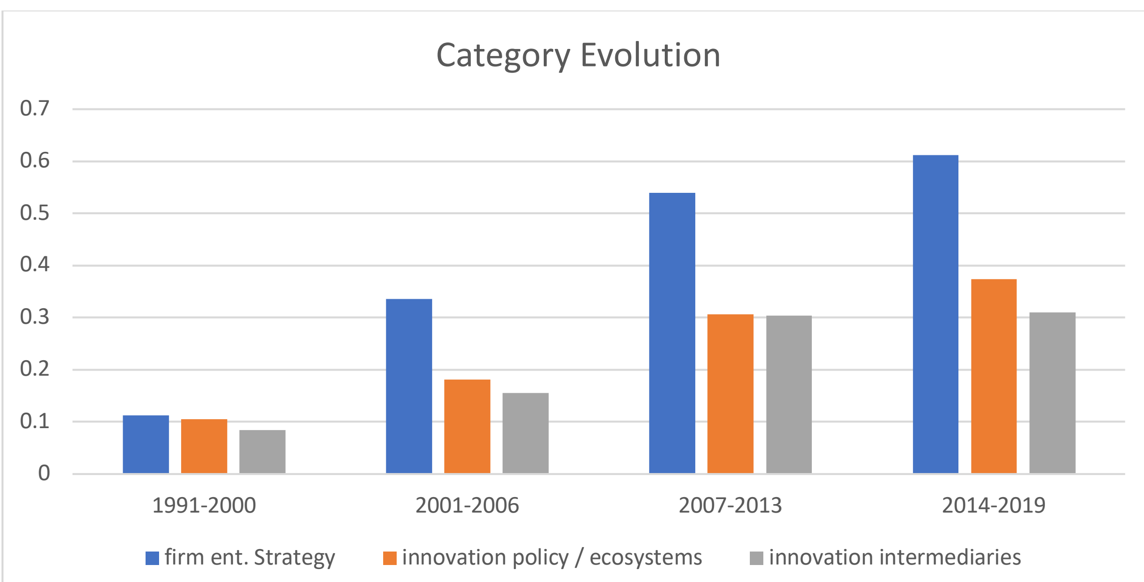

Figure 1b. **Publication activity in TIM journals related to science and innovation separated by Entrepreneurial Strategy, Innovation Policy and Innovation Intermediaries theme**

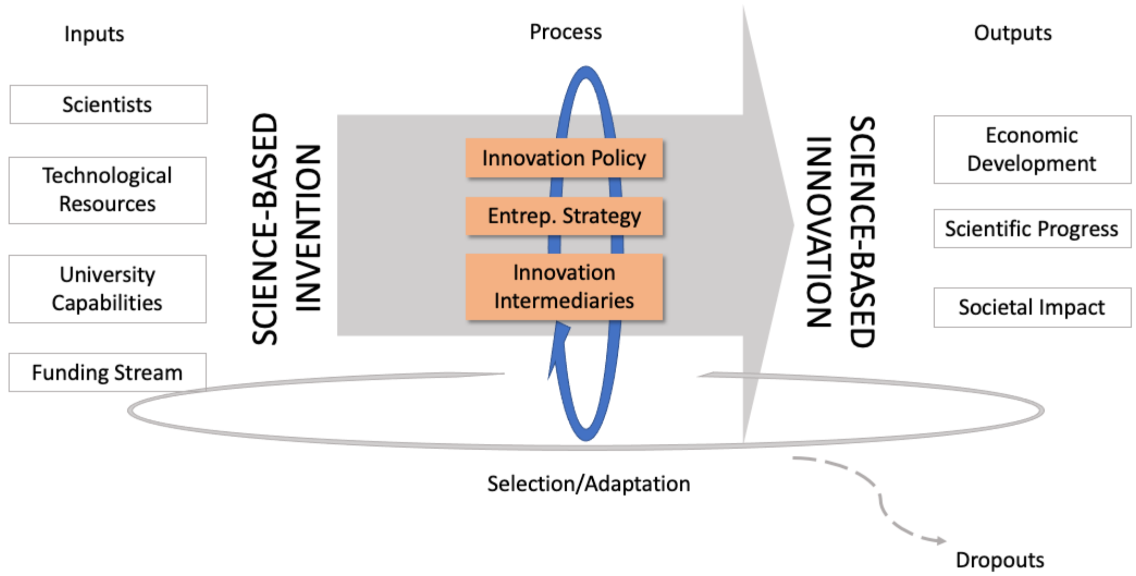

Figure 2. **An analytical framework of "science innovation"**

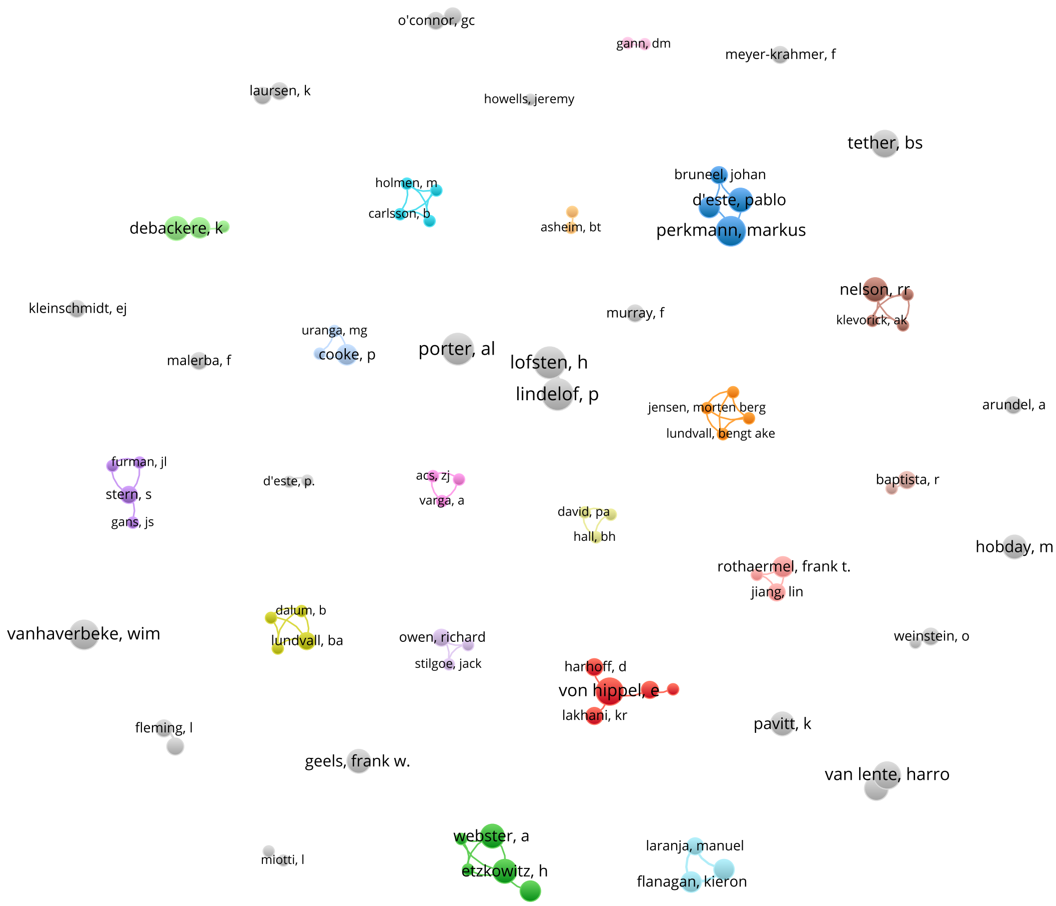

Figure C1. A map of co-authorship

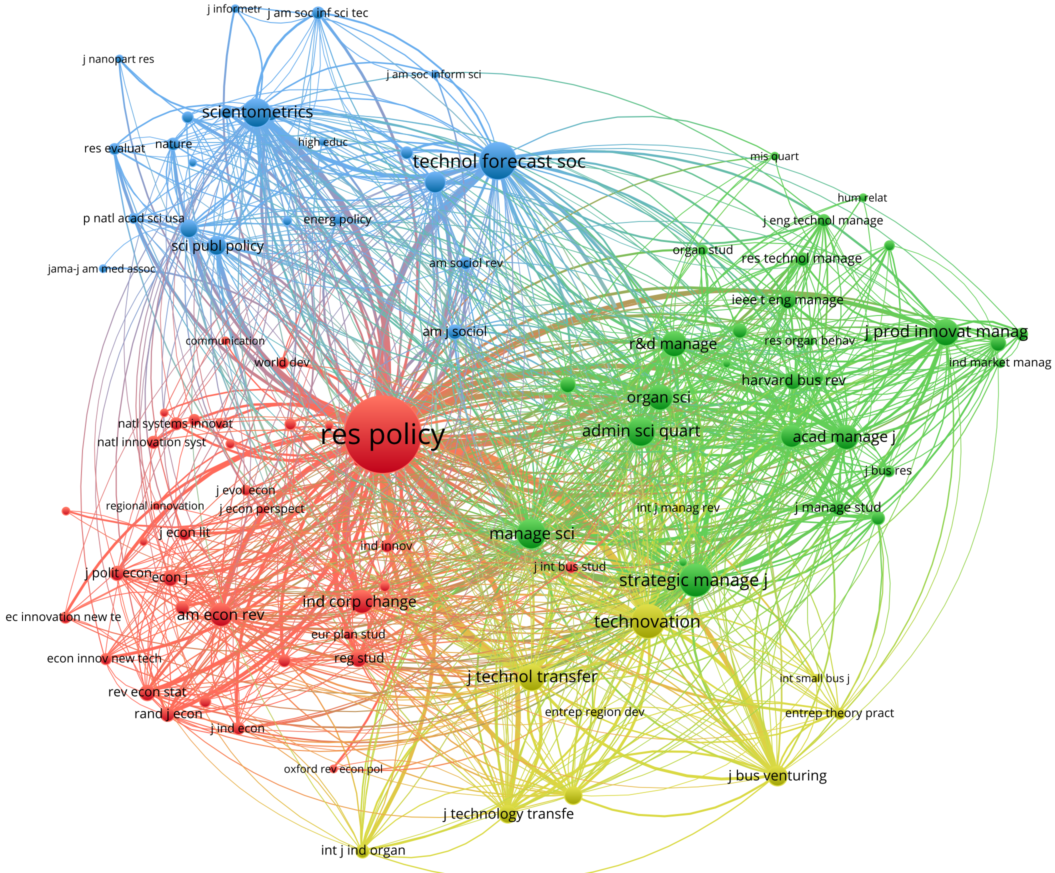

Figure C2. **A map of journal co-citation**

Essay 2:

Impact of Partnerships, Patenting and Uncertainty on Innovation Performance: Evidence from the Emergence of a Personalized Medicine Ecosystem

Andrew Park
Elicia Maine

Beedie School of Business
Simon Fraser University
500 Granville Street
Vancouver, British Columbia, Canada

Abstract

Personalized medicine is a rapidly growing subsector within medicine and biotechnology, revolutionizing medicine through customized approaches to patient care. We investigate how the management of uncertainty can influence the innovation performance of personalized medicine firms, which have been shown to operate under prolonged periods of technical and environmental uncertainty. To do this, we use a mixed methods approach and make three key contributions to the innovation management literature. First, we conduct the first comprehensive data-driven examination of the emergence of the personalized medicine industry, through the identification, classification and analysis of personalized medicine firms in British Columbia, Canada. Second, using this novel and custom dataset, we investigate the impact of the technical uncertainty of these firms on innovation performance. A multivariate regression model is estimated to assess the impacts of technical uncertainty on two types of firm innovation performance. We find that firms that engage in strategic partnerships, strategic timing of patents and those that develop products of high technical uncertainty exhibit greater innovation performance. Third, using case studies of exemplars in the British Columbia personalized medicine innovation ecosystem, we argue that alliances and early patenting were central to the elite innovation performance of these exemplars, and can serve as a replicable uncertainty management strategy for

prospective personalized medicine firms. A better understanding of the emergence of a rapidly growing personalized medicine innovation ecosystem, and the factors that influence innovation performance of firms within it, can enable researchers, scientist-entrepreneurs and innovation policy makers to create and capture value in this ecosystem, which is expected to create breakthrough scientific research and knowledge-economy jobs.

Keywords: Innovation Ecosystem; Science-based businesses; Personalized Medicine; Uncertainty; Innovation Performance

Introduction

Science-based firms, such as those operating within the biotechnology and life sciences sectors, have been shown to exist under prolonged periods of sustained uncertainty, leading to long commercialization times and high capital costs (Pisano, 2006; Pisano, 2010; Maine & Seegopaul, 2016). However, despite the fact that these science-based firms make disproportionately positive contributions to global health, social and economic challenges, little research has been conducted on how uncertainty facing these firms affects their innovation performance. This research gap is relevant and important because identifying the determinants of innovation performance for highly technical science-based ventures such as personalized medicine firms, which we focus on in our study, can inform both innovation policy and firm strategy. In this paper, we create a novel and custom dataset around firms that comprise an emerging personalized medicine innovation ecosystem to analyze the relationship between technical uncertainty and innovation performance. In addition, we explore the uncertainty management strategies that influence innovation performance of personalized medicine firms.

We choose personalized medicine as the context for our study. Personalized medicine is a rapidly growing subsector within medicine and biotechnology and has become a new subdomain of research due to its tremendous potential for improving the way medicine is delivered today (Knowles, Luth & Bubela, 2017; Cullis, 2015). We choose this sector due to the varying levels of technical uncertainty that firms within it face, which allows for effective empirical analyses on the role of uncertainty on innovation performance. Furthermore, a better understanding of innovation performance of the personalized medicine innovation ecosystem has implications for innovation policymakers and entrepreneurs who wish to leverage its rapid growth and potential for improving global health, social and economic outcomes. Our study on the emergence of this ecosystem, and the relationship between uncertainty and innovation performance among its firms, makes several key contributions: 1) it defines the role of uncertainty on innovation performance, providing avenues for future research on the effects of uncertainty in the innovation management literature, 2) it provides scientist-entrepreneurs strategies to manage this uncertainty and capture value in this novel ecosystem through strategic partnerships and 3) it helps policymakers to better understand the evolution of a rapidly growing science-based ecosystem and align their incentives programs to support their desired economic and social outcomes.

Our paper proceeds as follows. First, we provide an overview of personalized medicine and related ecosystem studies and review the management literature which have relevance to uncertainty, innovation performance and industry emergence. We then describe our methods in identifying personalized medicine firms and their relevant innovation performance metrics, along with our quantitative approach in analyzing the relationship between uncertainty and innovation performance. Next, we present the results of our multivariate regression model on the relationship between uncertainty and innovation performance. We follow this by presenting qualitative case studies of exemplars in the British Columbia personalized medicine innovation ecosystem to demonstrate the how effective uncertainty management can lead to improved innovation performance. Finally, we draw implications for scholars, innovation policymakers and scientist-entrepreneurs in the emerging personalized medicine industry.

Literature Review

In this section, we review the literature on science-based businesses and industry emergence, focusing on the high uncertainty science-based ventures face. Next, personalized medicine and its related technologies are briefly summarized. We were not able to find any previous industry emergence studies on the personalized medicine industry, thus several reports on the broader biotechnology industry were identified and are described. The importance of understanding the evolution of a novel ecosystem to determine the factors (namely, uncertainty) that influence the innovation performance among its firms is then highlighted. We conclude by reviewing the literature on strategic partnerships and timing of patents, and how it is related to uncertainty management and innovation performance.

Uncertainty and the emergence of science-based innovation ecosystems

Science-based businesses, such as those in the personalized medicine industry, face higher levels of technical uncertainty over long time frames (Thomas et al., 2020; Pisano, 2006; Pisano, 2010; Maine & Seegopaul, 2016). These firms, which are largely responsible for breakthrough technologies that make significant global health, social and economic improvements, typically operate under conditions of very high risk, due to the high capital costs and investments involved in commercializing their products and the long timelines required for R&D and regulatory approval. Even after significant investment with financial resources and human capital, many science-based firms, such as personalized medicine firms, are unsuccessful in releasing their products and services, and even if they are successful, they often find difficulty in gaining market traction. Little research has been conducted on how varying levels of uncertainty affects innovation performance by these firms, thus our research question becomes, "do strategic partnerships, timing of patents and the level of technical uncertainty of personalized medicine firms have influence on innovation performance outcomes?".

To answer this question, we build and curate a customized dataset of personalized medicine firms through an industry emergence lens. The emergence of an industry can be strategically observed through the entry of firms with specific capabilities. Innovation management scholars argue that firm entry and exit reveal the phases of industry emergence and the relative importance of product and process innovation at each phase (Utterback, 1994; Utterback & Abernathy, 1975). For the emergence of a science-based ecosystem, entry into the industry can be assessed through artifacts which document the acquisition of specific technological capabilities (Maine et al., 2014). Identifying, classifying, and analyzing firms with such technological capabilities yields insight on the relationship between competitive strategy, including uncertainty management, and innovation performance in a nascent innovation ecosystem (Maine et al., 2014; Utterback and Abernathy, 1975). In the following subsection we briefly summarize personalized medicine and identify related industry reports that inform our data collection process.

What is Personalized Medicine?

Personalized medicine is a growing field within the life sciences domain that aims to take a customized approach to a patient's health and well-being. It is mostly discussed in the context of treating ailments and diseases by looking at a patient's genomic, metabolomic or microbiomic profile and matching treatments accordingly. However, it can also be implemented effectively as a prophylactic or preventive measure, for example, by customizing a patient's diet based on their lifestyle and family history of disease. A personalized methodology to creating novel treatment pathways could lead to notable improvements in global health outcomes. This personalized approach has led to an uptick in global science-based firms dedicated to this particular subfield of medicine (Swan, 2009).

Relevant regional innovation ecosystem studies

There are two categories of related prior empirical studies related to personalized medicine or biotechnology that we attempted to identify: 1) regional empirical data on personalized medicine innovation ecosystems and 2) biotechnology innovation ecosystems in the jurisdiction we examine. The evaluation of regional systems of innovation related to personalized medicine is sparse. We were only able to identify short commentaries on the state of personalized medicine ecosystems in California (Alex et al., 2016; Governor's Precision Medicine Advisory Committee, 2018) and Europe (Stratified Medicine Scotland, 2016). To the best of our knowledge, our study is the first to provide an empirical and quantitative analysis of this emerging sector using an innovation management lens. To do this, we focus on the personalized medicine ecosystem in British Columbia, Canada and aim to identify all personalized medicine firms operating in this jurisdiction.

While there were no studies identified in the extant literature that specifically analyzed the personalized medicine ecosystem using this approach, its parent industry, the biotechnology sector, has been studied in British Columbia by groups such as LifeSciences BC (2015) and the Centre for Policy Research on Science and Technology (CPROST) at Simon Fraser University (Holbrook, 2003). Holbrook examines the British Columbia biotechnology cluster, presenting metrics including age of firms, number of university spinoffs, and growth in the number of firms.

Another notable study of the biotechnology and life sciences cluster in British Columbia was jointly conducted by PricewaterhouseCoopers and LifeSciences BC (2015). It is largely a quantitative study that provides a snapshot of current LifeSciences BC member firms, including a categorical breakdown of that list by capability, aggregate revenue and headcount estimates. A notable gap relevant to our research is that none of these studies investigated personalized medicine firms, nor investigated potential mechanisms at the firm level which may influence innovation performance. Thus, we determined that we needed to create our own dataset of British Columbia personalized medicine firms. We use these predicate studies as models to determine the relevant metrics we wish to observe, and to guide our data collection process.

Uncertainty management through strategic partnerships and strategic timing of patents

In addition to the research objective of determining the influence of uncertainty on innovation performance of personalized medicine firms, we wish to investigate the strategies that exemplars have used to manage this uncertainty and enhance innovation performance. Previous research has shown that the acquisition strategic partnerships can improve innovation performance at both firm and industry levels (Laursen & Salter, 2014; Alexy, Bascavusoglu-Moreau & Salter, 2016; Christensen, Olesen & Kjaer., 2005). One strategy that firms use to acquire downstream alliance partners is the strategic timing of patents. It has been shown that patents serve as effective signalling mechanisms of venture quality to potential partners and investors; attracting both partners and funding is critical to de-risking a highly uncertain venture (Chesbrough, 2020; Maine & Thomas, 2017; Hsu & Ziedonis, 2008).

The mechanism of strategic partnerships in aiding innovation performance is likely explained by the fact that firms operating in highly uncertain environments require access to complementary assets that are generally unavailable to the emerging start-up. Prior research has shown that new firms with novel technologies can benefit from the complementary assets owned by incumbents and other related firms in their local ecosystems, including those with scientific capabilities (e.g., Hagedoorn, 1993) and sales and marketing channels (Rothaermel, 2001). In the case of biotechnology, start-ups working on drug discovery likely do not have the deep regulatory expertise and distribution networks to optimally commercialize their products after the R&D stage and often require strategic alliances for clinical trials, regulatory assistance and market launch (Niosi, 2003; Baum & Silverman, 2004).

Personalized medicine firms, which represent a subset of biotechnology (Milne, Cohen & Chakravarty, 2015; Allison, 2008; Zuckerman & Milne, 2012), face similar levels of high uncertainty and are strong cases to observe when determining the influence of strategic partnerships and uncertainty on innovation performance. In this paper, we supplement our quantitative analysis with case studies from two personalized medicine firms who leveraged strategic partnerships and strategic timing of patents to manage uncertainty.

Methodology

In this section, we describe the data sources used to identify, categorize and analyze the performance of the firms that underpin the British Columbia personalized medicine innovation ecosystem. A customized dataset of these firms was built as no such dataset was in existence. To the best of our knowledge, our study is the first in the innovation management literature to profile the emergence of this sector. We wish to empirically test the relationship between uncertainty and innovation performance of personalized firms and so we explain our choice of the salient variables and controlling factors in our dataset. We conclude by describing the analysis methods used to investigate the relationship between the level of technical uncertainty of personalized medicine firms and innovation performance.

Personalized Medicine firm sample

Firms are the most meaningful level of analysis when investigating industry emergence (Utterback, 1994). In order to create a dataset around the emergence of personalized medicine in British Columbia, we began with several databases, including S&P Capital IQ, LifeSciences BC (formerly BC Biotech) Press Releases, ReadyToRocket, University of British Columbia (UBC) Industry Liaison Office, Simon Fraser University (SFU) Spin-Off Companies List, LifeSciences BC Membership List, CPROST, and the BC Sciences Cluster Directory. The LifeSciences BC Press Releases archive was the most comprehensive data set available, and included data from January 2004, so we used this ass a historical cut-off. We reviewed each life science, biotechnology, pharmaceutical and digital health company in each of these databases to assess their capabilities in personalized medicine. We then cross verified this list by searching the USPTO database for assignees in the following major British Columbia cities, “Vancouver”, “Kelowna”, “Victoria”, “Burnaby”, “Surrey”, “Richmond”.

We reviewed the capabilities sections of each identified company’s website or press releases and included them in our list if they developed or were developing treatments that were customized to a component of a patient’s health profile. The keywords used to identify if the company had personalized medicine capabilities is presented in Appendix A. We verified the timing of development of personalized medicine capabilities for each firm through web searches, press releases, publications and patents. For each firm we also collected the following data: revenue, age, operational status, headcount, technical capabilities summary, level of technical uncertainty, spinout status, financing raised, number of strategic partners list of granted and in-review patents.

To create a visual representation of the emergence of the personalized medicine innovation ecosystem, we track the timing of entry and exit of firms with the technological capabilities described in the following subsection. To track firm exit, we categorized each firm as “active” or “defunct”. For each firm, if they were still listed as an active business on Google at the time of data collection and appeared to have a regularly updated website, we included them in the “active” category. If there was a press release that a firm was out of business, listed as inactive on Google, or there was no website, we included them in the “defunct” category.

Variables of the analysis

The main exposure variable in this study was derived from categorizing each firm in our dataset by their technical capability. We utilize two innovation performance outcomes based on existing literature that a firm may experience from the exposure measure: *value output* and *firm size*. Value output is based on the frequently used sales-related proxy for innovation performance seen in previous innovation management empirical research (Gunday, 2011; Jung, 2016; Ferreira, 2017). We operationalize value output by normalizing revenue by the age of the firm, as performed by Maine, Lubik & Garnsey (2012). Firm size is another innovation performance outcome measure, separate from value output, that is operationalized by the number of employees. It has been used in prior research as an indicator of the effectiveness of innovation strategies, as shown by an increase in the number of qualified workers (Yigitcanlar, 2018; Gunday, 2011). We provide further details on how these variables were derived and operationalized in the following subsections. In addition to the exposure and outcome variables, we collected data on patenting and partnerships and used them as controlling factors while measuring the influence of uncertainty on innovation performance.

Independent variable: uncertainty

We categorized the personalized medicine firm sample into “therapeutics”, “diagnostics”, “medical device” or “digital health” companies. Therapeutics companies are pharmaceutical companies or in some cases, medical device companies, who are developing drug-based treatments for disease. Diagnostic companies provide point of care, “omics” testing, or laboratory tests or supplies for determining disease state, disease progression or a patient’s state of health. Medical device companies develop implantable or external physical devices to treat disease. Digital health companies provide software or mobile solutions for housing or manipulating patient data, or diagnostic services using digital sensors embedded in consumer hardware. Table 1 provides examples of firms categorized in each of these subsectors. For the purposes of our multivariate regression model, we created an ordinal variable, *Uncertainty*, with therapeutics firms exhibiting high uncertainty based on work conducted by Maine & Seegopaul (2016) (assigned a value of 1) and diagnostics, digital health and medical device exhibiting lower uncertainty (assigned values of 2, 3 and 4 respectively).

Dependent variables: innovation performance

Firm revenue is representative of innovation performance through value capture, which is defined as the importance of a firm’s technology to customers as demonstrated through sales (Maine, Lubik & Garnsey, 2012). Value capture metrics such as revenue are important indicators of firm impact on an innovation ecosystem and allow us to compare a firm’s influence against others. Our key dependent variable is *value output (VO)*, which we derive from revenue data for each firm for the year preceding the year of data. We then normalize this revenue data by dividing revenue by the age of the firm. We include an additional outcome variable drawing from previous innovation management research: *firm size (FS)*, which is operationalized by the number of employees in the firm (Yigitcanlar et al., 2018).

Controlling factors: strategic partnerships and strategic timing of patents

In addition to collecting the exposure and outcome data for our regression model, we collected contextual data surrounding strategic partnerships and used this metric as a controlling factor while analyzing the influence of uncertainty on innovation performance. We operationalized strategic partnerships through a *normalized partnerships (Partn)* variable (defined as the number of strategic partnerships divided by firm age). Research has shown the acquisition of strategic partners can lead to downstream effects on commercial success (Zobel, Balsmeier & Chesbrough, 2016; Niosi, 2003; Baum & Silverman, 2014), thus we use this variable as a controlling factor, given their likely autonomous effect on innovation performance. The number of strategic partnerships was sourced for each firm from S&P Capital IQ and by reviewing archives of company press releases.

We test a second, binary controlling factor in our regression model, *strategic timing of patents (ST)* (i.e., whether the personalized medicine firm had a granted patent filed within five years of firm formation) based on previous work by Maine & Thomas (2017). Firms operating in conditions of high technical and market uncertainty use early patenting as signaling mechanisms to attract alliance partners (Hsu & Ziedonis, 2008; Maine & Thomas, 2017). Thus, because of its role as an early, signaling strategy to reduce uncertainty through funding and downstream alliances, we include this variable as another controlling factor given its likely autonomous effect on innovation performance.

To include this variable, we gathered the number of personalized medicine patents from each firm using a stepwise process. We first searched Google Patents using the firm's name as the assignee and the same list of keywords in the previous section in the body text and title search fields, then cross verified the results against the USPTO database. We reviewed the titles and abstracts of each patent to verify they were indeed related to personalized medicine. The verification was conducted by using our academic knowledge of biotechnology and personalized medicine. For example, ICO Therapeutics' patent on dosing regimens describes methods to customize doses based on a patient's specific response to the drug being administered, which is a strong example of personalized treatment (ICO Therapeutics Inc., 2010). The filing date of granted patents from the USPTO was captured and compared to firm entry date.

Analysis Techniques

The aims of this research are to create a dataset around the emergence of the personalized medicine innovation ecosystem and use that dataset to analyze firm innovation performance outcomes. We exclude defunct firms from our total sample of 94 firms, leading to 63 active firms for our analysis. We do this to remove biases from very old firms, or firms that had minimal or short-lived operations. Given that our study estimates a single regression model with more than one dependent variable, and we include controlling variables (*Partn* and *ST*) alongside our exposure variable (*uncertainty*), we conduct a multivariate multiple regression of active firms (n = 63) to test the relationship between uncertainty and innovation performance (operationalized by *VO* and *FS*).

To prepare the data for a multivariate analysis, the continuous variables, *VO*, *FS* and *Partn* are first checked for normality, and it is observed that all three are skewed and leptokurtic (Changyong et al., 2014). To improve normality, natural log transformations (*ln(VO), ln(FS), ln(Partn)*) are conducted on each of these variables. Table 2 shows the results of the data transformation; skewness and kurtosis are both lowered to controllable levels.

In multivariate regression models, the outcome variables should be at least moderately correlated. As a result, a correlation analysis was conducted first to examine the level of associations between the variables in our study. Table 3 shows that the two outcome variables (*ln(FS)* and *ln(VO)*) are correlated with each other.

Results

In this section we present an overview of the emerging British Columbia personalized medicine industry ecosystem, including growth patterns and descriptive statistics of the salient variables in our analysis. We then present the results of our multivariate regression and elucidate the links between uncertainty and innovation performance for personalized medicine firms.

Descriptive analysis of the emerging personalized medicine innovation ecosystem

By identifying, categorizing and investigating the 94 firms (63 currently active) whose focus is on personalized medicine or have a product related to personalized medicine, we observe the emergence of the personalized medicine innovation ecosystem in British Columbia (Figure 1). The resultant dataset around the emergence of these firms is used to generate the results of our regression model, which we review in the following subsection. A brief description of the historical emergence of this ecosystem is provided in Appendix A.

In terms of the independent variable, uncertainty, of the 94 firms, 50 were in the “therapeutics”, or *high uncertainty*, category, 24 were in “diagnostics”, and 13 were in “digital health” and 7 were in “medical device”, which comprise the *lower uncertainty* categories. Related to one of our controlling variables, *strategic timing of patents*, the majority of our personalized medicine firm sample had filed at least one personalized medicine patent: relevant patent filings were identified for 56 of the 94 firms. Related to our key outcome variable, *value output*, and our other controlling factor, *strategic partnerships*, out of the 63 active firms in our sample, 55 firms reported revenue and 60 firms reported more than one strategic partner.

Innovation performance by personalized medicine firms

Table 4 outlines the results obtained from the multivariate regression model. In this model, and in the correlation matrix in Table 3, there is a negative association between the *Uncertainty* ordinal variable and both innovation performance measures, with the correlation between *Uncertainty* and *ln(FS)* being significant. Given this loose association, this suggests that although high uncertainty therapeutics firms may in some way contribute to greater innovation performance, its precise role and influence on the relationship between innovation strategies such as a strategic partnering and strategic timing and innovation performance must be more deeply examined, for example, through case studies (which we conduct in this paper), or through a moderator analysis (an avenue for future research).

With respect to the effects of our controlling factor, *ln(ST)*, we see a significant association with value output (but not firm size), suggesting early patenting has an influence on innovation performance, which makes sense intuitively, given the incentive for firms that develop products of high sophistication to seek intellectual property protection. For our other controlling factor, *ln(Partn)*, we see a significant and positive association with our key outcome variable, *ln(VO)* but not for our secondary outcome variable, *ln(FS)*. This reveals an interesting finding in that the acquisition of strategic partners has a controlling effect on the relationship between firm uncertainty and firm innovation performance (specifically as it relates to firm value capture). In the following section, we more deeply explore the role *strategic partnerships* play in managing uncertainty through case studies of two exemplars in the British Columbia personalized medicine innovation ecosystem.

Discussion

In this section, we discuss our findings in the context of extant literature and elucidate how uncertainty influences innovation performance in the personalized medicine innovation ecosystem. Additionally, using two case studies of exemplars within our context, we examine how strategic partnerships allowed these exemplars to manage uncertainty and capture significant value from this emergent ecosystem.

Uncertainty as an influencer of innovation performance

While it is generally accepted that science-based businesses, particularly those in biotechnology and its related subsectors such as personalized medicine, operate under conditions of high uncertainty (Pisano 2006; Maine et al., 2014; Maine & Seegopaul, 2016), little research has been conducted on investigating the relationship between levels of uncertainty and innovation performance of these firms. We choose the personalized medicine industry as our context because of its emergence as a high potential sector to improve global social and economic outcomes, and because of the significantly varying levels of uncertainty among its firms, which serves as an ideal experiment to evaluate potential differences in innovation performance due to uncertainty. As no predicate studies or datasets existed on this emergent ecosystem, we created a novel and custom dataset of personalized medicine firms in British Columbia, using an industry emergence lens, which focuses on the firm as the unit of analysis (Utterback, 1994; Utterback & Abernathy, 1975).

We show that personalized medicine firms in British Columba that develop products of high technical uncertainty exhibit a loose connection to enhanced innovation performance. While this may initially appear counterintuitive, it has been noted that science-based ventures, while they face initial hurdles in survival and regulatory approval, once commercialized, have the potential to provide dramatically positive impacts to regional and global innovation ecosystems, through increased economic productivity and improved social and health outcomes (Niosi 2011; Pisano 2003; Pisano, 2006).

We also find support for the influence of *strategic timing of patents* on innovation performance. This is consistent with previous research that finds a positive influence of patenting on innovation outcomes (Hsu & Ziedonis, 2008; Park, Borah & Kotha, 2016; Zobel, Balsmeier & Chesbrough, 2016). Innovation scholars who have conducted work on patenting have noted the conceptual value of patenting as signaling or licensing mechanisms (Pierrard & Lavallee, 2019; Chesbrough, 2020) and have also tested their value explicitly through empirical work (Bjornali et al., 2017; Zobel, Balsmeier & Chesbrough, 2016).

We also observe that *strategic partnerships* are a controlling factor in our model. The influence of strategic partnering may be due to the fact that for highly uncertainty firms, such as those with personalized medicine capabilities, downstream alliance partners with capabilities related to financing, manufacturing, sales and marketing and distribution may improve their chances of commercialization success (Baum & Silverman, 2004; Chesbrough, 2003; Lahr & Mina, 2016; Niosi, 2003). From case studies we will present in this section, we suggest there may be a potential moderating effect of uncertainty and specific innovation strategies and innovation performance. That is, based on insights from our case studies, personalized medicine firms that operate under high technical uncertainty may actively engage in more alliances to improve innovation performance. A follow up study confirming and extending this interaction effect may be useful to better understand the mechanisms and effects of *Uncertainty* on the relationship between certain innovation strategies and innovation performance.

Based on our results, specifically for the role of strategic partnerships and strategic timing play in innovation performance, we suggest that science-based firms that operate under conditions of high uncertainty and those that engage in alliances and early patenting are more likely to create significant economic value if the resultant value of these capabilities is effectively appropriated. This finding is likely transferrable to firms operating in other science-based sectors such as quantum computing, artificial intelligence and advanced materials, potentially extending the external validity of our findings to other industries of high technical uncertainty. While we find evidence of the influence of strategic partnerships, strategic timing and uncertainty on innovation performance of personalized medicine firms, it is unclear what specific innovation management strategies highly uncertain firms employ to improve innovation performance. We investigate this further using cases of two exemplars in the British Columbia personalized medicine innovation ecosystem in the next subsection.

Innovation performance through the management of uncertainty

Numerous innovation scholars have noted the importance of strategic partnerships for emergent science-based firms, who may have breakthrough inventions but require downstream complementary assets to acquire regulatory approval and successfully commercialize their product or service (Laursen & Salter, 2014; Alexy, Bascavusoglu-Moreau & Salter, 2016; Christensen, Olesen & Kjaer., 2005). A key strategy firms use to attract partners with these complementary assets is signalling the quality of their capabilities through early patenting (Chesbrough, 2020; Maine & Thomas, 2017; Hsu & Ziedonis, 2008). Alliance partnerships are particularly relevant to our study given the fact that the personalized medicine innovation ecosystem is characterized almost exclusively by emergent science-based firms facing uncertain technical and market challenges. Two of arguably the most successful firms in the British Columbia personalized medicine innovation ecosystem, AbCellera and Zymeworks, display evidence of strategic partnerships, and we conduct a brief examination of their emergence in the following subsections. We choose these firms to conduct our case studies as they are both recent examples of high value creation firms (i.e., they are both high value creators and both had one of the largest Canadian biotechnology IPOs in history) that managed uncertainty through novel partnership strategies. These two examples support our quantitative analysis linking uncertainty and innovation performance with a case-based analysis of how a high uncertainty firm may produce high innovation performance.

AbCellera

AbCellera is an antibody solutions company founded by Dr. Carl Hansen, a former professor at the University of British Columbia (UBC). While he was trained as a physicist during his undergraduate studies at UBC, he saw the value in interdisciplinary research and pursued his PhD in microfluidics at the California Institute of Technology. After returning to UBC to join the Department of Physics and Astronomy, he continued his interdisciplinary microfluidics research and eventually gained interest in the antibody market.

AbCellera was founded in 2012, with the premise of being an end-to-end antibody solutions company. Since inception, Hansen prioritized AbCellera's services around helping other pharmaceutical and biotechnology partners to more effectively identify antibody candidates for their therapeutics and indications of interest (AbCellera Biologics Inc., 2020), indicating that Hansen has long recognized the value of early strategic partnerships. Furthermore, we see evidence of strategic timing of patents, which as previously discussed, serves as signalling mechanisms to potential alliance partners, in that AbCellera's key microfluidics patent was filed *before* firm formation. While the traditional method of drug discovery centered around wet lab research, AbCellera gained a competitive advantage in attracting alliance partners by integrating an artificial intelligence-backed computational platform, called Celium, to run *in silico* experiments. This platform allows AbCellera to, "accelerate wet lab experimentation … in a continuously iterative process … (to) find real molecules that have been optimized by nature" (AbCellera Biologics Inc., 2020).

By simulating traditional wet lab experiments computationally, AbCellera is able to lower costs and shorten drug discovery timelines for its pharmaceutical partners. As AbCellera forges partnerships with more pharmaceutical companies, data generated from their partnerships is continually fed back into Celium, improving its efficiency and accuracy, with then makes AbCellera's services even more compelling for other pharmaceutical companies. Alliance partners are critical to AbCellera not only in mitigating its high uncertainty environment (through continuous milestone payments from its partners) but also in continuing to improve its antibody discovery platform.

The competitive advantage derived from strategic partnerships has contributed to the company's rapid growth and recent capturing of headlines, as seen in its 119 partnership programs to date (AbCellera, 2021), its completion of the largest IPO in Canadian biotechnology history (Silcoff, 2020) and its co-development of the first FDA approved neutralizing antibody therapeutic for COVID-19, with its strategic partner, Eli Lilly.

AbCellera continues to strive towards integrating new capabilities, as seen in its ambitions in become a large scale, GMP antibody manufacturing company while continuing to build out its existing antibody discovery platform. The continual revenues generated from its strategic partnerships has allowed the firm to manage the uncertainty surrounding their long time to commercialization and capital intensive GMP manufacturing goals. Even with this manufacturing capability within its sights, AbCellera continues to recognize the importance of strategic partnerships. It has declared that the GMP manufacturing capability will be additive to its antibody discovery platform and together, they will be able to serve their pharmaceutical partners even more effectively, through a full end-to-end antibody platform solution.

Zymeworks

Zymeworks is a protein therapeutics company focusing on treatments for cancer, as well as for autoimmune diseases. It was founded by Dr. Ali Tehrani, who received his PhD in Microbiology and Immunology at UBC. Alternative pharmaceutical business models, predicated on being a strategic partner to other pharmaceutical companies, was of interest to Tehrani, even while he was still a graduate student at UBC (McCullough, 2016). He recognized early in his studies that the traditional drug discovery process was myopically focused on producing a single blockbuster drug, which was an inordinately risky proposition. Instead, he envisioned building a technology platform company to support drug development and help other biotechnology and pharmaceutical companies with their drug development processes.

He hypothesized that running computer simulations to model protein molecules and mimic their interactions with other molecules would add value to the traditional drug discovery process, which traditionally relies on the expensive and time consuming wet-lab process of trying millions of combinations of molecules and “fishing” for a serendipitous interaction. Tehrani recruited a software developer to build Zymeworks’ computational platform (the first evidence of a strategic partnership based on a complementary need for software engineering know-how) and raised the company’s first angel investment in 2001, based on the premise that, by becoming a drug development partner to other firms instead of trying to discover a blockbuster molecule themselves, Zymeworks would be able to dramatically reduce the uncertainty associated with the traditional drug development process, while also participating in the upside of a blockbuster drug discovery. Similar to AbCellera, we see Zymeworks engaging in strategic timing of patents, in particular their suite of early patents related to their core molecular modeling capabilities, which as previously discussed, signals venture quality to potential partners.

We observe numerous subsequent strategic partnership events, which ultimately allowed Zymeworks to continue to reduce uncertainty around its long-term success through shorter term milestone-based payments. Zymeworks attracted numerous big-name pharmaceutical and biotechnology partners to co-develop therapeutics, including Merck, Celgene, Eli Lilly and GlaxoSmithKline, all of whom utilize the company's computational platform to build novel oncology therapeutics for its disease targets (Zymeworks Inc., 2021). In turn, the data generated from each subsequent partnership program helps improve Zymeworks' computational platform, which then makes the platform more compelling for other potential partners. In 2014, Zymeworks placed in the top ten health technology companies in terms of financing raised and in 2017 the company completed the largest Canadian biotechnology IPO in over a decade (Silcoff, 2017).

Similar to AbCellera, Zymeworks has benefited from its strategic partnership-based uncertainty management strategy by now being able to turn its attention to a much more ambitious target: to develop and commercialize its own oncology therapeutics. While Zymeworks' partnership-based contract research model, backed by the competitive advantage derived from its computational engine, was instrumental in de-risking the company's long-term prospects, it has now created its own drug pipeline, which includes two leading breast cancer drug candidates. While developing its own therapeutics is much more capital intensive, if successful, these therapeutics could further accelerate Zymeworks' commercial expansion and innovation performance.

Implications for policy and practice

Our study has implications for managers of science-based firms operating under conditions of high uncertainty. In consideration of our finding that strategic timing of patents has a relationship with firm value capture, personalized medicine firm founders working in highly uncertain technologies and markets can consider early patenting, not only to protect their intellectual property, but to signal venture quality to potential alliance and downstream value chain partners. As seen in our analysis of the importance of strategic partnerships in managing uncertainty to improve innovation performance, firm founders can de-risk their larger therapeutics ambitions through partnership projects that generate short term revenue; ideally these projects will be configured in a way that will successively build towards their longer timeline, capital intensive projects. This stepwise uncertainty mitigation strategy has been explored previously through a real options approach. In this approach, firms use choice as a strategic asset, where they defer having to decide on making a large investment (such as a drug discovery project) but still retain the future right to make the investment (McGrath, 2004). Using real options, firms can configure their investment decisions so that they do not immediately make large resource outlays for high potential projects but make small investments in the short term to preserve access to future opportunities (McGrath, 2003).

Innovation policymakers can also support the growth of the personalized medicine innovation ecosystem based on the findings from our study. Given the noted association between strategic timing of patents and innovation performance, policymakers are encouraged to carefully evaluate and weigh the benefits of patent protection to value capture, against other scholarly arguments for an open science model. Some of these arguments (e.g., Williams 2013; Edwards, 2016; Gold, 2019; Gold, 2021) suggest there are benefits to open data sharing in facilitating collaborative networks and reference the success of the Structural Genomics Consortium in accelerating genomics research. Policymakers can investigate of both sides of this argument and shape intellectual property and university technology licensing office policies accordingly. Furthermore, given the importance and high potential of personalized medicine firms working in highly uncertain domains, innovation policymakers can structure their funding regimes to help manage this uncertainty, with a carefully designed mix of hiring, grant funding and tax credit support.

Conclusion

The advent of personalized medicine has not only been a paradigm shift in medicine, but it has also spurred new venture formation within and outside the traditional biotechnology industry. Although there is a growing interest in studying the innovation ecosystem potential of personalized medicine, whose firms are characterized by high technical uncertainty, little relevant empirical data and analysis currently exists investigating the relationship between uncertainty and innovation performance. Through a carefully curated and analyzed dataset of the British Columbia personalized medicine innovation ecosystem, we offer insight into the emergence of this science-based innovation ecosystem and the role of uncertainty on innovation performance of the firms within it.

We find evidence of the influence of strategic partnerships, strategic timing and technical uncertainty on innovation performance by personalized medicine firms. This phenomenon may be explained by the fact that although firms that face high uncertainty may have initial difficulty in commercializing their products, once commercialized, their breakthrough capabilities may be more likely to create significant social and economic value. Interestingly, our study shows that even within the personalized medicine ecosystem, which is generally characterized as exhibiting high uncertainty, the varying levels of uncertainty within its firms produces heterogenous effects on innovation performance.

In addition to elucidating the influence of partnerships, patenting, uncertainty on innovation performance in the personalized medicine ecosystem, we investigate two exemplars within the jurisdiction of our context, Zymeworks and AbCellera and examine the uncertainty management strategies they employed to become high innovation performers. We find that strategic partnerships and timing of patents were significant contributors to their innovation performance, and similar strategies in utilizing alliance partnerships may be beneficial to prospective personalized medicine firms. We also provide implications for innovation policymakers and practitioners who wish to participate in, and effectively support the growth of this emergent ecosystem.

The growth of the personalized medicine innovation ecosystem has significant potential for improved social and economic outcomes. Personalized medicine could be the advent of a new paradigm of targeted patient care. During the global pandemic of COVID-19, personalized medicine firms such as AbCellera were central to vaccine and therapeutics solutions. Companies such as Zymeworks, another company that utilized strategic partnerships to navigate its uncertain environment, are expected to play a significant role in accelerating oncology related therapies. The emergence of a regional personalized medicine innovation ecosystem can lead to improved health and social outcomes, more technology-based jobs, infusions of capital, and heightened interest from researchers and industry practitioners regionally and globally.

References

AbCellera Biologics Inc. (2020). 2020 Form S-1. Retrieved from https://www.sec.gov/Archives/edgar/data/1703057/000119312520299507/d29983ds1.htm

AbCellera. (2021). AbCellera Reports Q1 2021 Business Results. Retrieved from https://www.abcellera.com/news/abcellera-reports-q1-2021-business-results

Alex, K., Park, L., Baca, E., …Grieshammer, U. (2016). *Report to the State of California Legislature*. The Governor's Office of Planning and Research.

Alexy, O., Bascavusoglu-Moreau, E. & Salter A. J. (2016). Toward an aspiration-level theory of open innovation. *Industrial and Corporate Change*, 25(2), 289–306.

Alexy, O., George, G., & Salter, A. J. (2013). Cui bono? The selective revealing of knowledge and its implications for innovative activity. *Academy of Management Review*, *38*(2), 270-291.

Allison, M. (2008). Is personalized medicine finally arriving?. *Nature Biotechnology*, *26*(5), 509-517.

Baum, J. A., & Silverman, B. S. (2004). Picking winners or building them? Alliance, intellectual, and human capital as selection criteria in venture financing and performance of biotechnology startups. *Journal of Business Venturing*, *19*(3), 411-436.

Bjornali, E. S., Giones, F., & Billstrom, A. (2017). Reveal or conceal? Signaling strategies for building legitimacy in cleantech firms. *Sustainability*, 9(10), 1815.

Changyong, F. E. N. G., Hongyue, W. A. N. G., Naiji, L. U., Tian, C. H. E. N., Hua, H. E., & Ying, L. U. (2014). Log-transformation and its implications for data analysis. *Shanghai Archives of Psychiatry*, *26*(2), 105.

Chesbrough, H. W. (2003). *Open innovation: The new imperative for creating and profiting from technology*. Harvard Business Press.

Chesbrough, H. (2020). Innovation Imperatives from Covid-19. Forbes. Retrieved from https://www.forbes.com/sites/henrychesbrough/2020/03/18/innovation-imperatives-from-covid-19/?sh=32e20d6d6fb1

Christensen, J., Olesen M. & Kjaer J. (2005). The industrial dynamics of open innovation – evidence from the transformation of consumer electronics. *Research Policy*, 34, 1533–1549

Cullis, P. (2015). *Personalized Medicine Revolution* (pp. 1-161). Vancouver/Berkeley: Greystone Books.

Edwards, A. (2016). Perspective: Science is still too closed. *Nature*, *533*(7602), S70.

Ferreira, J. J., Fernandes, C. I., & Raposo, M. L. (2017). The effects of location on firm innovation capacity. *Journal of the Knowledge Economy*, *8*(1), 77-96.

Gold, E. R. (2021). The fall of the innovation empire and its possible rise through open science. *Research Policy*, *50*(5), 104226.

Gold, R. (2019). Should Universities Get Out of the Patent Business? *Centre for International Governance Innovation*. Retrieved from https://www.cigionline.org/articles/should-universities-get-out-patent-business

Governor's Precision Medicine Advisory Committee. (2018). *California Initiative to Advance Precision Medicine*. Retrieved from https://www.eventbrite.com/e/governors-precision-medicine-advisory-committee-public-session-registration-47454423458

Gunday, G., Ulusoy, G., Kilic, K., & Alpkan, L. (2011). Effects of innovation types on firm performance. *International Journal of Production Economics*, *133*(2), 662-676.

Hagedoorn, J. (1993). Understanding the rationale of strategic technology partnering: Interorganizational modes of cooperation and sectoral differences. *Strategic Management Journal*, *14*(5), 371-385.

Holbrook, J.A. (2003). *The Vancouver biotechnology cluster*. Centre for Policy Research on Science and Technology, Simon Fraser University.

Hsu, D. H., & Ziedonis, R. H. (2008, August). Patents as quality signals for entrepreneurial ventures. In *Academy of Management Proceedings* (Vol. 2008, No. 1, pp. 1-6). Briarcliff Manor, NY 10510: Academy of Management.

ICO Therapeutics Inc., (2010). Dosing regimens for treating and preventing ocular disorders using c-raf antisense. ICO Therapeutics.

Jung, D., Kim, Y., Suh, Y., & Kim, Y. (2016). Perceived innovation barriers and open innovation performance: insights from Korea. *International Journal of Knowledge-Based Development*, *7*(2), 125-142.

Knowles, L., Luth, W., & Bubela, T. (2017). Paving the road to personalized medicine: recommendations on regulatory, intellectual property and reimbursement challenges. *Journal of Law and the Biosciences*, *4*(3), 453-506.

Lahr, H., & Mina, A. (2016). Venture capital investments and the technological performance of portfolio firms. *Research Policy*, 45(1), 303-318.

Laursen, K., & Salter A. (2014). The paradox of openness: appropriability, external search and collaboration. *Research Policy*, 43(5), 867–878.

LifeSciences British Columbia & PricewaterhouseCoopers. (2015). *The life sciences sector in BC: economic impact now and in the future*. LifeSciences British Columbia. Retrieved from http://lifesciencesbc.ca/wp-content/uploads/2015/06/LifeSciences-BC-Sector-Report-2015.pdf

Maine, E., Lubik, S., & Garnsey, E. (2012). Process-based vs. product-based innovation: Value creation by nanotech ventures. *Technovation*, *32*(3-4), 179-192.

Maine, E., & Seegopaul, P. (2016). Accelerating advanced-materials commercialization. *Nature Materials*, *15*(5), 487-491.

Maine, E., & Thomas, V. J. (2017). Raising financing through strategic timing. *Nature Nanotechnology*, *12*(2), 93-98.

Maine, E., Thomas, V. J., Bliemel, M., Murira, A., & Utterback, J. (2014). The emergence of the nanobiotechnology industry. *Nature Nanotechnology*, *9*(1), 2-5.

McCullough, M. (2016). How Zymeworks is building the next great Canadian drug company. *Canadian Business*. Retrieved from https://www.canadianbusiness.com/innovation/zymeworks/

McGrath, R. G., Ferrier, W. J., & Mendelow, A. L. (2004). Real options as engines of choice and heterogeneity. *Academy of Management Review*, *29*(1), 86-101.

McGrath, R. G., & Boisot, M. (2003). Real options reasoning and the dynamic organization: Strategic insights from the biological analogy. *Leading and managing people in the dynamic organization*, *201*.

Milne, C. P., Cohen, J. P., & Chakravarthy, R. (2015). Where is personalized medicine in industry heading?. *Nature Reviews Drug Discovery*, *14*(12), 812-814.

Neter, J., Kutner, M. H., Nachtsheim, C. J., & Wasserman, W. (1996). Applied linear statistical models.

Niosi, J. (2003). Alliances are not enough explaining rapid growth in biotechnology firms. *Research Policy*, 32(5), 737-750.

Niosi, J. (2011). Complexity and path dependence in biotechnology innovation systems. *Industrial and Corporate Change*, 20(6), 1795-1826.

Park, U. D., Borah, A., & Kotha, S. (2016). Signaling revisited: The use of signals in the market for IPO s. *Strategic Management Journal*, *37*(11), 2362-2377.

Pierrard, S., & Lavallee, E. (2019). Open innovation: A shift to new intellectual property models? Lavery Lawyers. Retrieved from https://www.lavery.ca/en/publications/our-publications/3155-open-innovation-a-shift-to-new-intellectual-property-models.html

Pisano, G. (2006). Profiting from innovation and the intellectual property revolution. *Research Policy*, *35*(8), 1122-1130.

Pisano, G. P. (2010). The evolution of science-based business: innovating how we innovate. *Industrial and Corporate Change*, *19*(2), 465-482.

Rothaermel, F. T. (2001). Incumbent's advantage through exploiting complementary assets via interfirm cooperation. *Strategic Management Journal*, *22*(6-7), 687-699.

Silcoff, S. (2017, June 4). Zymeworks IPO bears good tidings for Canadian biotechnology. *Globe and Mail*. Retrieved from https://www.theglobeandmail.com/technology/zymeworks-ipo-bears-good-tidings-for-canadian-biotechnology/article35198952/

Silcoff, S. (2020, December 16). AbCellera closes record biotech IPO as underwriters exercise option to buy shares; total proceeds US$555.5-million. *Globe and Mail*. Retrieved from https://www.theglobeandmail.com/business/article-abcellera-closes-record-biotech-ipo-as-underwriters-exercise-option-to/

Stratified Medicine Scotland. (2016). *The Scottish precision medicine ecosystem*. Stratified Medicine Scotland. Retrieved from http://www.stratmed.co.uk/media/1151/pme_near-final_071016_service-broker-model-and-diagram-of-pme.pptx

Swan, M. (2009). Emerging patient-driven health care models: an examination of health social networks, consumer personalized medicine and quantified self-tracking. *International Journal of Environmental Research and Public Health*, *6*(2), 492-525.

Thomas, V. J., Bliemel, M., Shippam, C., & Maine, E. (2020). Endowing university spin-offs pre-formation: Entrepreneurial capabilities for scientist-entrepreneurs. *Technovation*, *96*, 102153.

Utterback, J. (1994). Mastering the dynamics of innovation: How companies can seize opportunities in the face of technological change. *University of Illinois at Urbana-Champaign's Academy for Entrepreneurial Leadership Historical Research Reference in Entrepreneurship*.

Utterback, J. M., & Abernathy, W. J. (1975). A dynamic model of process and product innovation. *Omega*, *3*(6), 639-656.

Williams, H. L. (2013). Intellectual property rights and innovation: Evidence from the human genome. *Journal of Political Economy*, *121*(1), 1-27.

Yigitcanlar, T., Sabatini-Marques, J., Kamruzzaman, M., Camargo, F., Moreira da-Costa, E., Ioppolo, G., & Palandi, F. E. D. (2018). Impact of funding sources on innovation: evidence from Brazilian software companies. *R&D Management*, *48*(4), 460-484.

Zobel, A. K., Balsmeier, B., & Chesbrough, H. (2016). Does patenting help or hinder open innovation? Evidence from new entrants in the solar industry. *Industrial and Corporate Change*, *25*(2), 307-331.

Zuckerman, R., & Milne, C. P. (2012). Industry perspectives on personalized medicine. *Nature Reviews Drug Discovery*, *11*(3), 178-179.

Zymeworks, Inc. (2021). Form 10-K. Retrieved from https://www.annualreports.com/HostedData/AnnualReports/PDF/NYSE_ZYME_2020.pdf

Tables

Table 1. Personalized Medicine Industry Subsectors

Subsector	Definition	Examples
Therapeutics	Firms developing drug-based treatments for disease	AbCellera, Aquinox, Celator
Diagnostics	Firms providing point of care, “omics” testing, or laboratory tests or supplies for determining disease state	Boreal Genomics, Augurex, Microbiome Insights
Medical Device	Firms developing customized implantable or external device-based treatments for disease	Life360 Innovations, Microdermics
Digital Health	Firms providing software or mobile solutions for housing or manipulating patient data, or diagnostic services using digital sensors	MetaOptima, Careteam

Table 2. Skewness and kurtosis results of data transformation

	VO	FS	Partn	In(VO)	In(FS)	In(Partn)
Skewness	2.709	5.921	1.077	-.558	.355	-.084
Kurtosis	7.777	37.021	.254	.685	.705	-1.201

N=63

Table 3. Descriptive Statistics

	ln(VO)	ln(FS)	ln(Partn)	Uncertainty	ST	Mean	SD
ln(VO)	1.00					6.066	1.283
ln(FS)	.478**	1.00				3.396	1.316
ln(Partn)	.374**	.100	1.00			-.923	1.000
Uncertainty	-.027	-.258*	.146	1.00		1.889	.969
ST	.382**	.279*	-.057	-.217	1.00	.49	.504

N = 63. ** $p < 0.01$; * $p < 0.05$.

Table 4. Multivariate regression model results (coefficients)

	ln(VO)	ln(FS)
ln(Partn)	.468**	.241
	(.167)	(.192)
ST	.910**	.628
	(.334)	(.384)
Uncertainty	-.025	-.228
	(.181)	(.209)

N=63. ** $p < 0.01$; * $p < 0.05$. Standard errors in parentheses.

Figures

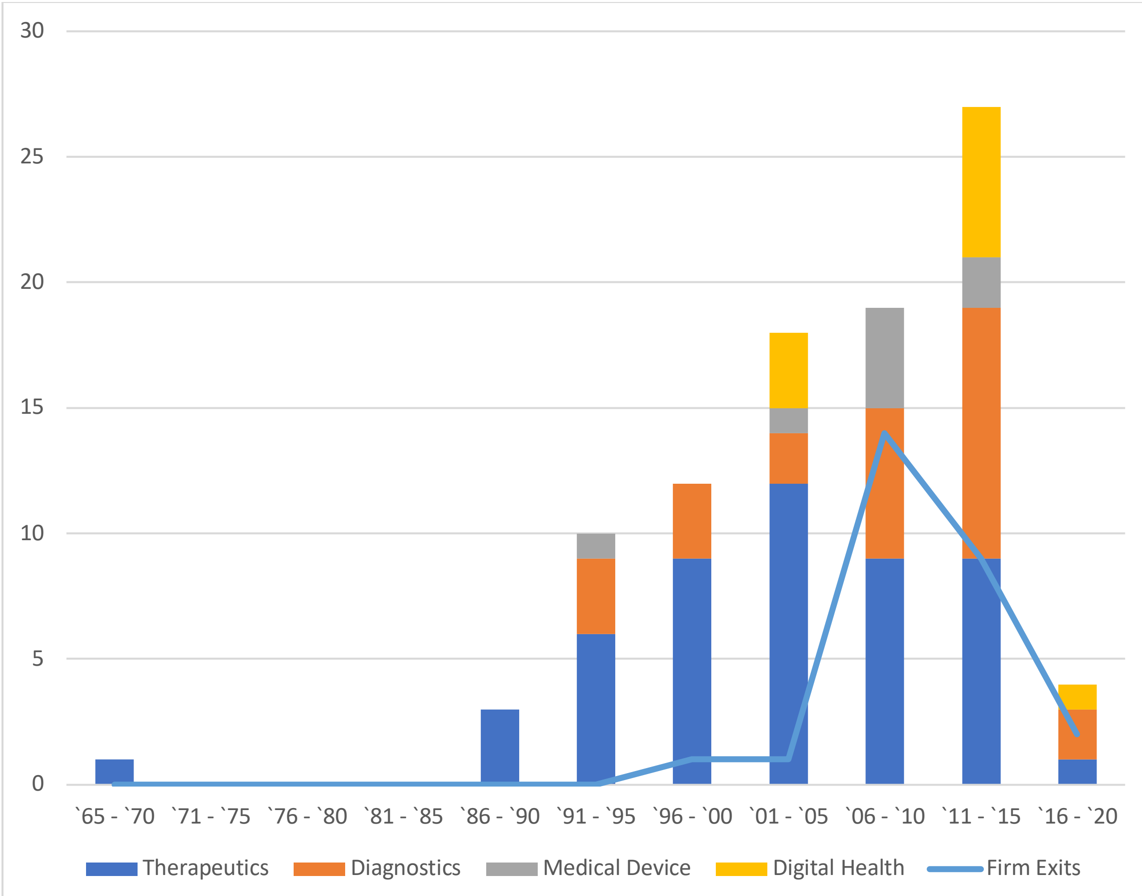

Figure 1. The evolution of the personalized medicine innovation ecosystem.

Keywords used to identify personalized medicine firms

“targeted treatments”, “sensitive diagnostics”, “genetic testing”, “biomarker testing”, “gene delivery”, “genomics based”, “microbiomics”, “metabolomics”, “antigen targeting”, “guided optimization”, “precision medicine”, “precision health”, “next-generation sequencing”, “microarray”, “machine learning”, “pharmacogenomics”, “cell signaling”, “customized”, “translational cancer research”, “early cancer detection”, “real time monitoring”, “tracking”, “home monitoring”, “medication monitoring”, “digital profile”, “body contours”, “data provenance” and “rapid diagnostics”.

Description of the emergence of the British Columbia personalized medicine innovation ecosystem

The first venture initiating the personalized medicine innovation ecosystem in British Columbia was RepliCel, a University of British Columbia spinoff founded in 1967 to develop dermatological treatment solutions for acute bacterial infections. 20 years later, the next firms, Cardiome Pharma, Angiotech and QLT were founded, with capabilities in developing customized therapeutics and medical devices, and the innovation ecosystem was built steadily after that. Over the next 15 years, the number of new entries with technological capabilities in personalized medicine, primarily in therapeutics and diagnostics continued to build. The first digital health personalised medicine firms were founded between 2001 and 2005, and account for an increasing proportion of new entrants. Firms entered the personalized medicine innovation ecosystem in increasing numbers each measured period until 2015, with new entrants in therapeutics decreasing in both absolute number and proportion of new entrants after 2005. Regarding the technical capabilities and patenting activity of these firms, in total, 242 filed patents were identified which were assigned to, or previously assigned to one of the firms in our sample. 120 of the 242 patents were granted while the remainder were active or abandoned applications. There was a wide range of patent filing dates, from 1987 to 2016, with many patents having been filed by company founders before the company founding date.

Essay 3:

Whether and When to Reveal: Open Innovation Mechanisms Within an Emerging Personalized Medicine Innovation Ecosystem

Andrew Park

Elicia Maine

Beedie School of Business

Simon Fraser University

500 Granville Street

Vancouver, British Columbia, Canada

Abstract

Drawing on and contributing to the Open Innovation literature, our study explores the boundary conditions of the effectiveness of Open Innovation strategies within emerging innovation ecosystems. Namely, we propose a relationship between the use of Open Innovation by emergent Personalized Medicine firms in British Columbia and their value outputs. We test our hypothesis empirically by quantifying the use of the Open Innovation mechanisms of Selective Revealing, Strategic Timing and Strategic Partnering by each of the firms in our sample, categorized by level of uncertainty, and comparing them to the value output of each of these firms. We find Open Innovation activities have a positive effect on value outputs for Personalized Medicine firms. Additionally, firms who operate in environments of high uncertainty and who employ these Open Innovation mechanisms enjoy higher value outputs than firms who operate in environments of low uncertainty. Thus, we argue that Open Innovation plays an important role in stimulating the economic performance of emerging science-based ecosystems.

Keywords: Open Innovation; Innovation Ecosystems; Science-based businesses; Personalized Medicine; Uncertainty; Selective Revealing

Introduction

Open Innovation, which is defined as the purposive inflow and outflow of knowledge and resources to accelerate innovation (Chesbrough, 2003), is a key strategy employed by science-based businesses, such as biotechnology, nanotechnology and pharmaceutical ventures, which operate under prolonged and high degrees of uncertainty. Given the timelines, complexity, and commercialisation costs involved, attracting investors and alliance partners with complementary assets is vital (Maine & Garnsey, 2006; Perkmann & Walsh, 2007; Rasmussen, 2008; Pisano, 2010). Alliance partners of science-based ventures are typically large incumbents with complementary technical capabilities, in such areas as clinical trials and manufacturing, and/or commercial resources, such as widespread distribution channels.

Attracting alliance partners is a prudent strategy for science-based businesses, but they are faced with difficult choices with respect to which partners to approach and how much information regarding their capabilities to divulge. On one hand, they must reveal enough of their secret sauce to signal that their venture is of high quality (Hsu & Ziedonis, 2008); on the other hand, they cannot reveal so much that their technology is copied. Although patents may be perceived as a protective, and therefore closed mechanism, scholars argue that patenting enables Open Innovation through enhancing the signalling, selecting and functioning of strategic partnerships (Pahnke, Katila & Eisenhardt, 2015; Ruckman & McCarthy, 2016). In investigating the demand side of patent licensing, Ruckman and McCarthy (2016) find that positive reputational signals, which include prior research outputs, increase the likelihood of a biopharmaceutical firms' ability to out-license a patent, even if similar patents from other firms already exist. Thus, prior revealing of capabilities, patenting and signaling appear to work synergistically when science-based businesses attempt to attract alliance partners.

Adding further to this dilemma, Openness and value capture are not consistently correlated across firms and the relationship may be radically different across different industries. For example, an open strategy employed by a large American software incumbent such as IBM provides only marginal benefit to value capture (West, 2003). Similarly, Gimenez-Fernandez and Sandulli (2017) find there is a point of diminishing (and even negative) returns on innovation performance for a firm when cooperating and outsourcing strategies are used. On the contrary, Maine and Garnsey (2006) describe the case of a science-based venture in the advanced materials sector which did not realize value capture until they advertised their capabilities to prospective partners who helped them achieve success in commercialization.

Even less is known about the relationship between Open Innovation and value capture in emerging science-based innovation ecosystems. Personalized Medicine is one such context. While there is a small set of papers that examine Personalized Medicine (Swan, 2009; Knowles et al., 2017), as far as can be ascertained, there are no Open Innovation studies conducted on this sector. From a policy perspective, a better understanding of emerging industries, including Personalized Medicine, using an Open Innovation lens would have broad societal and socioeconomic benefits (Chesbrough & Bogers, 2014) such as the creation of more knowledge economy jobs.

Since Chesbrough's (2003) seminal publication on Open Innovation, a stream of work (West, 2003; Bogers et al., 2017; Clausen & Rasmussen, 2011; Alexy et al, 2013) on open strategies has emerged, often documenting the positive outcomes experienced by large American software companies who engage in open-source strategies. Subsequently, authors have attempted to identify boundary conditions of Open Innovation. Specifically, advocates for Selective Revealing (Henkel et al., 2014) note that in some situations, being strategic about what and when to reveal information may lead to better value capture outcomes for emerging ventures.

Authors have also explored the link between the use of various Open Innovation mechanisms. For example, Zobel, Balsmeier and Chesbrough (2016) find that a firm's patent stock has a positive effect on the number of interorganizational partnerships. Regardless, these advocates don't explain *why* Open Innovation affects value capture. Other scholars note the lack of theory development in the Open Innovation literature (Dahlander, Frederiksen & Rullani, 2008; Hopkins et al., 2011; Hopkins, Tidd & Nightingale, 2013), arguing that Open Innovation researchers are too embedded in their chosen contexts and need to do a better job of building theories that have external validity, for example through defining specific Open Innovation mechanisms and elucidating the conditions under which these mechanisms fail to positively impact value capture.

Moreover, most Open Innovation research has focused on specific case studies or a limited set of firms; few empirical studies have been conducted at the industry or ecosystem level. Moreover, noting the narrow set of industries examined, numerous scholars (Dahlander & Gann, 2010; Armellini, Kaminski & Beaudry, 2014) have noted the need for contexts from other industries, to assess the external validity of current Open Innovation research. Recently, there has been an expansion of contexts within the Open Innovation literature (Zobel, Balsmeier & Chesbrough, 2016; Armellini, Kaminski & Beaudry, 2014; Bianchi et al., 2011), however, the seminal works in this body of research are still based on studies of multinational software firms.

A significant amount of Open Innovation work has been conducted on American software firms which operate in environments of low uncertainty (i.e., when an end product is conceptualized, from a technical perspective, it is likely to be built as expected; Dahlander & Gann, 2010). In contrast, science-based firms have a lower probability of bringing a conceptualized product to fruition, where the end result functions as predicted (Maine & Seegopaul, 2016). Additionally, it is unclear how operating in an uncertain environment affects resultant value capture when using Open Innovation strategies. In this paper, we answer the research question, 'why and under what conditions do the Open Innovation mechanisms of Selective Revealing, Strategic Timing and Strategic Partnering affect value capture by Personalized Medicine firms?'

Our study makes several contributions to the Open Innovation literature. First, we examine why Open Innovation influences value capture of science-based firms. We propose a theory explicating why Open Innovation affects firm value capture, and how this relationship is moderated by uncertainty. We hypothesize that Open Innovation activities have a positive effect on value capture. Further, we hypothesize that the effect of Open Innovation activities is heterogenous across firms of high and low uncertainty. In order words, when a science-based firm operates in an uncertain environment and their technology is highly uncertain, more Open Innovation leads to higher value capture. These hypotheses challenge the overwhelmingly positive sentiment surrounding Open Innovation (e.g., Brunswicker & Ehrenmann, 2013; Chan, 2013; Chesbrough & Crowther, 2006; Hopkins, Tidd & Nightingale, 2013; Coad et al., 2021). A rethinking of the merits of Open Innovation encourages further research from the scholarly community on the boundary conditions of Open Innovation.

Second, we test our hypotheses in the emerging Personalized Medicine sector that is radically transforming medicine and clinical practice (Cullis, 2015). In so doing, we use a context outside the American software domain and one which includes science-based firms of different Personalized Medicine subsectors. Further, we examine differences in value capture from Open Innovation across the four major subsectors of Personalized Medicine from highest to lowest uncertainty: therapeutics (firms that research and create treatments for disease, typically pharmaceutical companies), medical device (firms that create implantable or external device-based treatments for disease), diagnostics (firms that create methods to detect disease) and digital health (firms that build software applications for disease monitoring). While we are aware of a study that has explored the size of the firm as a moderator between openness and innovation performance (Vahter, Love & Roper, 2014), we have not yet encountered such a study on uncertainty or science-based firms. We hypothesize that uncertainty moderates the relationship between Open Innovation and value capture.

Third, we contribute to the debate on whether patents impede or enable Open Innovation in emerging scientific fields. We find evidence that strategic timing of patents contributes to value capture by firms in an emerging Personalized Medicine innovation ecosystem and suggest that it is the signaling value of patents that enhance Open Innovation through attraction of investors and alliance partners.

This paper is organized as follows. In the next section, we review the current state of Open Innovation and Selective Revealing research and identify a major gap in the corpus of literature: there is a lack of theory and empirical work regarding the linkage between openness and value capture. Next, we propose 2 novel hypotheses linking Open Innovation and value capture, which is moderated by uncertainty. Specifically, we propose that Open Innovation allows firms to enjoy greater value capture under conditions of high uncertainty while under low uncertainty, Open Innovation has less of an effect on value capture. We then describe the methodology of investigating this question in the context of Personalized Medicine firms, present and discuss findings of our sample of firms and offer suggestions and avenues for future research.

Theoretical Framework and Hypotheses

Open Innovation has emerged as an increasingly studied stream within the management of innovation literature and has yielded interesting insights into the benefits of using open strategies, particularly during the early stages of firm formation. Science-based businesses have been an understudied context within the Open Innovation literature. This science-based venture context has been studied, however, in a separate stream of management of innovation literature, namely that of innovation ecosystems.

A focal point in the science-based innovation ecosystem corpus of literature has been the need for start-up firms to acquire downstream partners in the industry value chain and access complementary assets to their core technologies. Herein lies the link to Open Innovation: one of the objectives for firms in using an Open Innovation strategy is to attract alliance partners and complementary assets early in their formation, in order to optimize their chances of survival and value capture. However, innovation ecosystem research does *not* discuss how open or closed strategies affect value capture for science-based firms.

We contribute to the field of innovation research by better defining the boundaries of Open Innovation research by incorporating a new context and drawing on related work in the innovation ecosystems literature. In the next section, the current state of Open Innovation research is reviewed. The Personalized Medicine industry (a type of science-based venture) is then described, along with its four subsectors, and why it is an important context for expanding our knowledge of Open Innovation. Finally, we illustrate the parallels to previous research that has been done on innovation ecosystems, in particular the commonalities with Open Innovation regarding the acquisition of alliance partners and complementary assets. Figure 1 serves as a roadmap for this section and illustrates the timeline of Innovation Ecosystem research, Open Innovation research and how the concepts of science-based businesses and the need for attracting alliance partners link the two.

Open Innovation

Open Innovation was coined by Chesbrough (2003) to describe the trend of technology-based firms acquiring capabilities and technical know-how through partnerships with external partners and acquisitions of smaller firms. This is in contrast to the Closed Innovation model of investing solely in internal R&D and resisting inter-firm knowledge sharing (West, 2003). Since Chesbrough's pioneering work, the field of Open Innovation has been further refined, studied, and debated at multiple levels (Bogers et al., 2017). Scholars generally agree that Open Innovation strategies include active management of knowledge inflows and outflows, and this purposive approach is helpful in appropriating value from both internal and external R&D (Chesbrough, 2003; Chesbrough & Bogers, 2014). For example, a software firm may carefully choose which open-source code libraries they wish to integrate into their own codebase, and which parts of their own code they wish to release to the open-source community. Consequently, we argue that the use of Open Innovation activities in science-based firms (specifically, Personalized Medicine firms) positively relates to firm value capture.

Previous Open Innovation literature has found patenting as an indicator of openness (Laursen & Salter, 2014; Hagedoorn, Lokshin & Zobel, 2014), but the link between patenting, openness and innovation outcomes has been heavily debated in prior research, which we discuss throughout this paper. For example, several scholars have argued that formal IP initially enables open activities (see discussions on Selective Revealing and Strategic Timing that follow) but that a long-term focus on patenting may be detrimental to openness and related performance outcomes (West & Gallagher, 2006).

The joint efforts of interdependent parties, or strategic partnerships, is another proxy for openness that has been studied in Open Innovation research (Zobel, Balsmeier & Chesbrough, 2016; Kapoor & Furr, 2014). This operationalization is related to patenting, as formal IP may enable these collaborations, which is particularly helpful to new firms or firms with highly novel technologies that may benefit from downstream strategic alliances (Arora & Merges, 2004). Given that IP (in the form of Selective Revealing and Strategic Timing) and Strategic Partnerships have all been utilized and debated as proxies for openness, we consider all three as Open Innovation mechanisms in this paper. We put forward the following hypothesis:

H1: Open Innovation activities have a positive effect on a firm's value capture, i.e., firms who engage in Open Innovation activities exhibit higher value capture than their less open counterparts.

Some scholars argue that Open Innovation, as currently practiced, while arguably beneficial to value *capture* (e.g., generating revenue and profits (Priem, 2007)), is detrimental to value *creation* (e.g., making scientific discoveries through knowledge labor and subsequently introducing novel products and services to the market (Bowman & Ambrosini, 2000)) in the innovation ecosystem as a whole (Edwards, 2016; Williams, 2013). For example, Williams (2013) finds that some forms of intellectual property protection can impede scientific discovery, noting that Celera's contract law-based IP led to a 20-30% decrease in related research. In contrast, in terms of value capture, which is the focus of our empirical analysis, Open Innovation strategies can be helpful for firms who have a product they are ready to commercialize but are reliant on frequent exchanges of downstream complementary assets, partnerships and financing.

As the field of study has developed, more scholars have been arguing that openness in and of itself is not a panacea, and the relationship between its practice and value capture is nuanced. For example, Kotha and Srikanth (2013) argue that firms who engage in Open Innovation practices must ensure that incentives among actors are aligned and mutually beneficial behavior is enforced (ideally through shared visibility) or else bargaining power may shift too heavily in favor of one party. It is becoming evident that the boundary conditions of Open Innovation need to be further refined, and certain moderators exist in the link between open strategies and value capture that need to be defined and measured. In light of this, a more nuanced and muted form of Open Innovation research has emerged, known as *Selective Revealing*.

Selective Revealing and the Need for New Contexts

Some scholars favor a hybrid strategy between Open and Closed Innovation, called Selective Revealing, which was coined by Henkel (2006). In Selective Revealing, firms still operate with an Open Innovation mindset, but carefully consider when and which of their capabilities to reveal. West (2014) cautions against a wholesale Open Innovation approach, noting that more often than not, a Closed Innovation strategy is preferred, particularly when the firm is in a position of high leverage, as employing an Open Innovation strategy can carry innumerable risks. He states, "We don't assume that a firm that has an alliance portfolio will use alliances for every project, product or technology, so why would we assume this for open innovation?" (West, 2014, 6). The core message of Selective Revealing proponents is that the value of Open Innovation is heavily context-dependent and further research is needed to understand when and how to seek alliance partners and complementary assets.

We aim to add clarity to this context-dependent relationship by choosing the burgeoning Personalized Medicine industry as a new context to expand the Open Innovation body of literature. The Personalized Medicine industry offers cases of firms with measurable and varying degrees of uncertainty, which makes it an ideal context for evaluating the relationship between Open Innovation and Value Output, with uncertainty as a moderator. A brief introduction to Personalized Medicine and its applicability to Open Innovation follows.

Personalized Medicine, Science-based Businesses and Uncertainty

Personalized medicine is a growing field within the science-based business domain that takes a customized approach to a patient's health and well-being. It favors treating ailments and diseases by looking at a patient's genomic, metabolomic or microbiomic profile and matching treatments accordingly over a one-size-fits-all approach. The one-size-fits-all approach of traditional (non-Personalized) medicine relies heavily on identical treatments for large groups of people; this traditional approach, while fast and cheap, suffers from inconsistency in treatment outcomes, as different people may react differently to the same treatment. Personalized Medicine can also be implemented effectively as a preventive measure, for example, by customizing a patient's diet based on their lifestyle and family history of disease. A Personalized approach to creating treatment pathways could lead to notable improvements in global health outcomes (Cullis, 2015). Increased advocation for this approach has led to an uptick in the founding of global science-based firms dedicated to this particular field (Swan, 2009).

While Personalized Medicine is a novel field of study in the management of innovation literature, it is a subdomain of science-based business research, which has been studied extensively. Science-based businesses, termed by Pisano (2006), are technology firms who face higher levels of uncertainty over longer time frames compared to their counterparts in other areas such as manufacturing, oil & gas, and information technology (Maine et al., 2012; Pisano, 2006; Pisano, 2010; Maine, Soh & Dos Santos 2015). Because of this uncertainty, science-based businesses, such as Personalized

Medicine ventures, face significant pressure early in their life cycles to attract complementary assets, including venture capital funding, to prolong their survival. This need for firms in emerging ecosystems to partner with these other entities to improve their chances of survival is largely driven by the level of uncertainty in their technologies and the environments in which they reside (Pisano, 2006; Pisano, 2010; Maine & Seegopaul, 2016).

Consequently, firms operating under environments of high uncertainty can use various open strategies, such as publishing research and patenting early, to signal that their capabilities are of high quality to Venture Capitalists and other potential alliance partners (Hsu & Ziedonis, 2008; Park et al., 2016). Furthermore, science-based businesses can use a portfolio of patents and research outputs to build reputational credibility, which not only attracts alliance partners but increases the likelihood of successfully licensing out their patents (Ruckman & McCarthy, 2016). These strategies can aid firms operating under environments of high uncertainty by helping them attract partners to gain external assets early in their formation. In this paper, we attempt to elucidate the link between open strategies (including patenting and seeking strategic partnerships) and firm success (measured by value capture) and the influence of uncertainty on this link. We predict the following:

> *H2: The effect of Open Innovation activities on value output is heterogenous across Personalized Medicine firms of high and low uncertainty, such that it is stronger for firms who exhibit high technical uncertainty compared to firms who exhibit low technical uncertainty.*

This work makes a theoretical contribution by highlighting the role of uncertainty as a moderator in the relationship between Open Innovation and Value Capture, as seen in Figure 2.

Methodology

In this section, the method used to collect and categorize firms with Personalized Medicine capabilities is explained. Next, the data sources used to identify and categorize Personalized Medicine companies in British Columbia, Canada are described. The methods used to collect Personalized Medicine patent and partnership counts from these companies, which serve as indicators of Open Innovation activity are also then described. Finally, the methods used to calculate and assess value captured by each of these companies are explained.

Personalized Medicine Firm Sample

In order to create a dataset around the emergence of the Personalized Medicine ecosystem in British Columbia, Canada, we first gathered existing related industry reports. These included studies of the biotechnology sector (LifeSciences British Columbia & PricewaterhouseCoopers, 2015; Holbrook, 2003). Next, we utilized several databases, including ReadyToRocket, University of British Columbia (UBC) Industry Liaison Office, Simon Fraser University (SFU) Spin-Off Companies List, LifeSciences BC (formerly BC Biotech) Press Releases, LifeSciences BC Membership List, CPROST, BC Sciences Cluster Directory and S&P Capital IQ. The LifeSciences BC Press Releases archive was the most comprehensive data set available, and included data from January 2004, so we used this data as a historical cut-off. We reviewed each life science, biotechnology, medical device, diagnostic, pharmaceutical and digital health company in each of these databases to assess their capabilities in Personalized Medicine, since not all these firms have Personalized Medicine capabilities and ended up with a dataset of 94 firms.

We then cross verified this list by searching the USPTO database for assignees in the following cities, ‘Vancouver’, ‘Kelowna’, ‘Victoria’, ‘Burnaby’, ‘Surrey’, ‘Richmond’, which comprise the largest municipalities in British Columbia, by population. We kept patent title and body searches broad in the USPTO database and included the following keywords: ‘Cancer’, ‘Gene’, ‘Diagnostics’, ‘Therapeutic’ and ‘Digital Health’ since these are commonly listed capabilities by Personalized Medicine firms. We verified this list of capabilities by using our academic knowledge of biotechnology and Personalized Medicine and this list was further cross-checked by an independent professor of Molecular Biology and Biochemistry at the University of Calgary. We reviewed the capabilities sections of each identified company’s website or press releases and included them in our list if they developed or were developing treatments that were customized to a component of a patient’s health profile, which is by definition, a Personalized Medicine approach. The keywords used to identify whether the firm had Personalized Medicine capabilities is listed in the Appendix.

Strategic Partnerships

As an indicator of Open Innovation activity, we drew on Zobel, Balsmeier and Chesbrough's (2016)'s work in using strategic partnerships as a proxy for Open Innovation activity. Other scholars have also used interorganizational relationships as an indicator of openness and note that cross-firm cooperation is needed by emergent firms to access complementary assets unavailable to the emerging start-up (Laursen & Salter, 2014; Alexy, Bascavusoglu-Moreau & Salter, 2016; Christensen, Olesen & Kjaer., 2005). We reviewed and collected the number of strategic partnerships (partnerships related to operational activities such as R&D and distribution and not ones related to financing, accounting or administrative services) by consulting the S&P Capital IQ database, company websites and press releases.

Patents: Selective Revealing and Strategic Timing

Contrasting Viewpoints of Patents in Open Science

As an additional indicator of Open Innovation activity, we identified firms that had at least one granted patent, which represents our 'Selective Revealing' variable. We acknowledge that not all patenting activity may be indications of purposeful Open Innovation strategy and the viewpoint that patenting or other forms of intellectual property protection serve as clear proxies for Open Innovation is not one that is unanimously held. For example, Williams (2013) observes that after Celera protected its sequenced genes using contract law, follow-on scientific research activity on these genes declined by over 20%. Other scholars are more explicit about the downsides of patenting on innovation outcomes (Bubela & Cook-Deegan, 2015; West, 2003; Perkmann & Schildt, 2015). Several scholars examine the Structural Genomics Consortium as an innovation intermediary that has spurred substantial follow-on research and brokered productive industry-researcher collaborations through its patent-free, open data model (Gold, 2021; Gold 2019; Edwards, 2016; Perkmann & Schildt, 2015).

However, the value of patenting in early capabilities revealing strategies has been demonstrated through empirical research on the influence of patenting on innovation outcomes (Hsu & Ziedonis, 2008; Park et al., 2016; Zobel & Chesbrough, 2016). Interestingly, Williams conducted follow-up efforts to her case study on Celera and found that gene patenting specifically (in comparison to other forms of intellectual property) had no quantifiable effect on follow-on innovation (Sampat & Williams, 2019; Williams, 2016). Other scholars have either discussed the conceptual value of patents to Open Innovation as signalling or licensing mechanisms (Pierrard & Lavallee, 2019; Chesbrough, 2019) or used them as Open Innovation variables in empirical work (Bjornali et al., 2017; Zobel & Chesbrough, 2016).

In light of the opposing viewpoints on the validity of patents as a proxy for open innovation, we drew from other empirical and conceptual work that specifically targeted patents that were filed early in a firm's formation in order to signal venture quality and attract alliance partners (Maine, 2017; Bjornali et al., 2017; Hoenig & Henkel, 2015; Hsu & Ziedonis, 2008). While the existence of a granted patent (i.e., our 'Selective Revealing' variable) may be subject to debate, we argue that consistent with these studies on early signalling strategy, the early filing of a patent is a clear and purposeful Open Innovation mechanism. Consequently, we identified firms that patented early in their formation, leading to our 'Strategic Timing of Patents' variable, which we define below.

Patent Collection

We searched for Personalized Medicine patents published by each firm in our list of Personalized Medicine companies. We first searched Google Patents using the firm's name as the assignee and the Personalized Medicine keywords (see Appendix) in the body text and title search fields. We reviewed the titles and abstracts of each patent to verify they were indeed related to Personalized Medicine. For example, ICO Therapeutics' patent on dosing regimens describes methods to customize doses based on a patient's specific response to the drug being administered, which is an example of Personalized treatment (ICO Therapeutics, 2010).

We then performed the same search on the USPTO database for cross verification. The results were generally consistent between the two databases, although the Google Patents database produced additional results. These additional results are partly driven by the fact that Google Patents allows for greater flexibility in matching inventor names to search queries. For example, a search on Google Patents for 'Paul Harris' also returns results for 'Paul C. Harris'. Patents identified using this approach were included in our list of Personalized Medicine patents developed by British Columbia firms. In addition to quantifying the number of Personalized Medicine patents for each firm, we set a binary Yes/No indicator for firms who have at least one granted patent, which represents our ‘Selective Revealing’ variable. Additionally, following Hsu and Ziedonis (2008) and Maine and Thomas (2017) we labeled firms who have a granted patent with a priority date within 5 years of firm founding as engaging in *Strategic Timing* of patents. These firms are labeled as ‘Strategically Timed’ with a Yes/No indicator.

Categorization and Uncertainty

Firms who are no longer in business may affect the validity of our results, so they were identified and separated in our firm sample: if a firm was only in existence for a short period and became defunct several decades ago, it is not a viable indicator of the modern link between Open Innovation and value output. Thus, we split the firms into ‘active’ and ‘defunct’ firms. For each firm, if they were still listed as an active business on Google as of July 2018 and appeared to have a regularly updated website, we included them in the ‘active’ category. If there was a press release that a firm was out of business, listed as inactive on Google, or there was no website, we included them in the ‘defunct’ category.

Firm Capabilities and Uncertainty

We further grouped the companies into categories by capability: ‘therapeutics’, ‘medical device’, ‘diagnostics’ or ‘digital health’ companies. This categorization allowed us to understand the differences in value capture resulting from the employment of Open Innovation strategies for the different types of Personalized Medicine firms, who, in turn, operate under different levels of uncertainty. Therapeutics firms typically exist in environments of high uncertainty, whereas digital health firms exist in environments of low uncertainty (Maine & Seegopaul, 2016). Diagnostics and medical device firms operate in environments of medium uncertainty, as their costs and timelines to commercialization are higher than those of digital health firms but lower than those of therapeutics firms.

Therapeutics ventures are pharmaceutical companies who are developing drug-based treatments for disease. Medical device companies develop implantable or external physical devices to treat injury or disease. Diagnostic companies provide point of care, ‘omics’ testing, or laboratory tests or supplies for determining disease state, disease progression or a patient’s state of health. Digital health companies provide software or mobile solutions for housing or manipulating patient data, or diagnostic services using digital sensors embedded in consumer hardware and feature a lower level of uncertainty than the other categories due to the relative certainty in producing a functional software-based product. Table 1 lists each of these subsectors, with example firms and their levels of uncertainty.

Measures

Open Innovation

We draw on the Open Innovation mechanisms of Selective Revealing, Strategic Timing and Strategic Partnering and categorize each firm accordingly. We labeled each firm as having engaged in Selective Revealing (denoted as *SR*) if they received a granted patent with a Personalized Medicine capability. We labeled each firm as having engaged in Strategic Timing (denoted as *ST*) if they received a granted patent with a Personalized Medicine capability within 5 years of firm founding. This Strategic Timing measure has also previously been used by Maine and Thomas (2017). We use SR and ST in a correlation and matched comparison analysis.

We conduct a deeper quantitative analysis using Strategic Partnerships as our key Open Innovation mechanism. We created a *Partn* continuous variable which is the total number of strategic partnerships for a firm, divided by the numbers of years since founding. We normalize this continuous variable to control for the advantage older firms have in accumulating a greater number of strategic partners. We use the *Partn* independent variable as our key regressor to conduct hierarchical linear modelling (HLM). We choose this measure because of the high relevance of strategic alliances to science-based firms. Other Open Innovation scholars have created or have drawn from other empirical measures of openness for their specific contexts. For example, Barge-Gil (2013) uses self-reported levels of collaboration for his study on a wide variety of Spanish firms, Mawson and Brown (2017) utilize the number of acquisitions as a proxy for openness and Kim and Ahn (2019) use Laursen and Salter’s (2006) suggested scale of search breadth and depth for openness studies on manufacturing firms.

Uncertainty

We operationalize *Uncertainty* through an ordinal variable whose value is approximately inversely related to the level of technical uncertainty. Specifically, therapeutics firms are given a value of “1”, diagnostics firms a value of “2”, digital health firms a value of “3” and medical device firms a value of “4”.

Value Output and Firm Size

Value output is defined as the importance of a firm’s technology to customers as demonstrated through sales (Maine et al., 2012) and is used as a proxy for value capture in this study. Similar sales-based metrics have been used as proxies for innovation performance in management literature (Gunday, 2011; Jung, 2016; Ferreira, 2017). Value output metrics are important indicators of firms’ impact on an innovation ecosystem and allow us to compare a firm’s influence on the industry against others, particularly as a result of Open Innovation. Drawing on previous empirical papers that use sales as a proxy for innovation performance, we further operationalize value output by dividing the most recent year revenue of each firm by the age of firm, as seen in Maine et al. (2012). The normalization of revenue by age of firm was conducted to debias firms who may have had the advantage of operating for a much longer period of time than newer firms. We label this variable *VO*. We use *VO* as the dependent variable in our HLM and we observe additive cross-level main effects VO and Partn and an interaction term between Partn and Uncertainty, labeled *ln(Partn)_x_Uncertainty*.

While *VO* is the focus of our analysis, our initial regressions from Essay 2, which we build on in this paper, also consider Firm Size, proxied by headcount and natural log transformed to a *ln(FS)* variable, as an innovation performance indicator. This is based on prior empirical work that utilizes an increase in the number of qualified employees as an innovation outcome (Yigitcanlar, 2018; Gunday, 2011). Firm Size is not normalized by the age of the firm due to the propensity for many therapeutics firms to receive a significant amount of investment (e.g., through Venture Capital funding) and then hire many employees but not generate any revenue in the short term. Thus, firm age is less likely to be of benefit to firms when that benefit is measured by Firm Size.

Analysis

We conduct our analyses based on our entire sample and 2 additional sub samples of the data collected. We examine the totality of firms in our sample in a correlation matrix, comparing value outputs of firms with varying levels of uncertainty and use of Selective Revealing and Strategic Timing. We also conduct a separate descriptive analysis on the top 20 firms in our sample, ranked by value output, to establish a robustness check. We then perform a matched comparison between high/medium vs. low value output firms and compare their value outputs. In this matched comparison, we choose 8 pairs of firms, where each pair is composed of 2 firms in the same level of uncertainty (e.g., therapeutics) with similar founding dates and different levels of value capture (i.e., high/medium vs. low). This matched pairwise comparison technique not only serves as an additional testing technique to support the results of our HLM, but also allows researchers to identify deeper nuances in individual firm cases (Eisenhardt, 1989).

We begin our quantitative analysis by referring back to the multivariate regression in Essay 2 to review influence of our key variables in a single regression model. Specifically, we include our exposure variables (*ST*, *ln(Partn)*, *Uncertainty*) and our dependent variables (*ln(VO)*, *ln(FS)*) in this model. To satisfy the normality requirements for a multiple regression analysis, in Essay 2, we checked the continuous variables *VO* and *FS* (dependent variables) and *Partn* (independent variable) using a skewness and kurtosis test (Changyong et al., 2014) and determined the data are not normally distributed. After conducting a natural log transformation on these variables, which are labeled *ln(VO), ln(FS)* and *ln(Partn)*, it is observed that normality was significantly improved, as seen in Essay 2 and shown again in Table 2. The correlation matrix in Table 3 shows that the dependent variables are correlated with each other, which is desirable in a multivariate regression.

Building on the multivariate regression from Essay 2, to test our hypotheses, we conduct a HLM of active firms (n = 63) to determine the relationship between the variables in the multivariate regression, and specifically, the relationship between Open Innovation activity, with *ln(Partn)* chosen as the key regressor, and value output. We model the natural log transformed value output, a continuous variable represented by *ln(VO)*, as follows:

$$ln(VO) = \beta_0 + \beta_1 ln(Partn) + \beta_2 Uncertainty + \beta_3 ln(Partn)*Uncertainty$$

where the main variable of interest is our key Open Innovation mechanisms: natural log transformed normalized number of partnerships, which is a continuous variable represented by *ln(Partn)*. *Uncertainty* is a dummy variable which indicates the level of technical uncertainty. The final interaction term allows us to observe the treatment effect that *Uncertainty* has on *ln(VO)*. To illustrate the moderating effect of *Uncertainty*, we plot the interactive effect of *Uncertainty* on *ln(VO)*.

Results

The emergence of the personalized medicine innovation ecosystem in British Columbia is depicted and analysed in this section, with Personalized medicine firms as the main unit of analysis. A dataset of all BC firms with Personalized medicine capabilities was created, along with their Personalized medicine patents, revenues, number of partners, number of employees, financing raised and spin-out origin. The first three metrics contribute directly to our HLM aimed at elucidating the relationship between Open Innovation mechanisms and value output. The remaining metrics contribute to our understanding of other firm growth and may also be correlated to value output and to each other. These firms are categorized into subsectors with varying levels of uncertainty (Table 1). The Open Innovation mechanisms of Selective Revealing, Strategic Timing and Strategic Partnering were proxied through patenting, founding and partnership data, and compared with value capture over time. As described in this section, Open Innovation was found to positively impact value capture in this emerging innovation ecosystem, moderated by uncertainty.

Personalized Medicine Firm and Patent Sample

British Columbia firms with Personalized Medicine capabilities were identified and categorized into one of four subsectors: therapeutics, medical device, diagnostics, or digital health (Tables 1-3). In total, 94 firms were identified, with 63 currently active and 31 defunct. Of the 94 firms, 50 were in the ‘therapeutics’ category, 24 were in ‘diagnostics’, 13 were in ‘digital health’, and 7 were in ‘medical device’. 10 of the 94 firms were Simon Fraser University spinouts (6 now defunct) and 32 were University of British Columbia spinouts (12 now defunct). 37 firms had publicly released Venture Capital fundraising data ranging from $0.8 million to $181.7 million in US dollars; while this does not necessarily mean the remaining companies did not raise Venture Capital funds (potentially due to non-disclosure agreements) it does give directional information on the proportion of firms who opted to go the Venture Capital funding route.

Value Output

As seen in Table 4, out of the top 20 firms ranked by Value output. 11 out of the top 20 firms were therapeutics firms. 10 of these top 20 companies were University of British Columbia spinouts, primarily in therapeutics. The majority of therapeutics firms were founded more than a decade ago, which is consistent with the expected commercialization timelines of science-based ventures (Pisano, 2010; Maine & Seegopaul, 2016; Maine et al, 2015).

Selective Revealing, Strategic Timing, Strategic Partnerships

The majority of Personalized medicine firms in the BC Innovation ecosystem rely on patenting to protect their intellectual property. 242 patents filed with the USPTO were identified, which were assigned to, or previously assigned to one of the 94 firms. 120 of the 230 patents were granted while the remainder were active or abandoned applications. Figure 3 shows the growth over time of Personalized medicine patents, firm founding, and firm exits assigned to British Columbia entities, broken out by year. We observe an uptick in firm exits around 2008, which could have been due to the economic recession. There is a spike in firm founding after 2010, which could be due to a market recovery after the recession, coupled with the founding of the Personalized Medicine Initiative in British Columbia. Consequently, there is an increase in the number of patent applications and granted patents that coincide with the increase in the number of firms founded.

The specific Open Innovation mechanisms of Selective Revealing and Strategic Timing appear to be related to commercialization success. A matched comparison analysis shows that the majority of higher value capturers exhibit the innovation mechanisms of Selective Revealing and Strategic Timing, compared to a minority of low value capturers. Table 3 shows a correlation matrix between the variables of our analysis, which supports the matched comparison. All three open innovation mechanisms, including Strategic Partnerships, are positively correlated to Value output, but not necessarily to Firm Size. This may be explained by the fact that many therapeutics companies are successful in raising significant Venture Capital investment due to the promise of its drug candidate, and thus have hired many employees, but have not yet generated any significant revenue.

The results of the multivariate regression model are provided in Essay 2 and shown again in Table 5. It is observed that *ln(Partn)* and *ST* both have significant and positive associations with *ln(VO)* but not with *ln(FS)*. This suggests that both Strategic Timing of patents and Strategic Partnerships play a role in determining innovation performance, as measured by value output. There is little evidence of a significant effect of the controlling factor *Uncertainty* on *ln(VO)*, and will be tested further in the HLM, per the hypothesis that it serves as a moderator on the relationship between Open Innovation and value output. Using our key regressor, *ln(Partn)*, our key dependent variable, *ln(VO)* and *Uncertainty*, we subsequently present the results of our tests to determine the relationship between these three variables.

Table 6 shows the results of the HLM, with successive additions of *ln(Partn), Uncertainty* and the interaction term in each model as the regressors and *ln(VO)* as the dependent variable. Regarding our hypotheses, these results suggest that a Personalized Medicine firm's value output increases with its engagement in Strategic Partnerships. The coefficient of *ln(Partn)* is positive and significant in the multivariate regression and the first two models of the HLM, suggesting support for H1, specifically for Strategic Partnerships.

In order to draw inferences with respect to H2, we refer to the third model for Strategic Partnerships in Table 8 and observe that the interaction term is significant in Model 3. Post hoc probing to investigate the moderating effect of *Uncertainty* is performed by plotting significant interactions as suggested by Aiken & West (1991) (Figure 4). High uncertainty therapeutics firms generally exhibit a stronger link between *ln(Partn)* and *ln(VO),* providing support for H2. The lowered significance of *ln(Partn)* in the third model is explained by the interesting crossover interaction effect of medical device firms, which was caused by a single firm with a very large revenue and partnership number. This crossover effect is a potential avenue for future research, with would include more data points from a broader set of personalized medicine firms in different jurisdictions. These regression results and associated figure of the interaction effect of *Uncertainty* on *ln(VO)* elucidate the relative effect of uncertainty on the link between Strategic Partnerships and value output.

Discussion

We show that the use of the Open Innovation mechanisms of Strategic Partnerships by Personalized Medicine firms in British Columbia is associated with higher value outputs and is moderated by uncertainty. We observe that Selective Revealing and Strategic Timing of patents are positively associated with value output in our correlation and matched comparison analysis. This suggests that timing a patent early in a firm's formation can play an important role in a firm's commercialization success. We argue that, consistent with Ruckman and McCarthy (2016) and Hsu and Ziedonis (2008), Strategic Timing of patents acts to improve the reputational status of the recently founded firm, allowing it to emit positive signals and increase its chances of attracting alliance partners and investors.

Based on our regression results, the Open Innovation mechanism of Strategic Partnerships aids in the commercialization process of a science-based venture through reputational signalling and the acquisition of complementary assets through alliances. The importance of the acquisition of complementary assets in the commercialization efforts of firms with high technical uncertainty has been frequently observed in the innovation management literature (Maine & Garnsey, 2006; Perkmann & Walsh, 2007; Rasmussen, 2008; Pisano, 2010; Zobel, Balsmeier & Chesbrough, 2016). A novel finding from our research is that the relationship between Open Innovation and value capture is moderated by technical uncertainty. Although this may be implicitly understood in the context of biotherapeutics and the related Personalized Medicine industry, because of the high cost of clinical trials, this finding is likely to also be true in other science-based sectors such as quantum computing, artificial intelligence and advanced materials, which increases the external validity of our model to other industries of high technical uncertainty.

The Open Innovation mechanism of Strategic Timing is positively associated with value capture, which is consistent with the findings from Maine and Thomas (2017). However, McCarthy and Ruckman (2017) argue that to build positive reputational signals, a firm may need to extend its licensing timelines, potentially trading off early mover advantages in both patenting and licensing. Thus, further study into the Open Innovation mechanism of Strategic Timing as a method to attract alliance partners with complementary assets is warranted.

The value and execution of Open Innovation mechanisms has been questioned in the extant literature. Some authors are skeptical of Open Innovation practices, interestingly, for divergent reasons. West (2003) argues that closed, proprietary strategies are often preferred when firms are trying to optimize value capture. On the other hand, Gold (2019; 2021), argues for the benefits of a patent-free, open data model and references the success of the Structural Genomics Consortium in accelerating genomics research. A comparative study of science innovation ecosystems with and without open science alliances would be valuable to inform this debate.

Scholars in both camps have noted that Open Innovation theories to date have been underdeveloped and that observations noted in one context may not necessarily be transferrable to other contexts (Hopkins et al., 2011; Hopkins, Tidd & Nightingale, 2013; Coad et al., 2021). Furthermore, an Open Innovation policy question is whether the potential suppression in scientific advances suggested by some innovation scholars (Williams, 2013; Edwards, 2016) is worth risking for the increase in value capture by national and regional innovation ecosystems.

To address the need for improved external validity in the Open Innovation literature, we explore the boundary conditions of Open Innovation in this paper. In particular, we argue that Open Innovation practices are more valuable in contexts of high uncertainty. We observe that in the nascent and highly uncertain Personalized Medicine innovation ecosystem, cooperative strategies, especially in the early years of firm formation, can lead to higher future value outputs. Additional avenues for research that can further bolster the external validity of our conclusions can be drawn from exploratory work from other innovation management scholars, including Chesbrough and Bogers (2014) and Lee, Olson and Trimi (2012), who investigated the effects of Open Innovation strategies on overall ecosystem growth, and Bathelt and Cohendet (2014), who studied the physical settings in which Open Innovation activity occurred, and linked their findings to ecosystem value capture.

We address the criticism of Open Innovation literature set forth by Dahlander and Gann (2010): that the contexts chosen in the existing body of work are too often centered on American software companies such as Microsoft and the Linux Foundation. We study and apply Open Innovation theory and concepts to a separate and emergent Personalized medicine industry. Consistent with scholars who argue that uncertainty moderates strategic decisions (Hannah & Eisenhardt, 2018; Maine et al., 2015), we find the importance of Open Innovation to value output to be moderated by uncertainty. Specifically, we observe that firms which operate in environments of high uncertainty, and which employ Innovation mechanisms enjoy higher value outputs than firms which operate in environments of low uncertainty and who do not utilize these mechanisms.

Conclusion

Through examination of the emergence of the Personalized Medicine innovation ecosystem in British Columbia and the commercialization patterns and strategies of the therapeutics, diagnostics, medical device and digital health firms within it, we find evidence of the importance of Open Innovation mechanisms of Strategic Timing and Strategic Partnerships to value capture by Personalized Medicine ventures. We advance the Open Innovation dialogue by shedding light on the competing positions of authors such as Henkel et al. (2006) who note a positive correlation between early revealing of capabilities and firm competitiveness and others (West, 2003; Williams, 2013; Edwards, 2016) who dispute the logic of Open Innovation in emerging science fields. We find an Open Innovation strategy to be helpful in a science-based venture’s commercialization efforts, particularly for firms with highly uncertain technologies.

In addition to our scholarly contributions, our findings have important implications for practitioners and policy makers. Emerging innovation ecosystems open up enormous potential for social and economic value capture. In the case of Personalized Medicine, it could be the advent of a new paradigm of targeted patient care. The growth of a Personalized Medicine innovation ecosystem has significant potential for improved social and economic outcomes through more research, more knowledge-based jobs, infusions of capital, and heightened interest from international researchers and industry practitioners. We find that early patenting and strategic partnering is positively associated with value outputs for Personalized Medicine firms, moderated by the technical uncertainty of the firm. If these Open Innovation mechanisms are indeed critical to the commercialization success of these firms, then loosening constraints on patenting and facilitating the licensing of those patents for emerging science-based firms should be a serious consideration for innovation researchers and policymakers.

References

Alexy, O., George, G., & Salter, A. J. (2013). Cui bono? The selective revealing of knowledge and its implications for innovative activity. *Academy of Management Review*, *38*(2), 270-291.

Alexy, O., Bascavusoglu-Moreau, E. & Salter A. J. (2016). Toward an aspiration-level theory of open innovation. *Industrial and Corporate Change*, 25(2), 289–306.

Armellini, F., Kaminski, P. C., & Beaudry, C. (2014). The open innovation journey in emerging economies: an analysis of the Brazilian aerospace industry. *Journal of Aerospace Technology and Management*, *6*(4), 462-474.

Arora, A., & Merges, R. P. (2004). Specialized supply firms, property rights and firm boundaries. *Industrial and Corporate Change*, *13*(3), 451-475.

Autio, E. & Thomas, L. (2014). *Innovation Ecosystems*. The Oxford Handbook of Innovation Management.

Barge-Gil, A. (2013). Open strategies and innovation performance. *Industry and Innovation*, 20(7), 585-610.

Bathelt, H., & Cohendet, P. (2014). The creation of knowledge: local building, global accessing and economic development—toward an agenda. *Journal of Economic Geography*, *14*(5), 869-882.

Bianchi, M., Cavaliere, A., Chiaroni, D., Frattini, F., & Chiesa, V. (2011). Organisational modes for Open Innovation in the bio-pharmaceutical industry: An exploratory analysis. *Technovation*, *31*(1), 22-33.

Bjornali, E. S., Giones, F., & Billstrom, A. (2017). Reveal or conceal? signaling strategies for building legitimacy in cleantech firms. *Sustainability*, 9(10), 1815.

Bogers, M., Zobel, A. K., Afuah, A., Almirall, E., Brunswicker, S., Dahlander, L., ... & Hagedoorn, J. (2017). The open innovation research landscape: Established perspectives and emerging themes across different levels of analysis. *Industry and Innovation*, 24(1), 8-40.

Bowman, C., & Ambrosini, V. (2000). Value creation versus value capture: towards a coherent definition of value in strategy. *British Journal of Management*, *11*(1), 1-15.

Brunswicker, S., & Ehrenmann, F. (2013). Managing open innovation in SMEs: A good practice example of a German software firm. *International Journal of Industrial Engineering and Management*, 4(1), 33-41.

Bubela, T., & Cook-Deegan, R. (2015). Keeping score, strengthening policy and fighting bad actors over access to research tools. *Nature biotechnology*, *33*(2), 143-147.

Chan, C. M. (2013). From open data to open innovation strategies: Creating e-services using open government data. In 2013 *46th Hawaii International Conference on System Sciences*. IEEE.

Changyong, F. E. N. G., Hongyue, W. A. N. G., Naiji, L. U., Tian, C. H. E. N., Hua, H. E., & Ying, L. U. (2014). Log-transformation and its implications for data analysis. *Shanghai Archives of Psychiatry*, *26*(2), 105.

Chesbrough, H., & Bogers, M. (2014). *Explicating open innovation: Clarifying an emerging paradigm for understanding innovation. New Frontiers in Open Innovation*. Oxford: Oxford University Press.

Chesbrough, H., & Crowther, A. K. (2006). Beyond high tech: early adopters of open innovation in other industries. *R&D Management*, 36(3), 229-236.

Chesbrough, H. W. (2003). *Open innovation: The new imperative for creating and profiting from technology*. Harvard Business Press.

Chesbrough, H. (2020). Innovation Imperatives from Covid-19. Forbes. Retrieved from https://www.forbes.com/sites/henrychesbrough/2020/03/18/innovation-imperatives-from-covid-19/?sh=32e20d6d6fb1

Christensen, J., Olesen M. & Kjaer J. (2005). The industrial dynamics of open innovation – evidence from the transformation of consumer electronics. *Research Policy*, 34, 1533–1549.

Clausen, T., & Rasmussen, E. (2011). Open innovation policy through intermediaries: the industry incubator programme in Norway. *Technology Analysis & Strategic Management*, *23*(1), 75-85.

Coad, A., Nightingale, P., Stilgoe, J., & Vezzani, A. (2021). The dark side of innovation. *Industry and Innovation*, *28*(1), 102-112.

Cullis, P. (2015). *The personalized medicine revolution: how diagnosing and treating disease are about to change forever*. Greystone Books.

Dahlander, L., Frederiksen, L., & Rullani, F. (2008). Online communities and open innovation. *Industry and innovation*, *15*(2), 115-123.

Dahlander, L., & Gann, D.M., (2010). How open is innovation? *Research Policy*, 39 (6),699–709.

Freeman, C. (1989). *Technology policy and economic performance*. Great Britain: Pinter Publishers.

Edwards, A. (2016). Perspective: Science is still too closed. *Nature*, *533*(7602), S70.

Eisenhardt, K. M. (1989). Building theories from case study research. *Academy of Management Review*, 14(4), 532-550.

Ferreira, J. J., Fernandes, C. I., & Raposo, M. L. (2017). The effects of location on firm innovation capacity. *Journal of the Knowledge Economy*, *8*(1), 77-96.

Gimenez-Fernandez, E. M., & Sandulli, F. D. (2017). Modes of inbound knowledge flows: are cooperation and outsourcing really complementary? *Industry and Innovation*, *24*(8), 795-816.

Gold, E. R. (2021). The fall of the innovation empire and its possible rise through open science. *Research Policy*, *50*(5), 104226.

Gold, R. (2019). Should Universities Get Out of the Patent Business? *Centre for International Governance Innovation*. Retrieved from https://www.cigionline.org/articles/should-universities-get-out-patent-business

Gunday, G., Ulusoy, G., Kilic, K., & Alpkan, L. (2011). Effects of innovation types on firm performance. *International Journal of Production Economics*, *133*(2), 662-676.

Hagedoorn, J., Lokshin, B., & Zobel, A. (2014). The coalignment of open innovation with environmental contingencies and its effect on innovation performance. *Maastricht University Working Paper*.

Henkel, J. (2006). Selective revealing in open innovation processes: The case of embedded

Linux. *Research Policy*, 35(7), 953-969.

Henkel, J., Schöberl, S., & Alexy, O. (2014). The emergence of openness: How and why firms adopt selective revealing in open innovation. *Research Policy*, 43(5), 879-890.

Hoenig, D., & Henkel, J. (2015). Quality signals? The role of patents, alliances, and team experience in venture capital financing. *Research Policy*, *44*(5), 1049-1064.

Hopkins, M. M., Tidd, J., & Nightingale, P. (2013). Positive and negative dynamics of open innovation. In *Open Innovation Research, Management and Practice*. Imperial College Press London.

Hopkins, M. M., Tidd, J., Nightingale, P., & Miller, R. (2011). Generative and degenerative interactions: positive and negative dynamics of open, user-centric innovation in technology and engineering consultancies. *R&D Management*, *41*(1), 44-60.

Hsu, D. H., & Ziedonis, R. H. (2008). Patents as quality signals for entrepreneurial ventures. *Academy of Management Proceedings* 2008(1), 1-6.

Jung, D., Kim, Y., Suh, Y., & Kim, Y. (2016). Perceived innovation barriers and open innovation performance: insights from Korea. *International Journal of Knowledge-Based Development*, *7*(2), 125-142.

ICO Therapeutics Inc. (2010). *Dosing regimens for treating and preventing ocular disorders using c-raf antisense*. ICO Therapeutics.

Kapoor, R., & Furr, N. R. (2015). Complementarities and competition: Unpacking the drivers of entrants' technology choices in the solar photovoltaic industry. *Strategic Management Journal*, *36*(3), 416-436.

Kim, N. K., & Ahn, J. M. (2019). What facilitates external knowledge utilisation in SMEs?–An optimal configuration between openness intensity and organisational moderators. *Industry and Innovation*, 1-25.

Kotha, S., & Srikanth, K. (2013). Managing A Global Partnership Model: Lessons from the Boeing 787 'Dreamliner' Program. *Global Strategy Journal*, 3(1), 41-66.

Knowles, L., Luth, W., & Bubela, T. (2017). Paving the road to personalized medicine: recommendations on regulatory, intellectual property and reimbursement challenges. *Journal of Law and the Biosciences*, 4(3), 453-506.

Laursen, K., & Salter, A. (2006). Open for innovation: the role of openness in explaining innovation performance among UK manufacturing firms. *Strategic Management Journal*, *27*(2), 131-150.

Laursen, K., & Salter A. (2014). The paradox of openness: appropriability, external search and collaboration. *Research Policy*, 43(5), 867–878.

Lee, S. M., Olson, D. L., & Trimi, S. (2012). Co-innovation: convergenomics, collaboration, and co-creation for organizational values. *Management Decision*, 50(5), 817-831.

Maine, E., & Garnsey, E. (2006). Commercializing generic technology: The case of advanced materials ventures. *Research Policy*, 35(3), 375-393.

Maine, E., Lubik, S., & Garnsey, E. (2012). Process-based vs. product-based innovation: Value creation by nanotech ventures. *Technovation*, 32(3-4), 179-192.

Maine, E., & Seegopaul, P. (2016). Accelerating advanced-materials commercialization. *Nature Materials*, 15(5), 487.

Maine, E., Soh, P. H., & Dos Santos, N. (2015). The role of entrepreneurial decision-making in opportunity creation and recognition. *Technovation*, *39*, 53-72.

Maine, E., & Thomas, V. J. (2017). Raising financing through strategic timing. *Nature Nanotechnology*, 12(2), 93.

Mawson, S., & Brown, R. (2017). Entrepreneurial acquisitions, open innovation and UK high growth SMEs. *Industry and Innovation*, *24*(4), 382-402.

McCarthy, I. P., & Ruckman, K. (2017). Licensing speed: its determinants and payoffs. *Journal of Engineering and Technology Management*, *46*, 52-66.

Moore, J. F. (1993). Predators and prey: a new ecology of competition. *Harvard Business Review*, 71(3), 75-86.

Neter, J., Kutner, M. H., Nachtsheim, C. J., & Wasserman, W. (1996). Applied linear statistical models.

Oh, D. S., Phillips, F., Park, S., & Lee, E. (2016). Innovation ecosystems: A critical examination. *Technovation*, 54, 1-6.

Pahnke, E. C., Katila, R., & Eisenhardt, K. M. (2015). Who takes you to the dance? How partners' institutional logics influence innovation in young firms. *Administrative Science Quarterly*, 60(4), 596-633.

Park, U. D., Borah, A., & Kotha, S. (2016). Signaling revisited: The use of signals in the market for IPOs. *Strategic Management Journal*, 37(11), 2362-2377.

Perkmann, M., & Schildt, H. (2015). Open data partnerships between firms and universities: The role of boundary organizations. *Research Policy*, *44*(5), 1133-1143.

Perkmann, M., & Walsh, K. (2007). University–industry relationships and open innovation: Towards a research agenda. *International Journal of Management Reviews*, 9(4), 259-280.

Pierrard, S., & Lavallee, E. (2019). Open innovation: A shift to new intellectual property models? Lavery Lawyers. Retrieved from https://www.lavery.ca/en/publications/our-publications/3155-open-innovation-a-shift-to-new-intellectual-property-models.html

Pisano, G. (2006). Profiting from innovation and the intellectual property revolution. *Research Policy*, 35(8), 1122-1130.

Pisano, G. P. (2010). The evolution of science-based business: innovating how we innovate. *Industrial and Corporate Change*, 19(2), 465-482.

Priem, R. L. (2007). A consumer perspective on value creation. *Academy of Management Review*, *32*(1), 219-235.

Rasmussen, E. (2008). Government instruments to support the commercialization of university research: Lessons from Canada. *Technovation*, *28*(8), 506-517.

Ruckman, K., & McCarthy, I. (2016). Why do some patents get licensed while others do not? *Industrial and Corporate Change*, *26*(4), 667-688.

Sampat, B., & Williams, H. L. (2019). How do patents affect follow-on innovation? Evidence from the human genome. *American Economic Review*, *109*(1), 203-36.

Schiffauerova, A., & Beaudry, C. (2011). Star scientists and their positions in the Canadian biotechnology network. *Economics of Innovation and New Technology*, *20*(4), 343-366.

Swan, M. (2009). Emerging patient-driven health care models: an examination of health social networks, consumer personalized medicine and quantified self-tracking. *International Journal of Environmental Research and Public Health*, 6(2), 492-525.

Vahter, P., Love, J. H., & Roper, S. (2014). Openness and innovation performance: are small firms different? *Industry and Innovation*, *21*(7-8), 553-573.

West, J. (2003). How open is open enough?: Melding proprietary and open source platform strategies. *Research Policy*, 32(7), 1259-1285.

West, J. (2014). *Open innovation: Learning from alliance research. In Open Innovation through Strategic Alliances*. Palgrave Macmillan, New York.

West, J., & Gallagher, S. (2006). Challenges of open innovation: the paradox of firm investment in open-source software. *R&D Management*, *36*(3), 319-331.

Williams, H. L. (2013). Intellectual property rights and innovation: Evidence from the human genome. *Journal of Political Economy*, *121*(1), 1-27.

Williams, H. L. (2016). Intellectual property rights and innovation: Evidence from health care markets. *Innovation Policy and the Economy*, 16(1), 53-87.

Yigitcanlar, T., Sabatini-Marques, J., Kamruzzaman, M., Camargo, F., Moreira da-Costa, E., Ioppolo, G., & Palandi, F. E. D. (2018). Impact of funding sources on innovation: evidence from Brazilian software companies. *R&D Management*, *48*(4), 460-484.

Zobel, A. K., Balsmeier, B., & Chesbrough, H. (2016). Does patenting help or hinder open innovation? Evidence from new entrants in the solar industry. *Industrial and Corporate Change*, *25*(2), 307-331.

Keywords Used to Determine Personalized Medicine Capabilities

‘targeted treatments’, ‘sensitive diagnostics’, ‘genetic testing’, ‘biomarker testing’, ‘gene delivery’, ‘genomics based’, ‘microbiomics’, ‘metabolomics’, ‘antigen targeting’, ‘guided optimization’, ‘precision medicine’, ‘precision health’, ‘next-generation sequencing’, ‘microarray’, ‘machine learning’, ‘pharmacogenomics’, ‘cell signaling’, ‘customized’, ‘translational cancer research’, ‘early cancer detection’, ‘real time monitoring’, ‘tracking’, ‘home monitoring’, ‘medication monitoring’, ‘digital profile’, ‘body contours’, ‘data provenance’ and ‘rapid diagnostics’

Figures

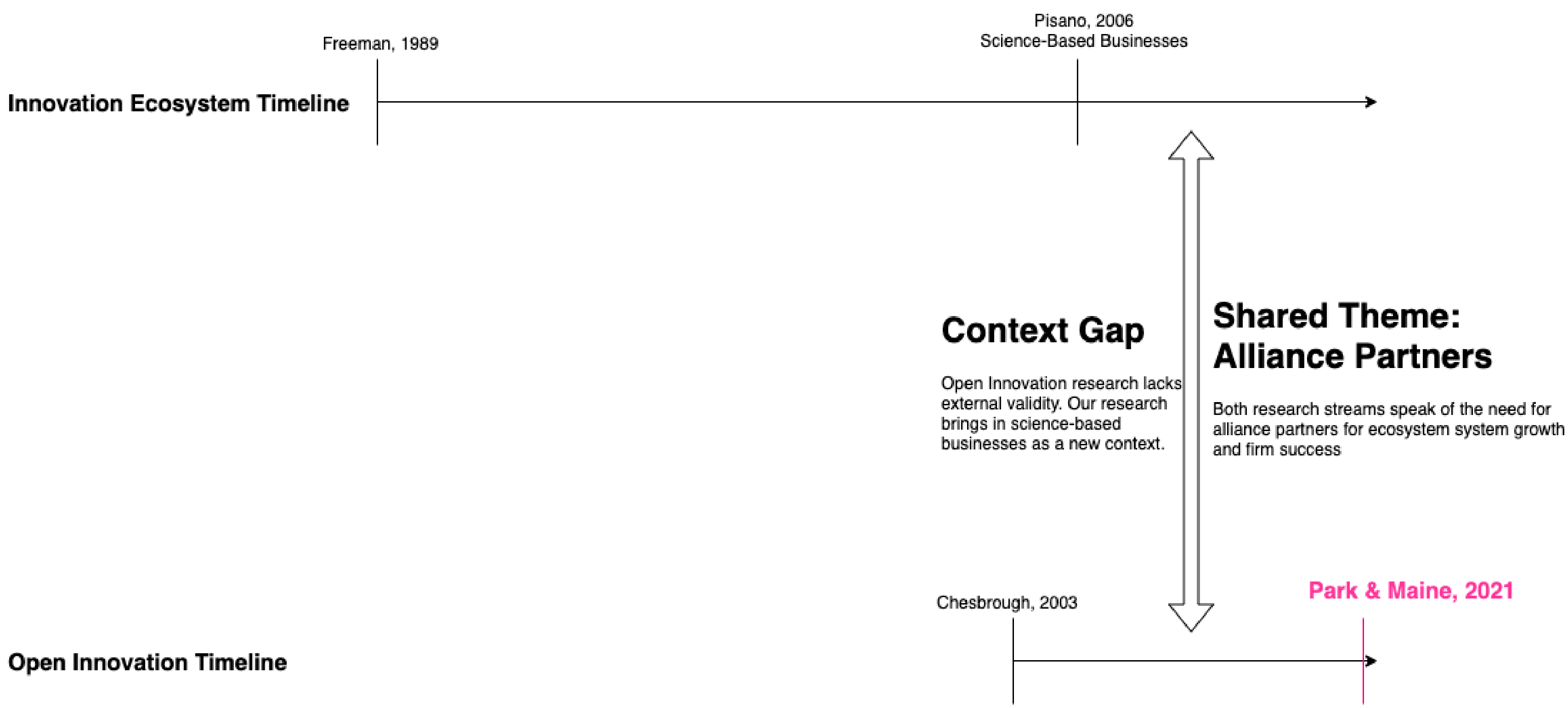

Figure 1. **The current state and missing gaps in Innovation Ecosystem and Open Innovation literature.**

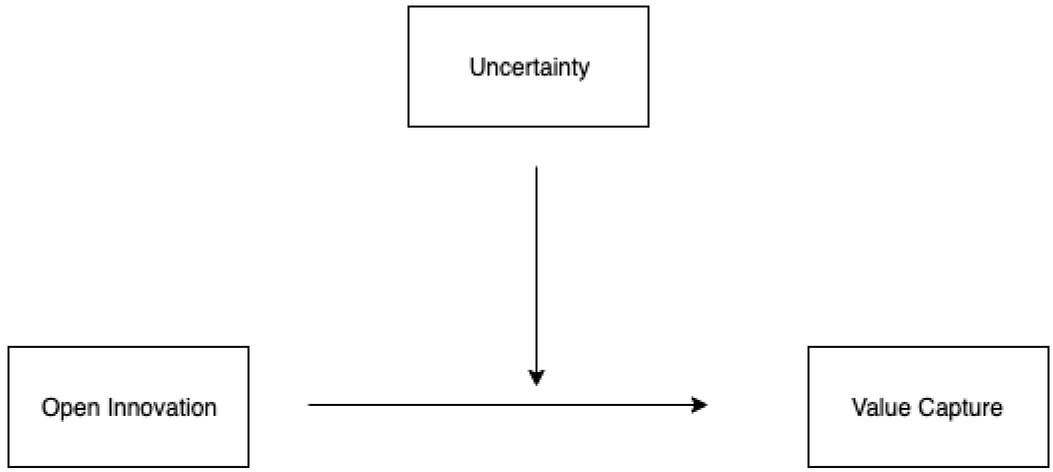

Figure 2. Open Innovation -> Value Capture Model

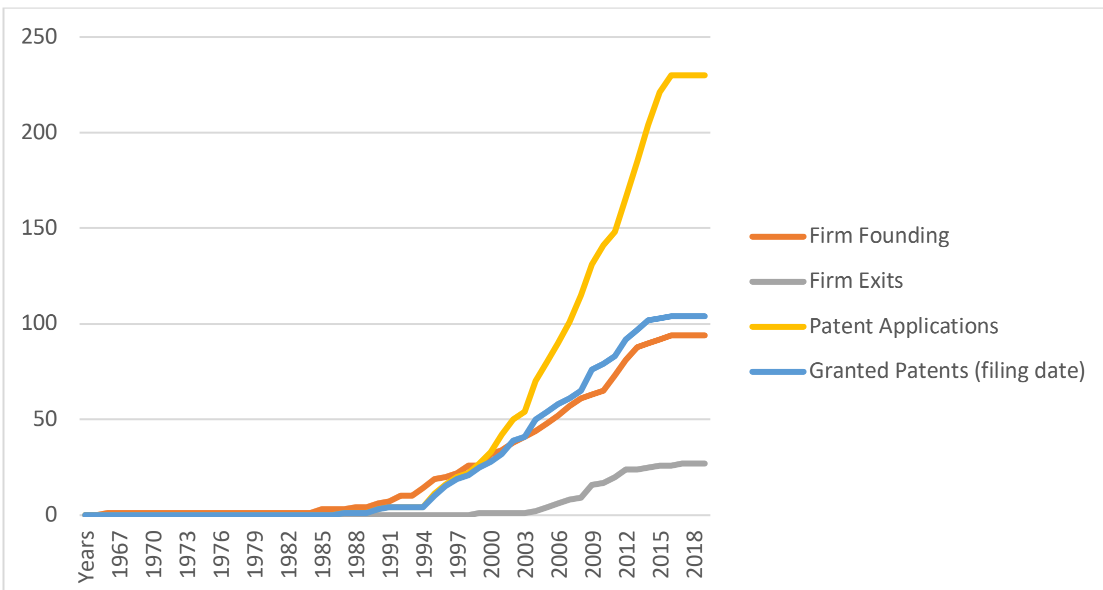

Figure 3. Open Innovation and Industry Emergence: Personalized Medicine Firms and U.S. Patents in British Columbia

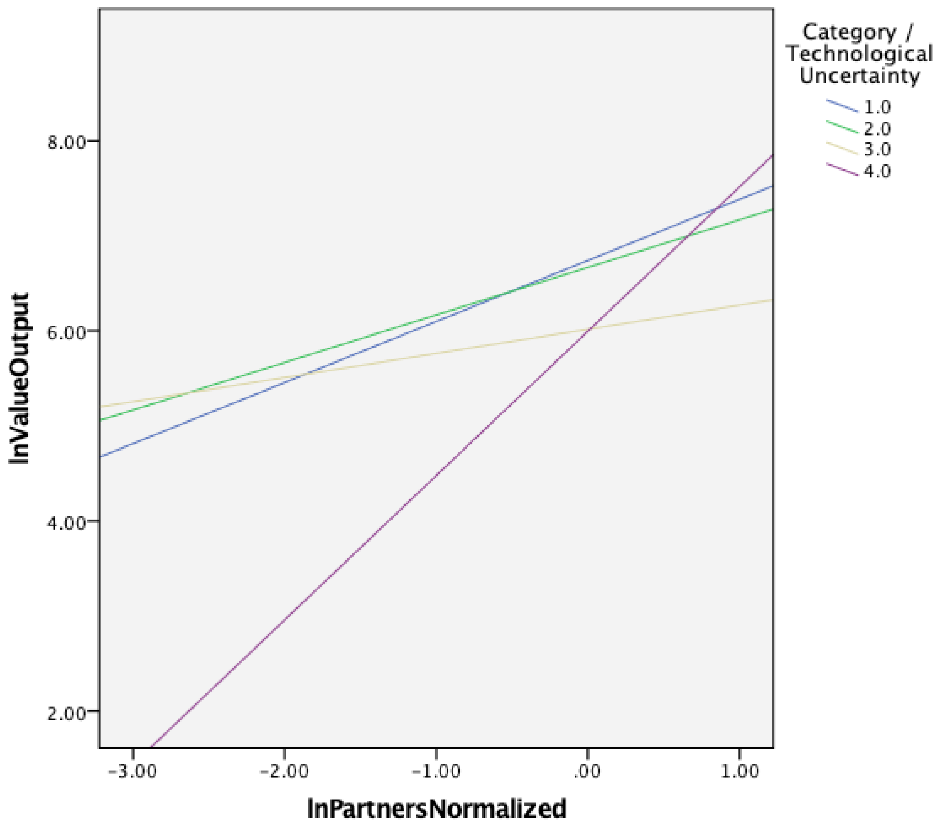

Figure 4. **The interactive effect of uncertainty on value output.**

Tables

Table 1. Personalized Medicine Industry Subsectors

Subsector	Definition	Examples	Level of Uncertainty
Therapeutics	Firms developing customized drug or device-based treatments for disease	AbCellera, Acuitas Therapeutics, Zymeworks	High
Diagnostics	Firms providing customized point of care, ‘omics’ testing, instrumentation or laboratory tests or supplies for determining disease state	Boreal Genomics, Augurex, Microbiome Insights, Precision Nanosystems	Medium
Medical Device	Firms developing customized implantable or external device-based treatments for disease	Life360 Innovations, Microdermics	Medium
Digital Health	Firms providing software or mobile solutions for housing or manipulating specific patient data, or diagnostic services using digital sensors	PHEMI, Headcheck Health	Low

Table 2. **Skewness and kurtosis results of data transformation**

	VO	FS	Partn	ln(VO)	ln(FS)	ln(Partn)
Skewness	2.709	5.921	1.077	-.558	.355	-.084
Kurtosis	7.777	37.021	.254	.685	.705	-1.201

N=63

Table 3. **Descriptive Statistics**

	ln(VO)	ln(FS)	ln(Partn)	Uncertainty	ST	SR	Mean	SD
ln(VO)	1.00						6.066	1.283
ln(FS)	.478**	1.00					3.396	1.316
ln(Partn)	.374**	.100	1.00				-.923	1.000
Uncertainty	-.027	-.258*	.146	1.00			1.889	.969
ST	.382**	.279*	-.057	-.217	1.00		.49	.504
SR	.344*	.261*	.022	-.221	.671**	1.00	.68	.469

N = 63. ** $p < 0.01$; * $p < 0.05$.

Table 4. Firm Data on the Top 20 Active BC Companies Ranked by Value Output

Name	VC Raised mil. USD	Founding Year	Value Output	Select Revealing	Strategic Timing	Category	Spinout
StemCell Technologies		1993	6000	Y	Y	Therapeutics	BC Cancer Agency
Celator	57.2	1999	5263	Y	Y	Therapeutics	BC Cancer Agency
Zymeworks	181.7	2003	4167	Y	Y	Therapeutics	
Aquinox Pharmaceuticals	134.3	2003	3167	Y	Y	Therapeutics	UBC
AbCellera	0.9	2012	2500	Y	Y	Therapeutics	UBC
Wiiv Wearables Inc	11.9	2014	2375	Y	Y	Medical Device	
Telus Health		2008	1600	Y	Y	Digital Health	
Claris Healthcare		2012	1533	N	N	Digital Health	
Precision Nanosystems	19.4	2010	1438	Y	Y	Diagnostic	UBC
PHEMI	25	2013	1400	N	N	Digital Health	
symvivo		2013	1400	Y	Y	Therapeutics	
Qu Biologics	10.2	2007	1291	Y	Y	Therapeutics	

Name	VC Raised mil. USD	Founding Year	Value Output	Select Revealing	Strategic Timing	Category	Spinout
Aspect Biosystems	1	2013	1000	N	N	Therapeutics	UBC
Microdermics	1	2014	1000	Y	Y	Medical Device	UBC
Arbutus Biopharma	116	2007	973	Y	Y	Therapeutics	UBC
Verisante Technology Inc		2006	858	Y	Y	Diagnostic	UBC
VidaTherapeutics	8.1	2008	840	Y	Y	Therapeutics	UBC
Navigate Surgical		2011	800	Y	Y	Diagnostic	
Boreal Genomics	31.4	2007	773	Y	Y	Diagnostic	UBC
Acuitas Therapeutics		2009	630	Y	Y	Therapeutics	UBC

Value output is 2020 revenue divided by the difference between the year of data collection (2020) and the year of firm founding. VC Raised mil. USD was collected in 2020.

Table 5. Multivariate regression model results (coefficients)

	ln(VO)	ln(FS)
ln(Partn)	.468**	.241
	(.167)	(.192)
ST	.910**	.628
	(.334)	(.384)
Uncertainty	-.025	-.228
	(.181)	(.209)

N=63. ** p < 0.01; * p < 0.05. Standard errors in parentheses.

Table 6. Hierarchical Linear Modeling results

	ln(VO)		
	Model 1	Model 2	Model 3
ln(Partn)	.478**	.514**	.158
	(.171)	(.177)	(.103)
Uncertainty		-.152	-2.837**
		(.187)	(.276)
ln(Partn)_x_Uncertainty			.456**
			(.044)

N = 63. ** p < 0.01; * p <0.05. Standard errors in parentheses.

Conclusion

This dissertation examines the antecedents, outputs and process of the translation of breakthrough invention to innovation through the development of a novel science innovation framework and an empirical analysis of the emerging personalized medicine innovation ecosystem. While previous work has been conducted in the innovation ecosystem and Open Innovation literature on firm growth and in the context of American software firms, little is understood about the inputs, processes and outcomes related to the translation of invention to innovation in emerging science-based industries. Thus, my dissertation explores the following questions: “what factors influence the translation of science invention to innovation?”, “does the level of technical uncertainty of personalized medicine firms have an influence on innovation performance outcomes?” and “why and under what conditions do the Open Innovation mechanisms of selective revealing, strategic timing and strategic partnering affect value capture by personalized medicine firms?”.

The first essay, titled, “Invention to Innovation: Creating the Conditions for Impact from University Science” presents a novel framework on science innovation supported by a comprehensive bibliographic review of the Technology and Innovation Management field and evidence of current debates and practice drawn from the 2020 R&D Management Symposium. This study is motivated by the fact that universities have significant potential to deliver economic and social benefits (Bonnaccorsi & Piccaluga, 1994; Langford et al., 2006; Barirani, Beaudry & Agard, 2017; Thomas et al., 2020) but government funding for university research is insufficiently being translated into these desired outcomes (Arora, 2019; Guzman & Stern, 2020). This framework highlights the key inputs and outputs of science-based innovation and identifies salient mediators that influence the economic and social outcomes of the invention to innovation process and has relevance to the other two essays that comprise this dissertation.

Based on this framework, we offer several recommendations for scholars, university leadership, scientist entrepreneurs and innovation policymakers who can work in tandem to improve the effectiveness of government funded scientific research. Given the importance of scientist-entrepreneurs in generating the inputs to the invention to innovation process and the path-dependent nature of the decisions they make in the research lab, they can begin to develop the entrepreneurial capabilities necessary to support the commercialization of their inventions while incubating at their universities. Relatedly, innovation policy makers can support these scientist-entrepreneurs by funding specialized entrepreneurial training programs and by funding strategic intellectual property protection and patenting programs at University Technology Licensing Offices that align the economic incentives of scientist-entrepreneurs and their universities. It is also important for university leadership to craft their IP policies to align their motivations with those of scientist-entrepreneurs. Furthermore, they can create promotion and tenure frameworks that allow entrepreneurship activities to partially fulfill research and teaching obligations for scientists. Given the importance of star scientists in starting and nurturing science-based ecosystems and networks (Schiffauerova & Beaudry, 2011), it is critical for innovation ecosystem stakeholders to support these scientists and the growth of their spinoff ventures in order to achieve the innovation performance outcomes that drive economic and societal impacts.

The second essay, titled, “Impact of Uncertainty on Innovation Performance: Evidence from an Emerging Personalized Medicine Ecosystem” establishes, to my knowledge, one of the first analyses of a personalized medicine innovation ecosystem and empirically tests the relationship between uncertainty and innovation performance, elucidating the role technical uncertainty and its associated controlling factors, strategic timing of patents and strategic partnerships play in firm value capture. I find evidence of the influence of technical uncertainty on innovation performance by personalized medicine firms, and that strategic timing of patents and strategic partnerships are important factors in this relationship. The configuration of these three independent variables (uncertainty, strategic timing and strategic partnerships) and their roles on value output are further investigated in the third essay. The findings in this study are supported by the creation of a novel and custom dataset of British Columbia personalized medicine firms as no such dataset was in existence.

The controlling factors in this quantitative analysis, strategic timing of patents and strategic partnerships, are further explored through a qualitative, case-based study on two exemplars in the British Columbia personalized medicine innovation ecosystem: AbCellera and Zymeworks. These firms utilized strategic timing of patents and strategic partnerships to mitigate uncertainty and enhance innovation performance. These exemplars successfully acquired numerous early partnerships to extend their technical capabilities, reduce technical and market uncertainty and drive early revenue as they built their ambitious therapeutics pipelines. This strategy of actively de-risking clinical development processes could be extensible to other science-based ventures and contexts of high technical uncertainty and is a potentially fruitful area for future research.

These findings have several implications for scientist-entrepreneurs and policy makers. Scientist-entrepreneurs with nascent ventures of high technical uncertainty, such as personalized medicine ventures, can consider early strategic partnership opportunities to de-risk their long-term prospects through early, recurring revenue. These partnerships can be enabled by signalling venture quality through the strategic timing of patents. Early iterations of an envisaged, longer term therapeutic that have the potential to generate revenue can be leveraged to attract alliance partners and produce short term funding, which is a real options approach that has been explored in previous research (McGrath, 2003). Innovation policy makers can support these scientist-entrepreneurs and their contributions to the growth of a high potential science-based innovation ecosystem by funding and helping University Technology Licensing Offices to craft IP protection policies that not only produce benefits to the university but incentivize academic scientists to pursue the commercialization of their breakthrough inventions.

While the importance of the roles of uncertainty, strategic timing of patents and strategic partnerships is observed in the second essay, the specific configuration of these variables requires further investigation, which is the motivation for the third essay. The third essay, titled, “When and Whether to Reveal: Open Innovation Mechanisms Within an Emerging Personalized Medicine Innovation Ecosystem” extends the findings from the second essay and organizes the input and outcome variables in a novel model. This model shows a positive relationship between Open Innovation and value capture, moderated by uncertainty. By empirically testing this relationship, it is found that the Open Innovation mechanisms of strategic partnerships and strategic timing of patents positively affect value capture, but this effect is heterogenous across firms of varying uncertainty. This essay also incorporates a discussion on the Structural Genomics Consortium, which has been used as a case study to support an opposing viewpoint that patenting is counterproductive to open data exchange and that suppressing it actually enables Open Innovation; some scholars who support this opposing viewpoint suggest that patenting and Open Innovation are immiscible (Perkmann & Schildt, 2015; Williams, 2013; Sampat & Williams; 2019).

The third essay affirms the importance of patenting in the personalized medicine context and makes a distinction between “open data” and “open science”, where the latter is conducive to Open Innovation through patenting. It is important to note that numerous studies have been conducted supporting the use of patents as viable proxies for Open Innovation (Pierrard & Lavallee, 2019; Chesbrough, 2020; Bjornali et al., 2017), particularly due to their usefulness in signaling venture quality and attracting alliance partners (Hsu & Ziedonis, 2008; Park et al., 2016). Given the opposing viewpoints on the role of patenting in value creation, policy makers would benefit from carefully considering these perspectives, and shaping intellectual property and funding policies based on the specific characteristics of the ecosystems they wish to support, and to actively monitor the effects of their policies on the innovation outcomes of these ecosystems.

Like the previous two essays, these findings have important implications for scientist-entrepreneurs and policy makers. I argue that the Open Innovation mechanisms of strategic patenting and strategic partnerships are positively associated with innovation performance for personalized medicine firms, and that this relationship is particularly pronounced for firms that operate under conditions of high uncertainty. Innovation policy makers can pay close attention to these high uncertainty therapeutics firms. For instance, by designing and funding IP policies that loosen constraints on patenting and facilitate licensing of those patents to downstream alliance partners. Scientist-entrepreneurs can also consider these findings when deciding whether and when to patent their inventions, particularly if they are commercializing high uncertainty therapeutics and are trying to signal to downstream alliance partners that their ventures are of high quality.

Across these three essays and referring to the inputs, mediators and outputs of the science innovation framework in the first essay, several recommendations are proposed for key stakeholders in the science-based business and personalized medicine innovation ecosystems. First, innovation scholars can conduct more empirical work on novel, understudied metrics such as the achievement of global health outcomes and sustainability goals to measure the broad impact of inputs to the invention to innovation process. Second, university leadership can support academic scientist entrepreneurs by better aligning promotion and tenure decisions with entrepreneurship activities, and by creating a well-defined patenting policy that bridges the commercial incentives of both the scientist entrepreneur and the university. Third, scientist entrepreneurs can seek early, strategic patenting and partnerships to mitigate the high costs and long timelines that are associated with science-based ventures, and to enhance the value capture potential of their firms. Lastly, innovation policy makers can support the growth of emergent science-based ecosystems such as personalized medicine, by carefully designing patenting policies that balance the commercial value of patent protection and the open science value of fluid data exchange, by funding specialized entrepreneurial training programs for academic scientists, and by funding and guiding University Technology Licensing Office programs to produce IP policies that align the motivations of the university, their academic scientists and the regional and national innovation ecosystems.

References

Arora, A., Belenzon, S., Patacconi, A., & Suh, J. (2019). Why the US innovation ecosystem is slowing down. Harvard Business Review.

Barirani, A., Beaudry, C., & Agard, B. (2017). Can universities profit from general purpose inventions? The case of Canadian nanotechnology patents. *Technological Forecasting and Social Change*, *120*, 271-283.

Bjornali, E. S., Giones, F., & Billstrom, A. (2017). Reveal or conceal? signaling strategies for building legitimacy in cleantech firms. Sustainability, 9(10), 1815.

Bonaccorsi, A., & Piccaluga, A. (1994). A theoretical framework for the evaluation of university-industry relationships. R&D Management, 24(3), 229-247.

Chesbrough, H. (2020). Innovation Imperatives from Covid-19. Forbes. Retrieved from https://www.forbes.com/sites/henrychesbrough/2020/03/18/innovation-imperatives-from-covid-19/?sh=32e20d6d6fb1

Guzman, J., & Stern, S. (2020). The State of American Entrepreneurship: New Estimates of the Quantity and Quality of Entrepreneurship for 32 US States, 1988–2014. American Economic Journal: Economic Policy, 12(4), 212-43.

Hsu, D. H., & Ziedonis, R. H. (2008, August). Patents as quality signals for entrepreneurial ventures. In Academy of Management Proceedings (Vol. 2008, No. 1, pp. 1-6). Briarcliff Manor, NY 10510: Academy of Management.

Langford, C. H., Hall, J., Josty, P., Matos, S., & Jacobson, A. (2006). Indicators and outcomes of Canadian university research: Proxies becoming goals?. *Research Policy*, *35*(10), 1586-1598.

McGrath, R. G., & Boisot, M. (2003). Real options reasoning and the dynamic organization: Strategic insights from the biological analogy. *Leading and managing people in the dynamic organization*, *201*.

Park, U.D., Borah, A. and Kotha, S., 2016. Signaling revisited: The use of signals in the market for IPO s. Strategic Management Journal, 37(11), pp.2362-2377.

Perkmann, M., & Schildt, H. (2015). Open data partnerships between firms and universities: The role of boundary organizations. Research Policy, 44(5), 1133-1143.

Pierrard, S., & Lavallee, E. (2019). Open innovation: A shift to new intellectual property models? Lavery Lawyers. Retrieved from https://www.lavery.ca/en/publications/our-publications/3155-open-innovation-a-shift-to-new-intellectual-property-models.html

Sampat, B., & Williams, H. L. (2019). How do patents affect follow-on innovation? Evidence from the human genome. American Economic Review, 109(1), 203-36.

Thomas, V. J., Bliemel, M., Shippam, C., & Maine, E. (2020). Endowing university spin-offs pre-formation: Entrepreneurial capabilities for scientist-entrepreneurs. *Technovation*, 96-97, 102153.

Thongpapanl, N. T. (2012). The changing landscape of technology and innovation management: An updated ranking of journals in the field. Technovation, 32(5), 257-271.

Williams, H. L. (2013). Intellectual property rights and innovation: Evidence from the human genome. Journal of Political Economy, 121(1), 1-27.