Coping with Unresolvable Uncertainty: A Situational Analysis of Regenerative Medicine Venturing Activity

Abstract

Acquiring resources, such as knowledge, is a fundamental entrepreneurial task during venture development. However, high levels of uncertainty challenge resource identification and access, hence collaboration and knowledge exchange mechanisms are valuable. During high levels of perceived environmental uncertainty, entrepreneurs and new ventures are required to develop coping strategies to ensure venture formation and growth. Yet, entrepreneurial coping during high uncertainty is an understudied process. The regenerative medicine (RM) sector represents a unique context for studying entrepreneurial activity under high levels of uncertainty. We consider how uncertainty in RM venturing affects entrepreneurial behavior. Informed by long-form, narrative interviews, we propose a process model of RM venturing linking uncertainty, university culture, collaboration and coping. The use of selective revealing in RM venturing, and the effect of different coping responses on resource assembly and collaborative knowledge, is considered. Our findings advance theories of venture development during high uncertainty.

Keywords: uncertainty, coping, collaboration, knowledge, venturing, entrepreneur

Introduction

In high uncertainty environments, entrepreneurs struggle to identify which resources to assemble and coordinate (Alvarez and Barney, 2005). New ventures must acquire key resources such as finance, knowledge and partnerships (Jarillo, 1989), but high levels of perceived environmental uncertainty (PEU) inhibit entrepreneurial behavior and sense making (Milliken, 1987). As such, collaboration and knowledge exchange mechanisms become especially valuable for the development of deep capabilities needed to exploit opportunities (Powell *et al*, 1996; George *et al*, 2008). When PEU is high, entrepreneurs and ventures must develop coping mechanisms to avoid paralysis and ensure venture formation and growth. Despite important implications for theories of entrepreneurial behavior and venture growth, the development of entrepreneurial coping strategies under high uncertainty has not been rigorously studied.

The regenerative medicine (RM) sector represents a fruitful context for studying entrepreneurial activity under extremely high levels of PEU. RM research, which often involves the use of stem cells, is *"the process of creating living, functional tissues to repair or replace tissue or organ function lost due to age, disease, damage or congenital defects"* (NIH, 2006). RM is expected to address unmet clinical needs, enhance human health, and generate significant commercial benefits. However, extremely high levels of uncertainty have limited the development of the RM industry. Despite active research clusters in numerous geographic locations, including the UK (Jennifer, 2011), venturing has been slow and the venturing process unclear.

Venture development in RM has not been well studied. We study how uncertainty affects entrepreneurial behavior through a situational analysis of resource assembly in RM venturing activity. In particular, we ask two questions. First, what are the unique aspects of resource assembly in RM venturing? Second, how does knowledge, accessed through collaborations and

networks, affect RM venture formation and growth? Informed by a pilot survey and long-form narrative interviews, we propose a RM venturing process model. The results point towards the development of specific coping strategies to address high levels of PEU. These are linked to the development of collaborative knowledge during venture formation and growth. Our study opens new research directions linking entrepreneurial sense-making to venture growth when uncertainty cannot be resolved by information gathering or analysis. It specifically builds on recent investigations on selective revealing as an alterative form of collaboration (Alexy *et al*, 2013).

Contributions

This research makes three contributions to the scholarly literature. First, we investigate entrepreneurial activity in an understudied field characterized by unusually high uncertainty. Second, this study advances theories of venture development by proposing a preliminary model linking uncertainty, collaboration and coping. Third, we extend university-industry scholarship by showing the link between university culture and venture coping strategies.

Our research also provides important practical contributions to RM practitioners and technology transfer offices (TTOs).

Venturing in the Regenerative Medicine Field

The RM industry faces complex political and social forces, uncertain regulatory frameworks, unresolved intellectual property (IP) rights issues, and untested production and distribution systems (Hogle, forthcoming 2014). The investment and infrastructure requirements of RM commercialization have favored entrepreneurial activities with explicit links to university research programs. These ties, along with the complex technological innovations of RM research and the uncertain venturing process, create numerous development challenges for RM

entrepreneurs.

The dependency on the larger institution may create resource assembly challenges for new technology ventures (Powell *et al*, 1996). These firms must operate with little or no slack in their resource pool, limiting product-market and business model exploration and testing (George, 2005; Bock *et al*, 2012). The perception of high risk in RM venturing has limited investments by venture capitalists (VCs) and pharmaceutical companies. This has created a capabilities gap between RM innovation and commercialization (Mittra and Tait, 2012). Entrepreneurs may compensate for resource scarcity by accessing social networks to legitimize organizational narratives and access knowledge and financial resources (Aldrich and Martinez, 2001; Lounsbury and Glynn, 2001). We expect that RM entrepreneurs and ventures will rely on collaboration and networks to access resources, including knowledge, in order to exploit opportunities. The processes, however, have not been carefully investigated within the context of RM venturing activity.

Methods

To explore sense-making and behavioral processes, we utilize a primarily qualitative approach to better develop insights into socially constructed knowledge and events (Locke, 2001). A small pilot survey confirmed the relevance of key constructs, but the primary dataset consists of long-form, narrative interviews (McCracken, 1988).

Data

Information about the complete set of qualitative informants is provided in Table 1. This includes role, informant type, organizational affiliation and location.

Table 1 here

The lead author conducted face-to-face, long-form narrative interviews with informants between November 2012 and September 2013. Interviews were conducted in private facilities to prevent interruptions and ensure confidentiality. Informants were asked to tell their story of their participation in the commercialization of regenerative medicine innovation. Informants were given complete freedom to recount their narrative without interruption and with limited or no further direction. This narrative interview approach was utilized to minimize investigator bias, increase informant comfort and encourage informants to recount their own story in their own words, allowing them to focus on self-identified areas of interest. Legal and ethical controversies associated with RM require an especially sensitive approach to the collection of qualitative data. The open-ended, non-directed narrative approach helps to reduce staged responses and social desirability bias (Podsakoff *et al*, 2003). Informants were encouraged to talk until they felt that they had reached a self-determined conclusion. Following the informant-determined end of the main narrative, some informants were prompted to provide additional details on key areas of interest. Field notes were generated during and immediately after each interview to provide *in situ* interpretation to complement transcript coding. The duration of the interviews ranged from 16 minutes to 111 minutes, with the average length being approximately 60 minutes.

A small-scale pilot survey was utilized to confirm the relevance of key constructs and frame the coding of the narrative interviews. The survey was designed to elicit data on informant's perceptions of RM venturing. Survey questions included both closed and open-ended questions on facilitative and inhibitive factors to RM venturing activity. Question types and order were carefully considered to reduce common method biases (Podsakoff *et al*, 2003). The survey

was pre-tested by administration to an RM industry expert and an academic scientist to ensure clarity of design and relevance of the questions (Fowler, 2009).

The lead author obtained information on target informants from Edinburgh BioQuarter, the commercialization arm of research output from the College of Medicine and Veterinary Medicine at The University of Edinburgh. Informants were selected based on direct involvement in the commercialization of RM in one of the following 4 categories: 1) RM entrepreneurs, 2) academic scientists, 3) RM/life science support entities, 4) RM companies. We excluded for-profit third party support firms such as consultancies. We also excluded full-time students, even those with significant entrepreneurial intent. This ensured efficient and effective saturation of categories, providing sufficient data to account for all aspects of the phenomenon (Morse *et al*, 2002). Informants were not provided detailed information about the interview to prevent prejudicial preparation of information or materials. The final dataset includes 23 long-form narratives.

Procedures

Coding of the qualitative interviews was informed by the results of the pilot survey. Survey informants were selected from the RM informant target list and e-mailed regarding their participation. We invited 26 individuals to participate in the survey and received 15 responses, which represents a 58% success rate. Referrals by first-wave respondents to additional industry participants generated 7 additional responses. Therefore, a total of 22 responses were utilized in the pilot survey analysis. Since the pilot survey data was used primarily to inform the qualitative interview coding, we report only simple descriptive statistics.

Analysis of the RM venturing interview narratives was informed by grounded theory (Strauss and Corbin, 1990). First-order codes were generated via open-ended coding of the transcripts. These were triangulated against the results of the pilot survey to identify overlap and

gaps. Then, through a cycle of inductive and deductive reasoning, theoretical categories representing theoretical groupings of the first-order codes were identified. Finally, theoretical categories were organized into aggregate theoretical dimensions.

Findings

We first present the findings of the online pilot survey. Following this, we discuss the narrative interview findings.

Online pilot survey findings

Pilot survey findings are presented in Figure 1. Most informants agreed (45.45%) or strongly agreed (31.82%) that RM commercialization is challenging due to resource constraints, and that collaborations are required for commercialization. Informants agreed (45.45%) or strongly agreed (27.27%) that collaboration with academic institutions is a requirement for commercialization. Similarly, most informants agreed (40.91%) or strongly agreed (36.36%) that collaboration with hospitals is necessary for commercialization. However, the majority of informants disagreed (50.00%) that collaborations with "big pharma" (large pharmaceutical companies) are required for RM commercialization. Most informants agreed (45.45%) that collaborations provide RM ventures with access to resources and agreed (63.64%) that collaborations enabled capabilities to be acquired. Furthermore, informants agreed (54.55%) or strongly agreed (36.36%) that knowledge is exchanged during collaborations and disagreed (40.91%) with the statement that RM collaborations were difficult to manage. Informants also disagreed (36.36%) or neither agreed/disagreed (31.82%) that RM collaborations often fail to deliver. Most informants agreed (31.82%) that governmental funding could be accessed for commercialization. However, there were differing views as to whether VC funding could be

accessed, with 31.82% of informants being in agreement and 31.82% being in disagreement. There was high agreement (63.64%) amongst informants that unresolved regulatory issues are affecting RM commercialization. Also, most informants agreed (36.36%) that manufacturing, distribution and scale-up uncertainties are affecting RM commercialization. Most informants agreed (40.91%) that unrealistic timeframes are set for RM commercialization, and most agreed (31.82%) or strongly agreed (31.82%) that RM business models are unknown and unproven.

Figure 1 here

Narrative interview findings

Output of the interview findings is presented in Table 2, utilizing a multi-level data structure (Walsh and Bartunek, 2011). The first column of the table shows the prevalence (%) of first-order codes within the total (T) 23 interviews. The table also highlights the prevalence (%) of first-order codes for each category, which includes interviews with 6 entrepreneurs (E), interviews with 3 academics (A), interviews with 12 support entities (SE) and interviews with 2 RM companies (RC). We provide further discussion on first-order codes, theoretical categories and theoretical dimensions. Illustrative examples of first-order codes and theoretical categories are presented in Table 3.

Table 2 here

We review the theoretical dimensions revealed by the data and note specific examples to highlight findings and relevance.

Perceived environmental uncertainty (PEU). Our data shows high levels of PEU surrounding RM venturing. In consideration of Milliken's (1987) typology of uncertainty, RM

ventures face high levels of state, effect and response uncertainties. In particular, given the high levels of environmental unpredictability, RM ventures face higher levels of state uncertainty. Informants consistently reported high levels of funding uncertainties, discussing the difficulties in securing funding for commercialization purposes. This is illustrated in example A in Table 3. RM venturing requires this funding gap or "valley of death" between stem cell discovery and translation to be bridged. Yet, achieving this is problematic at present, since RM venturing generally exceeds current investor timeframes and investment limits. Nevertheless, example B illustrates how conditional approval could be implemented in order to ease the funding gap. This provides ventures with access to the market prior to obtaining comprehensive data on safety and efficacy, but with the provision that more data is provided in the near future.

High levels of uncertainty also surround manufacturing, scale-up and distribution, as highlighted in example C. This is consistent with prior research conducted on RM business models, which highlighted the problems faced by a bio-artificial liver device venture in distributing their product due to unavailable cryogenic solutions (Mastroeni *et al*, 2012). As such, we see in example D that to overcome distribution uncertainties, more localized RM treatments will be required where the patient travels to the site of production.

RM ventures also face high levels of regulatory uncertainty, especially unresolved IP rights issues, which is illustrated in example E. Legislative changes regarding the use of human embryonic stem cells (hESCs) has resulted in the shift to induced pluripotent stem cells (iPSC) but has required ventures to adapt their business model as a consequence. Whilst iPSC are seen as being more ethically acceptable, ethical uncertainties still surround the RM sector. Furthermore, scientific shifts are likely because stem cell science is still in its infancy.

It would appear that ventures focusing on tools or diagnostics are the most viable. This is because the financial resources required for commercialization of tools or diagnostics is

significantly lower than the financial resources required to commercialize therapeutics. Example F in Table 3 illustrates this. However, despite tools or diagnostic ventures being the most viable in the short-term, given the current uncertainty within the RM sector, young RM tools or diagnostic ventures are likely to face downstream uncertainties such as reimbursement uncertainties, as confirmed in example G.

Coupled with these uncertainties are high levels of risk, which results in investor skepticism (Giebel, 2005). Risk was consistently discussed, with the suggestion that China and the US has different perceptions of risk in comparison to the UK. In a slightly different context, entrepreneurs discussed risk in terms of the personal risk that they face in financing their venture, as illustrated in example H. In contrast, when financial resources were obtained through governmental bodies, without this funding having to be matched or offered on a loan basis, risk was mitigated for the entrepreneur or venture.

Many of the uncertainties discussed within the dataset are consistent with previous research (Plagnol *et al*, 2009). It is evident that some ventures are not fully committing to this sector and only deploying limited resources until uncertainty and risk are reduced. Therefore, if the sector is to see advancements in RM venturing, these uncertainties must be addressed. In achieving this, RM ventures are engaging in collaborations, legitimacy building and knowledge exchange mechanisms.

University entrepreneurial culture. RM venturing is primarily driven by university-led stem cell research. As such, university academic scientists may be expected to participate in commercialization activities. This requires the inventing entrepreneur to modify their role-identity, shifting from a scientific orientation to a more market-driven approach (Jain *et al*, 2009). However, as illustrated in example I, this often creates conflicting pressures as academics are

measured on research papers and grants, not commercialization outcomes. This tension could impact their motivation for commercialization (Ndonzuau *et al*, 2002; Etzkowitz, 1998).

Commercialization of university-led stem cell innovations will be influenced by the entrepreneurial culture embedded within the university and the TTO's policies and procedures (Degroof and Roberts, 2004; Di Gregorio and Shane, 2003). Clear TTO policies may enable greater levels of commercialization (Lockett *et al*, 2003). Policies rewarding academic entrepreneurial behavior and commercialization have been shown to result in greater levels of commercialization (Renault, 2006; Friedman and Silberman, 2003; Lach and Schankerman, 2004; Henrekson and Rosenberg, 2001). Furthermore, the business development capabilities of TTO staff can influence commercialization (Thursby and Kemp, 2002; Lockett and Wright, 2005). Some staff may lack the technical and entrepreneurial understanding that is required to commercialize stem cell science (Lockett *et al*, 2005), which is highlighted in example J. RM venturing will, therefore, ultimately depend on universities deinstitutionalizing their traditional academic culture and adopting a more commercially oriented and entrepreneurial one (Scott, 2001; Dacin *et al*, 2002).

Coping strategies. In order to address high levels of PEU, entrepreneurs or ventures will be required to engage in coping strategies (Milliken, 1987). Our findings show entrepreneurs and ventures engaging in collaborations and legitimacy building in order to address the high levels of PEU.

The majority of collaborations are taking place for resource assembly purposes and improving particular processes, as highlighted in examples K and L respectively. They also provide access to funding and can build the legitimacy of a particular venture. Collaborations with industry and academia appear to be the most dominant types of collaboration within the

dataset. Collaborations with the National Health Service (NHS) are also vitally important for RM venturing, as they enable access to clinicians. However, gaining access to the NHS and forming a collaborative partnership is currently challenging, as illustrated in example M. Collaborations involving support entities provide ventures with access to executives with expertise in new venture development. They also facilitate in connecting ventures with investment communities. However, despite the benefits of collaborations, the costs associated with collaborations were evident, as shown in example N.

In addition to the role of collaboration in addressing the high levels of PEU, uncertainty reduction is also possible as a consequence of legitimacy building. When high amounts of uncertainty and controversy surround a novel technology, legitimization of this technology becomes essential and can result in ventures acquiring critical resources (Jain and George, 2007). Legitimacy building can be achieved through entrepreneurial narratives, resulting in the creation of new wealth (Lounsbury and Glynn, 2001; Martens *et al*, 2007). Entrepreneurial stories were evident within the dataset as a means of legitimacy building and serving to reduce uncertainty, as highlighted in example O. To enhance legitimacy ventures should protect their technology, widely publicize their technology and influence key stakeholders (Jain *et al*, 2009). Example P highlights the protection of stem cell research. Publicizing technology through raising awareness is documented in example Q. The influencing of key stakeholders is illustrated in example R.

Collaborative knowledge. Coping strategies impact on resource assembly and enable the access of knowledge for venture formation and growth. Research on absorptive capacity (Cohen and Levinthal, 1990; Zahra and George, 2002) and tacit knowledge suggests that the sophisticated, technological requirements of life science entrepreneurship make it unlikely that new ventures will possess sufficient internal knowledge and must, therefore, collaborate and

engage in resource exchange mechanisms to become competitive. Our findings highlight the exchange of knowledge and communication between the various actors operating within the RM sector. Knowledge is accessed through collaborations and networks, as illustrated in examples S and T respectively. This can be especially valuable as it can enable capability development. This is supported in example U, where we see knowledge being accessed via collaboration with a university in order to develop capabilities. Accessing knowledge through NHS collaborations is also shown to be particularly useful, as this can identify relevant disease areas and markets to target. This is highlighted in example V. Such knowledge exchange mechanisms can result in learning. However, informants did discuss the difficulties in exchanging knowledge due to the language differences between the various actors within the sector and due to the tacitness of RM knowledge. This is illustrated in example W.

Social networks have been suggested to be an important mechanism for the assembly of resources and in the creation and exchange of knowledge (Aldrich and Martinez, 2001; Ardichvili *et al*, 2002). Within the RM sector there are several life science communities that have been established, with the aim of ensuring successful RM venturing. The Scottish Stem Cell Network (SSCN) was formed in 2002 and was tasked with building a RM community and delivering RM commercialization. This network connected the scientific community and SME community, and served to bridge the gap between the different languages spoken by the various actors within the RM sector. SSCN closed in January 2012 due to the lack of further governmental backing. In its place the Cell Therapy Catapult was formed in London, which is funded by the UK government and is charged with growing the UK stem cell sector. This is to be achieved through the advancement of RM research and bridging the translational gap, resulting in commercialization. In addition, knowledge transfer networks have been established. The Health Knowledge Transfer Network is concerned with delivering innovation within the health sector,

which includes the medical biotechnology, medical technology, diagnostics and pharmaceutical industries. They organize events and workshops where industry actors can meet in order to share ideas and gain access to potential collaborators. The network also acts as a facilitator for the identification of new sources of funding. In example X we show knowledge access via networks, which assists the assembly of financial resources

Venture development. Accessing knowledge through collaborations and networks can enable RM ventures to form and grow. During this venture development period, ventures may continue to engage in coping strategies, resulting in additional collaborative knowledge. However, RM venture development is challenged due to a lack of slack resources. Financial resources are fundamental for venture formation and growth (Cassar, 2004), yet our data shows that entrepreneurs and ventures struggle to acquire financial resources. Governmental funding appears to be available for basic scientific RM research and to progress RM research to phase one/two studies. However, access to funding for clinical stage research and to deliver this research to market is currently challenging, as illustrated in example Y. At present, entrepreneurs and early stage RM ventures are required to match governmental funding with their existing financial resources, which is difficult. This is shown in example Z.

Currently, RM business models are unknown and unproven. Since RM is an evolving sector, it is reasonable to expect that RM business models will differ from the dominant life science business models and, as a result of the highly uncertain environment, it is probable that RM business models may evolve through a trial-and-error process (Heirman and Clarysee, 2004; Loch *et al*, 2008; Costa and Levie, 2012). Business model evolution through trial-and-error was exemplified within the dataset. When complexity and uncertainty are high, ventures may run multiple parallel business models and select the best performing one (Loch *et al*, 2008), as

illustrated in example AA. This example documents how a RM venture ran two separate business models due to the high levels of uncertainty surrounding the sector. One focused on RM services, whilst the other focused on a RM tools business model. It transpired that there was not the market demand for the service business model and, therefore, the tools business model was adopted. Informants also discussed uncertainty surrounding their own business model, in some cases discussing business model failure or changes to their current business model due to a lack of market demand. This highlights that RM business models cannot be predicted *ex ante*. Entrepreneurs discussed their desire to become players in the RM therapeutics market but due to the high uncertainties and costs of being involved in this market, all were prevented from operating in this space. However, example BB illustrates a venture that is combining a business model focusing on tools with the desire to develop cell-based therapeutics, which hints towards business model innovation (George and Bock, 2012). Although, it remains unclear whether this venture is truly innovating their business model because business model innovation requires a deep understanding of market trends and sufficient resources to direct towards novel opportunities (Bock *et al*, 2012; Johnson *et al*, 2008). Therefore, it appears from the dataset that RM ventures focusing on tools or diagnostics may have a clearer path to a viable business model than those focusing on therapeutics, as previously discussed.

Outcomes. Currently the economic impact of the entire RM market is estimated to be between $2-5 billion, which is expected to exceed $11 billion by 2020, contributing to a substantial reduction in healthcare costs (Tait *et al*, 2011). University-led RM venturing has the potential to result in significant economic gains. However, it should not be forgotten that failure is an unavoidable aspect of any entrepreneurial venture and even if universities are successful in

transferring their technology, they should not always expect the economic gains to accrue to their local area (Miner *et al*, 2001; Bock, 2012).

The economic impacts of university-led technology transfer can be significant but technologies emanating from the university, most often than not, will require vast amounts of investment and time in order to become commercially viable (Bock, 2012). Informants, especially RM support entities, were especially concerned with RM venturing positively impacting the local economic environment. However, there was some concern as to whether the local environment could retain this innovation. Furthermore, the immediate visible economic gains for RM are not always apparent, as benefits are not instantaneously observable, which can affect investment. Example CC illustrates this.

Despite the high uncertainty surrounding RM venturing, suggestions for the trajectory of the market were forthcoming. One entrepreneur suggested that ventures should collaborate with the NHS to enable widespread commercialization. This will provide access to clinicians who are best placed to offer suggestions on disease areas and indications. The disease areas to focus on should be "orphan" diseases, as taking an orphan drug to market requires less financial capital and is less time intensive. As such, orphan drugs could serve as the exemplar to the RM industry, providing greater confidence in the market and enabling further investment. Furthermore, NHS collaboration provides access to NHS patients and the opportunity for clinical trials to be conducted. This can provide gradual safety and efficacy data, and along with conditional approval, this could prevent the need for large-scale efficacy trials, which are highly expensive and currently hindering RM venturing. Another future scenario, as suggested by an academic scientist, views RM venturing initially relying on the use of regenerative tools and technologies in drug screening. Over the next ten years, the industry will begin to see bespoke RM therapies as processing costs reduce. This could involve cells being taken from a patient, grown up in culture

and then introduced back into the patient in order to repair the degenerative tissue or organ. Eventually, as we witness more scientific advances in the RM field, there will be widespread use of RM therapies for tissue or organ repair.

Informants also discussed the timeframes involved for RM scientific progression and widespread venturing**.** The expected timeframes for taking RM science to market differs amongst the actors operating within the sector. VCs, SMEs and the UK government do not understand the timeframes involved in taking RM science to market, according to entrepreneurs and RM support entities. VCs, SMEs and the UK government expect a much quicker return on investment and as a consequence, this has serious implications for RM funding and, ultimately, commercialization. This is illustrated in example DD. A more reasonable timeframe for investors to see a return on their investment was suggested to be 10-30 years. In terms of scientific progressions, it was suggested that it could be 50 years before there is large-scale use of stem cells.

Table 3 here

Our data also highlights differences in the way in which each category of informant addresses the high levels of PEU and their approach to RM venturing. We have previously shown, in Table 2, the differences in the prevalence (%) of each first-order code between all 4 categories of informants. To further illustrate the differences between categories and their approach to RM venturing, we highlight in Figure 2 the average occurrence (%) of each theoretical dimension per informant category. This suggests the formation of two distinct lenses in informants' approach to RM venturing.

Lens 1 consists of entrepreneurs and RM support entities. Both approach venturing in a similar way and have similar perceptions of uncertainty, including the significance and effect of uncertainty. Both categories lack slack resources and place more emphasis on the venture

development stage of the venturing model. They also both face similar PEU concerns, especially in relation to funding uncertainties. However, some differences are visible. For example, entrepreneurs appear to be relying on coping strategies less than any other category. Whilst further research is required in order to fully understand why this is the situation, we suggest that it is likely to be as a result of collaboration costs, which were evident within the dataset for the entrepreneur category.

Lens 2 consists of academics and support entities. They place a high emphasis on coping strategies, particularly collaborations, in addressing high levels of PEU. These collaborations progress scientific developments and improve current RM processes. Both categories are similarly concerned with the outcomes of RM venturing, especially in terms of innovation and economic development.

Figure 2 here

Discussion

Following the findings we present a RM venturing process model. Given the high levels of PEU surrounding RM venturing, we discuss alternative collaboration mechanisms. We extend the discussion to reflect on the effects of different coping strategies on resource assembly and collaborative knowledge. The effect of uncertainty on institutional culture is also considered.

A process model of RM venturing

Based on our findings we propose a RM venturing process model. This model is presented in Figure 3 and shows that high levels of PEU affect RM venturing. Also, since RM venturing is driven by university-led stem cell research, the entrepreneurial culture embedded within the university will determine successful RM venturing. In an attempt to overcome PEU and ensure

successful venturing, RM ventures engage in coping strategies. Coping responses include collaborations and legitimacy building, which enables the assembly of resources and development of collaborative knowledge, resulting in venture formation and growth. As ventures continue to develop they may engage in further coping strategies, resulting in additional collaborative knowledge development. The final part of the model is the outcome of the venture, which may be a success and lead to economic gains, or it may be a failure.

Figure 3 here

Collaboration under unresolved uncertainty

Our findings indicate that entrepreneurs rely on coping strategies less than any other category. We have shown collaborative costs to exist during collaborations and highlighted unwilling collaborators. In addition, given the high levels of PEU, high partner uncertainty is expected. Under conditions of high collaboration costs, unwilling collaborators and high partner uncertainty, it is possible that RM entrepreneurs and new ventures rely on selective revealing as an alternative strategic mechanism to known collaboration mechanisms (Alexy *et al*, 2103). Through the selective revealing of knowledge, the focal collaborating firm attempts to induce the external collaborating firm to become more similar to them with respect to the production of knowledge. However, the use of selective revealing strategies in RM venturing may be problematic. If RM entrepreneurs and new ventures lack knowledge, or hold incorrect knowledge, we propose that the use of selective revealing in RM venturing will create collaborative networks of ignorance. This will have serious implications for the development of collaborative knowledge and venture outcome, since opportunity recognition depends on individuals mentally comparing new information with prior knowledge through a cognitive process of structural alignment (Grégoire *et al*, 2010). Therefore, if entrepreneurs or new

ventures lack knowledge, or if incorrect knowledge has been selectively revealed, opportunity recognition will be affected.

Coping strategies: resource assembly and collaborative knowledge

Coping with uncertainty is a three-staged process. It involves *primary appraisal* in which individuals evaluate the threats to themselves. *Secondary appraisal* considers the response options available in order to deal with these threats. *Coping* with these threats relies on implementing the response options available and involves the use of two coping functions: a *problem-focused* coping and an *emotion-focused* coping (Lazarus and Folkman, 1984). During stressful situations individuals will utilize both types of coping functions in addressing the particular problem. However, problem-focused coping tends to predominate when individuals perceive that they can address the particular situation and emotion-focused coping prevails when the situation is less controllable (Folkman and Lazarus, 1980).

In this study we have shown that coping strategies include collaborations and legitimacy building. These depend on culture and uncertainty, and enable resource assembly and collaborative knowledge development. Such coping responses are examples of problem-focused coping strategies, as they reduce or remove the high levels of PEU. Several forms of problem-focused coping have been identified, such as *specific interpersonal efforts to alter the stressful situation* or the *seeking of social support* (Folkman *et al*, 1986b). The specific problem-focused coping form implemented by entrepreneurs is likely to have differing effects on resource assembly and collaborative knowledge development. For example, RM entrepreneurs implementing problem-focused coping, in which they seek social support, may find that they are unable to assemble resources and develop collaborative knowledge. This is because this form of coping relies on entrepreneurs obtaining external advice, assistance or knowledge. Yet, the

potential existence of networks of ignorance is likely to result in access to incorrect advice, assistance or knowledge. This will have serious implications for venture outcomes.

Emotion-focused coping strategies enable entrepreneurs to manage their emotions in relation to the uncertainty and are most suited to uncontrollable situations. Therefore, they are especially valuable to entrepreneurs and ventures during RM venturing due to the high levels of unresolvable uncertainty surrounding RM. Several forms of emotion-focused coping strategies exist, which can facilitate or inhibit problem-focused coping. These include: *wishful thinking*, *distancing*, *emphasizing the positive*, *self-blame*, *tension-reduction* and *self-isolation* (Folkman *et al*, 1986a). Again, we can expect resource assembly and collaborative knowledge development to proceed differently depending on which form of emotion-focused coping is adopted. For example, entrepreneurs relying on wishful thinking may fail to see potential flaws in their business model or RM technology. If they then collaborate for resource assembly and knowledge development purposes, homophily effects suggest that the collaborating firm will also fail to see the potential flaws. This will have serious consequences on venture formation and growth. Similarly, entrepreneurs who rely on distancing themselves from the high levels of PEU, may fail to assemble resources and develop collaborative knowledge.

Individuals differ in their coping responses (Carver *et al*, 1989) and, therefore, resource assembly and collaborative knowledge development will vary. In this study we have shown that RM informant categories differ in their coping responses to high levels of PEU. As such, we reported two lenses, which consisted of entrepreneurs and ventures in one lens, and academic and support entities in another lens. This suggests that there is not an objectively "correct" interpretation of the best commercialization path. Unresolvable uncertainty and variations in the best commercialization path, may lead to the grouping of RM informants based on homophily effects. This may have serious implications for venture outcome, as groups will either randomly

all succeed or fail based on whether their interpretation of the best commercialization path was accurate or not (Miner *et al*, 1996).

Institutional culture

RM venturing is driven by university-led stem cell research, which encourages venturing activity to be linked to university research and commercial outcomes. The embedded institutional culture and processes at the university and TTO are, therefore, likely to have an imprinting effect on the structure and characteristics of RM ventures which emanate from the university (Stinchcombe, 1965; Kimberly, 1975). At founding, new ventures are determined by the specific technological, economic, political and cultural resources that are available to them (Johnson, 2007). To ensure their survival and growth, they must follow strategies that are rewarded by their external environment (Kriaucinas and Kale, 2006). However, since RM ventures operate under extended periods of high levels of uncertainty, it is reasonable to suggest that imprinting effects will have unintended outcomes on the survival of young RM ventures. As such, imprinting effects, and also the inventing academic-entrepreneur's prior role-identity conflicts, presents significant challenges to RM venturing.

Practical Implications

Findings of this study present a novel picture of organizational coping under high levels of uncertainty. We suggest the need for entrepreneurs and new ventures to adopt coping strategies in response to the high levels of PEU, which can result in the development of collaborative knowledge and venture development. Entrepreneurs and new ventures, which fail to adhere to this, may find themselves unable to develop their business model.

Our findings are also especially useful to TTOs, who are charged with: (1) preventing the improper use of inventions, (2) boosting financial returns from IP, and (3) generating social benefits from university research (Siegel *et al,* 2004). We recommend that universities and TTOs, which expect to commercialize their stem cell research, need to consider balancing their academic and commercialization culture. However, given the high uncertainties surrounding RM commercialization, the risk–aversive nature of TTOs and their focus on short-term cash maximization, commercialization of university-led RM research is still likely to be challenging (Phan and Siegel, 2006).

This research also has implications to UK government policymakers, who are not only charged with ensuring that the UK remains at the forefront of RM research, but also with the commercialization of this research. Our proposed RM venturing process model provides an important contribution in ensuring that the UK exploits the commercialization aspect of RM research.

Limitations and Directions for Future Research

In this study we examined RM venturing under high levels of PEU. We relied on informants recounting their involvement in RM venturing through a narrative process and as a result, we developed a RM venturing process model. Whilst the results of this study appear to be robust, the extent to which the RM process model is a true reflection of the RM venturing field, can only be confirmed through empirical analysis that tests specific hypotheses. The inductively derived theories of RM venturing proposed in this study also require further testing, refinement and development through further empirical research. There are also limitations inherent to our dataset, since it is primarily limited to RM venturing informants located in Scotland. Therefore,

caution should be exercised in generalizing findings to other geographical or ecosystem boundaries. In addition, our dataset contains an overrepresentation of RM support entities.

Further empirical research is required to provide generalizable results of RM venturing. It would be especially useful to extend the small pilot survey to a large survey, which covers an international dataset. Furthermore, extension of interviews to other regions of the UK and internationally, is warranted.

We have suggested that RM entrepreneurs and ventures are relying on selective revealing. Further research is required to fully understand the existence and role of selective revealing in RM venturing, particularly the drivers and outcomes of this alternative form of collaboration mechanism. This is consistent with further research calls from Alexy *et al* (2013) and has the potential to reveal if RM ventures selectively reveal knowledge intentionally or unintentionally in order to shape the behavior of external actors.

We call upon further research to reveal the full nature of individual and organizational coping responses during opportunity exploitation and under high levels of PEU. This may distinguish which coping strategies are useful or detrimental in context. From this we can gain a deeper understanding of coping strategies for the assembly of resources, the development of collaborative knowledge and venture outcome. Our results emphasize the importance of research linking entrepreneurial cognition and decision-making to venture process, especially under high levels of uncertainty.

Conclusions

We investigated entrepreneurial activity within RM venturing, which is a sector characterized by unusually high levels of uncertainty. Our study advances theories of venture development by proposing a preliminary model linking uncertainty, collaboration and coping.

We show that under high levels of PEU, entrepreneurs and RM ventures engage in coping strategies for venture development. Coping strategies address the high levels of uncertainty and the scarcity of resources, and include collaborations and legitimacy building. These assist resource assembly and drive collaborative knowledge development, leading to venture formation and growth. Furthermore, we have progressed the understanding of university-industry scholarship by showing the potential link between university culture and venture coping strategies.

Tables and Figures

Table 1. Study Informant Information

Informant number	Informant's role	Category	Organization type	Organization location
1	Director of Operations	Support entity	Services	Edinburgh
2	Chief Executive Officer and Founder	Entrepreneur	Tools/Diagnostics/Services/Cell Therapies	Glasgow
3	Business Development Manager	RM company	Services/Research	Edinburgh
4	Chief Executive Officer and Founder	Entrepreneur	Services/Research/Consultancy	Edinburgh
5	Academic scientist	Academic Scientist	Research	Edinburgh
6	Senior Economic Development Officer	Support entity	Services	Edinburgh
7	Chief Executive Officer	Support entity	Services	Edinburgh
8	Business Development Executive	Support entity	Research	Edinburgh
9	Director and Academic	Academic scientist	Research	Edinburgh
10	Chief Executive Officer and Founder	Entrepreneur	Cell Therapies/Services	Manchester
11	Industry Liaison Manager	Support entity	Services	Glasgow
12	Technology Manager	Support entity	Services	UK wide
13	Chief Executive Officer and Founder	Entrepreneur	Tools/Diagnostics/Services/Research	Edinburgh
14	Chief Scientific Officer and Founder	Entrepreneur	Services	Glasgow
15	Chief Executive Officer	Support entity	Cell Therapies/Services/Research	London
16	Chief Executive Officer	RM company	Tools/Diagnostics	Royston
17	Outreach manager	Support entity	Services	Scotland
18	International Senior Executive	Support entity	Services	Scotland
19	Entrepreneur	Entrepreneur	Tools/Diagnostics	Edinburgh/ Glasgow
20	Chief Executive Officer	Support entity	Services	Edinburgh
21	Head of Business Development	Support entity	Services/Research	Edinburgh
22	Academic scientist	Academic scientist	Research	Edinburgh
23	Head of Business Creation	Support entity	Services/Research	Edinburgh

Table 2. Data Structure

Prevalence in study sample (%)*					First-Order Codes	Theoretical Categories	Theoretical Dimensions
Informant categories							
T	**E**	**A**	**SE**	**RC**			
61	83	67	50	50	Risk	Types of uncertainty	**Perceived environmental uncertainty (PEU)**
74	100	67	58	100	Funding issues		
43	33	67	42	50	Manufacturing, scale-up and distribution uncertainty		
39	50	0	42	50	Regulatory uncertainty		
17	17	33	17	0	Scientific uncertainty		
17	33	0	8	50	Ethics		
13	17	0	17	0	Reimbursement uncertainty		
39	17	33	58	0	Academic conflicts	Inventing entrepreneurs	**University entrepreneurial culture**
39	17	67	50	0	Academic motivations		
30	0	67	42	0	Academic metrics		
35	17	0	58	0	TTO business models and processes	TTO business models and processes	
91	83	67	100	100	Collaborations with industry	Collaborative partners	**Coping strategies**
74	33	100	83	100	Collaborations with academia		
39	17	33	50	50	Collaborations with NHS		
35	0	33	50	50	Collaborations with support entities		
39	67	67	17	50	Collaboration for sharing of resources	Collaborative outcomes	
30	17	33	25	100	Collaboration for process improvement		
22	0	67	25	0	Collaboration for funding purposes		
9	17	33	0	0	Collaboration costs		
4	17	0	0	0	Collaboration for legitimacy building		
61	83	67	58	0	Legitimacy building	Legitimacy building	
57	67	0	67	50	Knowledge transfer	Resource exchange mechanisms	**Collaborative knowledge**
70	50	100	75	50	Communication		
22	50	33	0	50	Learning		
26	17	33	33	0	Language differences		
57	50	33	75	0	RM and scientific communities	Networks	
87	83	67	92	100	Governmental funding	Funding sources	**Venture development**
61	83	33	58	50	VC funding		
35	0	100	33	50	"Big pharma" funding		
65	50	67	75	50	Spinout venture formation	Spinout venture formation	
57	100	33	33	100	Business models	Types of RM business models	
9	33	0	0	0	Integrated business model		
78	83	100	75	50	Resources	Existing resources	

30	17	33	33	50	Innovation	Economic development	**Outcomes**
30	0	0	58	0	Regional investment and growth		
65	67	67	58	100	Commercialization timeframes	Future scenarios	
9	17	33	0	0	Potential industry structure		

* Does not account for multiple occurrences within a single interview.

Table 3. Illustrative evidence

Example	Quote
A	"…simply because trying to find funding, I mean, the other issue in all of this is that to undertake anything is a hellish expensive process cause, I mean, we aren't even close to doing anything in terms of going into clinical trials, and if you started that realm you're talking mega bucks, and therein lies the big challenge for all of us." (CEO 1, support entity)
B	"And I think the industry is going to be moving to... call it different things: progressive licensing, conditional approvals, expanded access, it's all moving towards this…and again and again the House of Lords are talking about conditional approvals and asking people what they think of them, it's really clear that that's going to be how the system moves in the future…So it's not just doing phase one, two, three, get an approval and boom, start marketing. You're marketing it almost... not from day one, but once you've got some efficacy, and it's a gradual increase in exposure to the patients." (Entrepreneur 3)
C	"The second sort of major group of problems are in what I'd call manufacturing and supply chain issues…Lastly of course the major issue, how d'you get live cells to a patient or cells that are preserved and delivered to a patient or tissues that have been grown and implied, so the entire business model, manufacture and supply chain model is significantly different from what biotech and big pharma understands as their business model." (CEO 2, support entity)
D	"…but you can see where this, you know, is the whole process going to be very much more localized than you had with the pharmaceutical industry?" (Entrepreneur 3)
E	"The treatment of the patent regulations in Europe has also sort of blown things a bit in terms of people saying 'well, how do you develop something if you can't protect it?' you know, that's something else." (CEO 1, support entity)
F	"…now there's no way we're going to be doing clinical development on our own because we can't afford to do it…" (Business Development Manager, RM company)
G	"…reimbursement, that's the bit that's the missing piece at the moment." (Entrepreneur 3)
H	"Ok, so Neil and I sat down and talked about it and we, we, we had enough money for about another 6 months or something in the bank and we said we've got two choices; we can go find another processing partner, we can repair the issue with this processing partner, which was only beginning to unfold at the time, or we can do this ourselves, which we always wanted to do but were scared of the cost, the implications, weren't sure if we'd get regulatory approval so that we could commission a lab and try and raise money to do that, it's very difficult, it all a catch 22, raising money is a whole big catch 22……em, and, eh, so we took a decision to throw all the money at building a facility and doing it ourselves…" (Entrepreneur 1)
I	"Well, so yes, so that's obviously a very difficult area because there's a tension here isn't there? I mean academics as I've already said are judged by their papers and their grants…And, erm, spinouts take a lot of time and a huge amount of work, erm, in terms of putting it all together and then a lot of time promoting it and I think that group leaders find that extremely difficult because that's time that they're not doing their academic work and ultimately they will be judged with the current metrics much more on their academic work then they will on their commercialization work." (Academic scientist 2)
J	"I guess again that comes down to their tech transfer department to do that. Again, will they necessarily understand? I don't think so?" (Director of Operations, support entity)
K	"…so we have access to the cell lines, or at least some of them, from [company name]." (Business Development Manager, RM company)
L	"…the idea is that if we can work with them and take some of the processes and tune them up for proper manufacturing." (CEO 2, support entity)
M	"Access to the NHS is very challenging in Scotland, very challenging indeed and companies often feel that they would benefit – and they would benefit – from early conversations with the NHS where before they design their medical device, they get input from the end users and that's really challenging… But access to the NHS is something that comes up again and again and again, it's just something that's not happened in Scotland." (Industry Liaison Manager, support entity)
N	"…our processing partner and the processing partner failed the regulatory inspection in a blaze of glory…and the, em, the Human Tissue Authority, the regulator, suspended our human tissue authority license…" (Entrepreneur 1)
O	"…we had been talking to him, and talking to him, and talking to him, and he didn't, at first, believe that

	our technology did what it said it did because it is a paradigm shift for stem cell technology…and we get a lot of people who don't believe it, although less and less. We are able to show people stuff now that makes them realize that's it's the real deal…" (Entrepreneur 1)
P	"The other thing we managed to do is persuade, and this was the key I guess, was to persuade Scottish Enterprise that it was in their interest or Scotland's interest in developing the regen medicine to help fund the development of this capability…." (CEO 1, support entity)
Q	"…we've become active internationally as a mechanism of trying to demonstrate that UK is an attractive place to do this sort of work in and then we'll partner with potential inward investors to either set up manufacturing, you know, get clinical trials done, potentially being, if you like, the entry point into the European arena through the UK." (CEO 2, support entity)
R	"...guess [we have] being able to convince people…they may look back and say 'right, who let those idiots loose', I don't know [laugh] they may well say that now! But certainly at the time no, they were fairly relaxed in terms of, if you like, 'trusting' that we knew what we were doing or what we'd like to do." (CEO 1, support entity)
S	"I'm working, as I say, with [name of collaborator] and we are developing techniques which hopefully will have commercial applications in the future. So it's kind of using my communication skills and knowledge of embryology and his knowledge of transgenics and how that works." (Entrepreneur 2)
T	"…so there was a lot of work at that time about creating a network/a community which would almost act as the kind of interpreter or teach the others at least some of the key words from their different languages so they could at least understand each other when they were talking to each other." (Director of Operations, support entity)
U	"…we had a knowledge transfer partnership with the university… and really that was used to sort of develop our capability in creating cell lines that basically took on the form of hepatocytes." (Senior Economic Development Officer, support entity)
V	"So I think, you know, first thing you've got to sit down with medics and properly discuss indication." (Entrepreneur 3)
W	"The two communities are different aren't they…we speak a different jargon, speak a different language." (Academic scientist 1)
X	"But I did talk to the people in advance and I think this is quite a good thing to do as well is to talk to the TSB or whoever is awarding the grant that you're applying for and say 'look, we're thinking about doing this sort of thing, should we give up already or is this worth doing?' and I was told it was worth doing." (Business Development Manager, RM company)
Y	"…because at the moment people in regen med talk about a funding gap and you'll hear this from many people, but preclinical stuff... this kind of research and development that goes on in the university is great, it's all academic. You then sort of do proof of concept stuff which is fundable because it's fairly cheap, but then there's this clinical development which is extremely expensive and small companies can't afford it, universities certainly can't afford it." (Business Development Manager, RM company)
Z	"So all the funding that we get has to be matched and that's where a lot of people think that it's very easy cause all these grants are available, but nobody's prepared to take a huge mortgage out to pay for it or to pay the matching part because at the end of it they're not sure if they're going to get any money back." (Entrepreneur 4)
AA	"The other part to it which actually to be honest never really materialized, we also thought there was the opportunity of people actually utilizing our facilities to undertake that work, for them to actually come in and do that work, a bit like a hotel. In reality that bluntly didn't happen for whatever reasons…what we did with Cell Lab to some extent is move away... and started to moved away from a company that was... you could argue was almost a service company to one that would eventually 'have product or products' based on IP in one form or another, whether patented or not, that we could then market." (CEO 1, support entity)
BB	"…so we now have Oristem available in 6 countries…Now alongside all of that we have digressed into other products as well, so we have, em, actually got four products now. Oristem being the key product…And then the final product, erm, is called Thallocell. But also we have two other therapies, em, that we're working on as well. Em, one is an aesthetic medicine, so it's, em, cosmetics…So we would hope to engage in a clinical trial in Hong Kong in the next 6 months, em, with proof of concept first, kind of 10 people safety study…the cell type we have is ridiculously cool and, em, we have some amazing technology and we're trying to do so much with it. And then we have another idea which is

	around cardio, myocardio infarc." (Entrepreneur 1)
CC	"For renewable energy you can see windmills, you can see things going up, you can see things being built, you can see jobs being created, in regenerative medicine you can't see that and the output you would argue at the end of that might be that you're going to be using the current academic community, the current clinical communities, so the same people, not particularly new jobs created which is what they're all interested in; the output is when patients start getting better and the NHS costs go down." (Director of Operations, support entity)
DD	"I think it's just that complete dyssynchrony between the timescales involved for this and the timescales of most investors, even kind of public sector investors in this; they just can't wait that length of time and I guess even if you get... what we're beginning to get the impression that kind of regenerative medicine is beginning to lose its appeal even at Government level in Scotland now, just because there's nothing you can see for it." (Director of Operations, support entity)

Figure 1. Informants' Level of Agreement with Particular Statements

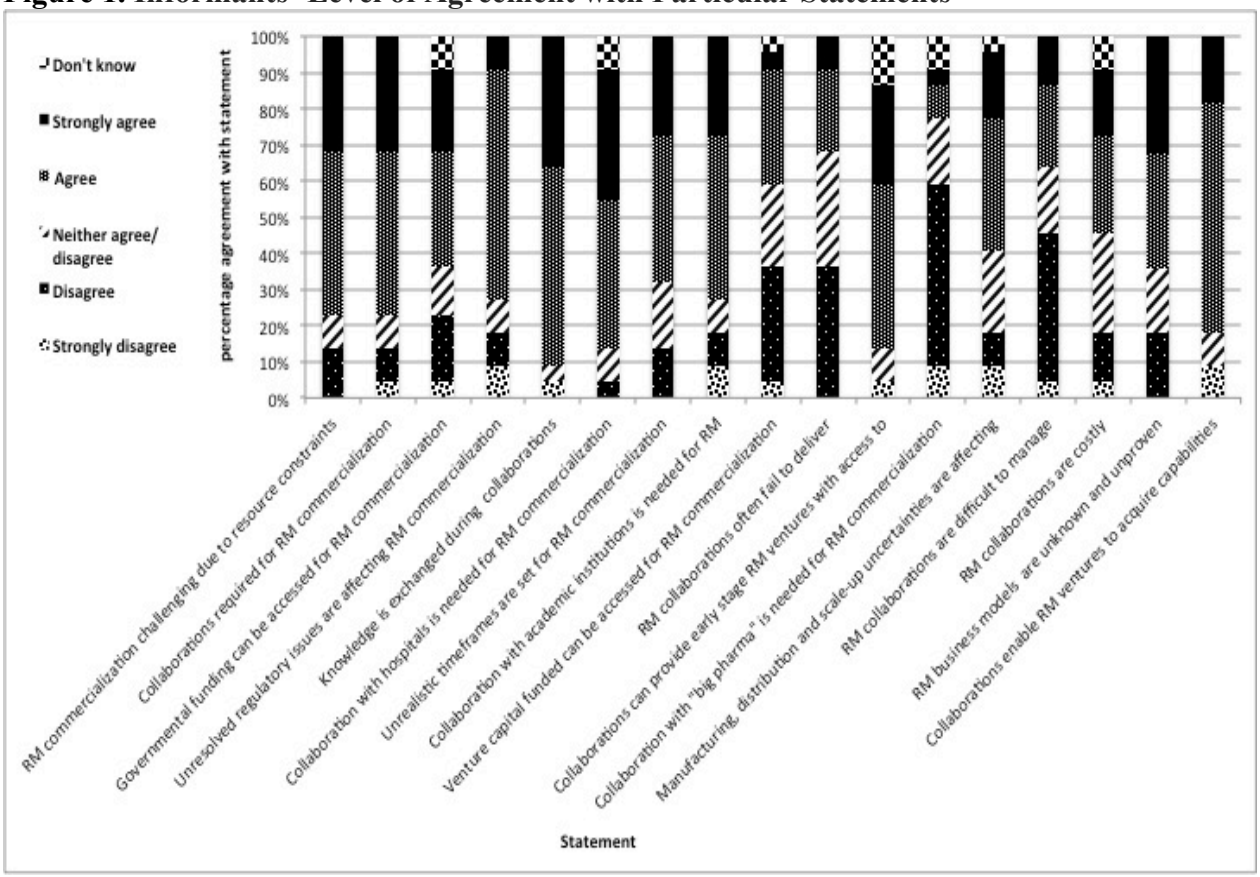


Figure 2. Revealed significance of uncertainty during narrative interview

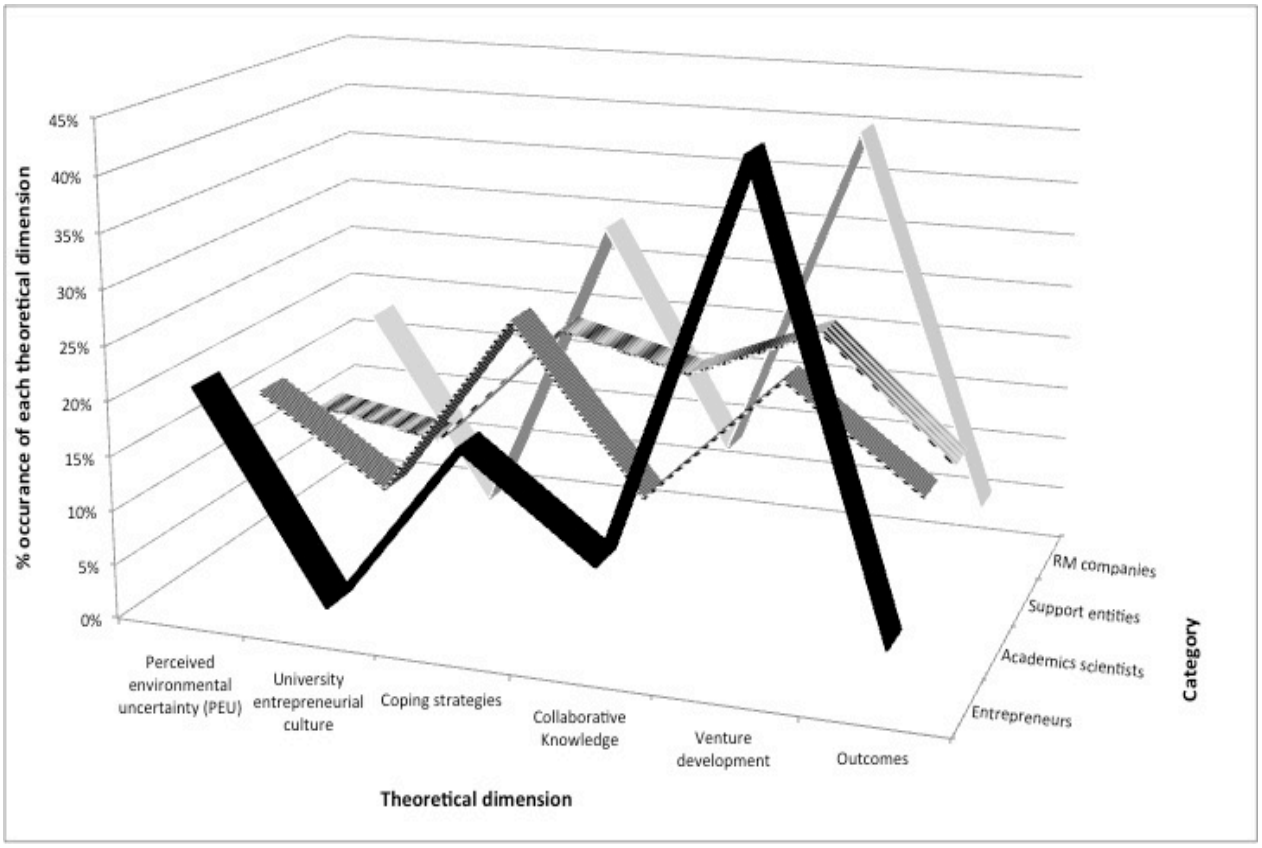
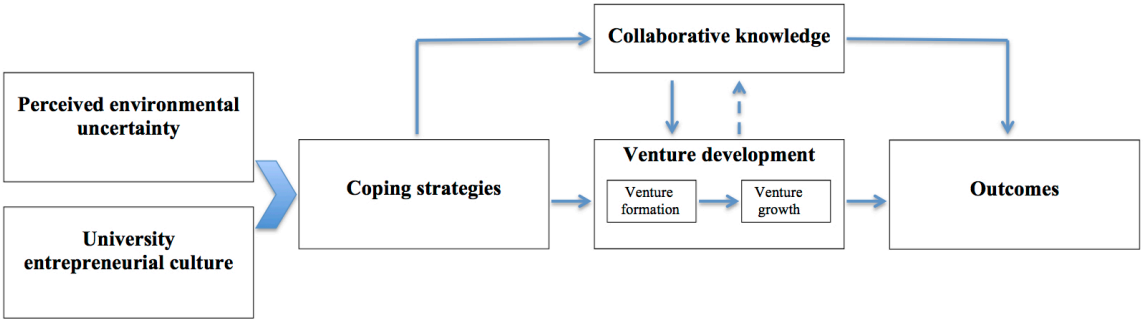


Figure 3. Process Model of RM Venturing



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