From temporary organizations to long-term collaboration

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Abstract
Antibiotic resistance is a growing problem and our main defence is developing new antibiotics. Different kinds of collaborations have been mentioned as a way to organize this development. ENABLE and Cepan is two collaborations that are focusing on early development of antibiotics. The partners in Cepan were all collaborating in ENABLE. This paper describes the partner selection process for the Cepan collaboration, with a focus on how interaction in ENABLE influenced the process. Preliminary findings show that earlier relationships, before ENABLE, were crucial for choosing two of the partners. For the last partner dependencies created in ENABLE became the deciding factor.

Introduction

Antimicrobial resistance (AMR) is a super-wicked problem (Levin et al. 2012), and we need new strategies to tackle this growing medical threat. Infections are the second most common cause of death worldwide and responsible for around 15 million deaths annually (Kraus 2008), and estimated to grow to 25 million in the year 2050 – 10 million due to resistance (O'Neill 2014). The best treatment against bacterial infections is the use of antibiotics. At present, the main strategy is to develop new antibiotics that can treat those infections that have become resistant to older antibiotics. Different kinds of collaborations, and especially public private partnerships, PPPs, have been suggested as an important way to organize research and development in the field of infectious diseases (see e.g. Munos 2011; So et al. 2011; So et al. 2012; Schultz 2013; Payne et al. 2015; Nathan 2015; Kirby 2015). In the pharmaceutical industry that historically has been very protective, new types of collaborations might be one of the changes that will generate a more open and tentatively inventive organisation, which is important when dealing with super-wicked problems (Levin et al. 2012). Most collaborations, and especially PPPs, will most likely be arranged as temporary organizations, instead of creating new permanent organizations, with actors from the wide range of expertise needed in the program. Creating efficient collaborations will be paramount to the success of the fight against AMR, and calls for a better understanding of how such collaborative temporary organizations work. There are already such collaborations that have been initiated on a multinational level, for example the Innovative Medicines Initiative[1] (IMI). One of the programs under IMI is the European Gram Negative AntiBacterial Engine[2] (ENABLE). ENABLE is a six-year project (2014-2020) focused on early development of antibiotics treating serious, systemic, resistant, Gram-negative[3] infections. The goal of ENABLE is (1) to identify three antibacterial lead programs, (2) identify two antibacterial candidate programs and (3) progress at least one program into clinical studies (for an overview of early drug development, see e.g. Nwaka & Ridley 2003). ENABLE is a competitive consortium, and unique in its combination of public funding and industrial focused drug development. Four partners that collaborated on a drug development program in ENABLE have been able to attract funding and started a new collaboration, called the Centre for Peptide-Based Antibiotics[4]. This makes ENABLE and Cepan interesting projects to study as new strategies to tackle the super-wicked problem of AMR.
On a more general level, innovation processes in a wide array of industries are increasingly managed in temporary inter-organizational projects (Jones & Lichtenstein 2008). Partner selection is one of the most important factors for alliance success (Hitt et al. 2000). There is great scholarly interest in alliance partner selection, using a variety of theories and approaches (Dacin et al. 2008). Two of these

[1] https://www.imi.europa.eu/
[2] http://nd4bb-enable.eu/
[3] Bacteria can be divided into Gram-positive and Gram-negative, with the latter type being generally more difficult to kill by antibiotics because they have two difficult-to-penetrate successive membranes that limit influx and multiple "pumps" which are capable of effluxing out substances meant to kill them.
[4] http://cepan.ku.dk/

approaches is the network approach and the embeddedness approach (Granovetter 1985; Uzzi 1997; Gulati 1995a; Gulati 1995b). One factor influencing partner selection in these approaches is prior interaction between organizations, as well as within the wider network. For example, networks and interdependencies are important factors for bringing firms together as alliance partners (Gulati 1995b). The concept of ties (see e.g. Granovetter 1973) is used extensively in this literature. However, these ties are to a large extent black boxed. The IMP literature have long recognized how firms are embedded in networks and how this leads to interdependencies (Håkansson & Snehota 1995). IMP scholars have developed the Activity-Resource-Actor model to analyse business interaction, which reveals some of the content in the ties that binds organizations together.

The aim of this paper is to open up the black box of previous ties using the Activity-Resource-Actor (ARA) model. It will examine which type of connection – activity links, resource ties and actor bonds – is of importance and when in the process of partner selection. It will also make an empirical contribution of how one collaboration project, ENABLE, leads to a new collaboration project called Cepan. ENABLE is a EU funded R&D consortium focusing on early development of antibiotics. Cepan is a privately funded project initiated by the University of Copenhagen (UCPH), an ENABLE partner, focusing on early development of a specific type of antibiotic. Cepan is funded by a grant from the Novo Nordisk Foundation Challenge Programme. Cepan is collaboration between UCPH, Statens Serum Institut (SSI) in Copenhagen, Latvian Institute of Organic Synthesis (LIOS) in Riga and National Medicines Institute (NMI) in Warszawa. All of these organizations are members of ENABLE.

Theory

Partner selection is critical for alliance success (Hitt et al. 2000). The literature on collaboration have covered this topic with an array of different theoretical approaches (Dacin et al. 2008). Some of the usual reasons mentioned are access to resources, access to new markets, reducing risk and organizational learning (ibid). There are differences in what actors look for depending on if the market is emerging or developed. In developed markets actors prioritize unique competences, market access and previous alliance experience (amongst other things)(Hitt et al. 2000). In emerging markets actors prioritize financial assets, technical capabilities and willingness to share expertise (ibid.). In both emerging and developed markets actors/companies prioritize complementary and managerial capabilities (ibid.). The social capital actors have, defined as the potentially beneficial relationships with external partners, also influence partner selection (Chung et al. 2000). Networks and interdependencies have been recognized as important for business relationship in the IMP literature (Håkansson & Snehota 1995; Håkansson et al. 2009). These factors are also important for bringing companies together in alliances (Gulati 1995b). Inter-organizational networks are important when choosing new partners, and a company that have no direct connection are more likely to enter an alliance if they have common partners (ibid.). The concept of interconnectedness is also important in the IMP literature (which reference?).

Prior connection and a history of interaction leads to trust between organizations (Gulati 1995a; Gulati & Sytch 2008). In the IMP literature, business relationships are developed through repeated interaction between actors over time, which can lead to adaptions in the activity links, resource ties and actor bonds between the actors (Håkansson et al. 2009). Furthermore, trust takes time to develop between actors (Håkansson & Snehota 1995), and it has been found that actors in the early stages of a relationship have an ambivalence period where formation of trust is non-existent (Gulati & Sytch 2008). In these early stages partners seem to "probe" each other, seeing if the other partner is trustworthy (ibid.). This is similar to the development of actor bond, which is a slow social process (Håkansson & Snehota 1995). It often starts with minor transactions in which little trust is needed due to the low levels of risk involved (ibid.). Thus, trust seem to be dependent on the temporal stage of the relationships (Gulati & Sytch 2008).

The type of uncertainty also seem to influence the choice of partner selection (Beckman et al. 2004). Using the concepts of exploration and exploitation, Beckman et al. found that actors use their network for exploitation of current knowledge in the network, while they explored new knowledge by forming new relationships with new actors. This is dependent on the type of uncertainty the actor faces. When facing market uncertainty, actors tend to exploit and reinforce their network. When facing company-specific uncertainty, but low market uncertainty, actors tend to explore and broaden their network of

alliances. It has also been found that process manageability and outcome interpretability dimensions of alliances influence partner selection (Shah & Swaminathan 2008). In certain types of alliances, such as R&D alliances, process manageability and outcome interpretability may be inherently lower due to the nature of R&D. Companies can then focus on building trust in order to enhance the probability of success of the alliance (ibid.). At the same time, the focus on trust have been criticised by Bierly and Gallagher (2007), which introduce the concept of strategic expediency to improve understanding of the partner selection process by focusing on the role of time pressure. In their critique Bierly and Gallagher put forth an argument that strategic expediency might help to shift attention to what is needed to make the alliance successful instead of focusing on partner selection and justification.

In the IMP literature the process of building trust between partners is analysed by looking at interaction, adaption and commitment. The ARA-model is used to analyse how activity links, resource ties and actor bonds are created and shaped between actors (Håkansson & Snehota 1995). These links, ties and bonds lead to adaption and commitment from the involved actors. Over time these interactions lead to the development of long-term business relationships. This approach might be useful to understand the partner selection process by giving attention to what type of previous connections, that is activity links, resource ties or actor bonds, are important at what stage of the relationship. Adaptions are critical for business relationships (Håkansson & Snehota 1995). Interactions, adaptions and commitment over time build business relationships, and trust can develop during this process. Social exchange relations often evolve in a slow process, starting with lower levels of transactions (ibid.). It is reasonable to think that activity links plays a more central role in the early stages of a relationship, compared to actor bond, which develops through social exchange. The case described below will give some preliminary findings supporting this statement.

Method

This study is part of an on-going research project for a PhD thesis. The aim of the larger research project is to expand current understanding in the fields of IMP and temporary organizations on how interaction is coordinated in large inter-organizational projects and how temporality influences these interactions. This is done with a single in-depth qualitative case study (Yin 2014) of the ENABLE project. The empirical material has been collected through interviews. A total of 47 semi-structured interviews have been done so far. Three of these have had a specific focus on the Cepan project and the partner selection process.

Almost all interviews have been transcribed and then analysed by first writing comprehensive narratives, followed by a more systematic search for particular evidence of how interactions between selected project members unfolded and how particular manifestations of temporality and time pressures relate with the emergence and development of selected relationships inside ENABLE. As an extension of these studies the development of the new program Cepan was included in the analysis with a focus on partner selection. This process follows the iterative logic of systematic combining put forth by Dubois and Gadde (2002), see next paragraph.

The interviews were complemented by documents and webpages produced in and for both ENABLE and Cepan by its members and initiators. The use of different sources of data for this research was based on the argument of triangulation by Dubois and Gadde (2002), according to which multiple sources of data contribute to the revelation of unknown and surprising aspects of a phenomenon, rather than checking the accuracy of the data (which is the triangulation argument used by Yin, 2014). Systematic combining is an iterative process where the empirical world, the framework of the research, theory and the case are developed together and in which each part directs and redirects the other parts (Dubois & Gadde 2002). Following this abductive or retroductive logic (Alvesson & Sköldberg 2000), the theoretical frame proposed above is accordingly more a result of this study, rather than an analytical frame created a priori and then simply applied to our case.

The case – ENABLE and Cepan

ENABLE is a EU funded six-year project (2014-2020) focused on early development of antibiotics. The goal of ENABLE is (1) to identify three antibacterial lead programs, (2) identify two antibacterial candidate programs and (3) progress at least one program in to clinical studies (for an overview of early drug development, see e.g. Nwaka & Ridley 2003). ENABLE is organized in three parts: (1) the management, (2) a drug discovery engine and (3) the portfolio (see figure X). The two most important

management teams for running ENABLE are the Consortium Management Office (CMO) and the Portfolio Management Committee (PMC). The CMO is responsible for the day-to-day running of ENABLE, and take decisions on how to distribute the ENABLE resources. The PMC decides on new applications from organizations that want to join ENABLE, as well as continuation of funding for programs active in ENABLE. In the event of termination of funding, the organization is still a member of the ENABLE project.

Organizations can enter ENABLE with their drug development program and become part of the ENABLE portfolio as hit-owners. Hit-owners receive funding from ENABLE for internal development, and access to the ENABLE drug discovery platform, called the hub. This consists of several different organizations with expertise in antibiotic drug development. Each program that enters ENABLE get a core-team assigned that consists of one or several representatives from the hit-owner, and several experts from the ENABLE hub. The program is co-led by the principal investigator from the hit-owner and one expert from ENABLE. The experts from ENABLE that are part of the core-team represent different platforms with competences needed for drug development. In figure X you can see the different platforms on the lower left side. In addition to their internal development, hit-owners "outsource" experiments to be performed in the hub. This is coordinated by the core-team representatives and then distributed to the different platforms.

The whole development process in ENABLE revolves around a three-monthly review process. This mean that every third month the PMC reviews each program in the ENABLE portfolio and decides whether it will continue to receive funding or not.

At the start of ENABLE the UCPH was one of the initial hit-owners in the project. Furthermore, UCPH is participating by running one of the chemistry hubs, and thus entered as both hit-owners and part of the drug discovery engine. The co-lead for the UCPH ENABLE program was a representative from NMI. NMI also did microbiology assays[5] for the UCPH program in ENABLE. In ENABLE, NMI had to develop a reliable way to test the UCPH compounds to generated good data. This was difficult, and took more than six month to get in place. LIOS was also involved in the UCPH program in ENABLE. LIOS contributed with their expertise and did preclinical assays and assessments for the UCPH program.

The funding for UCPHs development program was terminated in 2016. This was due to scientific challenges that needed basic research to solve, which is outside the scope of ENABLE. UCPH continued their research with other sources of funding, and in 2017 they obtained funding to run a new six-year project called the Center for Peptide-Based Antibiotics (Cepan). The overall aim in Cepan is to establish a drug discovery platform that focuses on peptide-based[6] antibiotics. Cepan can be envisaged as a complement to ENABLE were early hit and lead compounds are discovered, with focus on peptide-based structures. Compounds discovered in Cepan could tentatively continue in development through ENABLE or though other collaborations.

UCPH have had relationships with SSI and LIOS for a long time. However, UCPH had not collaborated with NMI before the ENABLE project. In Cepan, only UCPH and SSI has personnel directly funded by the project. SSI is also part of the management group in Cepan, together with UCPH. SSI is part of the management as they have direct funding of people and consumables from Cepan. LIOS and NMI are involved in Cepan as expert partners for test and evaluation of compounds as well as preparation of larger quantities; this is arranged as contract research for the specific tasks.

Partner selection

Not surprisingly, the first criteria for UCPH to consider partners for Cepan is that they have the scientific knowledge and technical expertise needed, and that they complement their own expertise. "You don't choose someone because he is a funny guy" as one UCPH respondent said.

SSI and UCPH, both located in Copenhagen, have a long relationship history. In Cepan, SSI contributes with *in vivo* expertise. UCPH did not have that many alternatives to get this kind of expertise in Cepan, unless they "[had to] search far away" (UCPH respondent). In addition, their long-

[5] An assay is an experimental setting that allows assessment or measurement of biological activities or other properties of the molecule(s).

[6] Peptides are molecule that consist of short chains of amino acid

term relationship clearly influenced the decision to get SSI involved in the project - "We have worked with SSI so much that it was the obvious choice" (UCPH respondent).
LIOS and UCPH have a long history of collaboration. One respondent at UCPH mentioned that he personally has had contact with them for at least 15 years. The services offered by LIOS are very similar to any contract research organization (CRO). Thus, UCPH could have chosen a CRO that offer similar services. However, the testing system used in Cepan is almost the same as they used in ENABLE, so most of the "infrastructure" was already in place. Furthermore, their previous relationship was crucial and the deciding factor for UCPH to reach out to LIOS and ask them to join this new project.
NMI, which UCPH did not have any relationship with before ENABLE, was clearly chosen for their expertise and the kind of activities they can do in Cepan. NMI contributes with microbiology expertise. As Cepan is complementary to the UCPH program previously worked on in ENABLE, it needed the same assays. Therefore, it was considered "hopeless" (UCPH respondent) to find another partner that should do the same thing as NMI had been doing and as such a much less attractive option.
One of the goals of LIOS in participating in ENABLE was to find other collaborations. The initiation of Cepan was very informal. When asked to recall any key events in the formation of the Cepan collaboration, the LIOS respondent said that he does not really remember. It was a phone-call or email from the UCPH respondent. He goes on and says:
"you know with established collaboration partners, if they have an opportunity they call and write an email. And you are just putting together the application and wait to see if it get funding or not"
This is also a clear manifestation of the importance of their previous relationship and the actor bond they have built up over the years. LIOS had no interaction with NMI in ENABLE, and when asked about this the LIOS respondent said that they rely on UCPHs choice of partner.
The reason that NMI agreed to be part of this new collaboration is more rational. The general goal is to participate in the development of new promising compounds. As they are part of the project like subcontractors this was a source of funding that would enable them to keep their employees busy. However, they also have hopes to get publications and scientific collaboration out of this new project, which was also the way it was discussed and the intention of the program. As NMI has established a way to generate good data in the assays that are critical in Cepan, UCPH seem more dependent on NMI than the other way around. At the same time, both partners describe the collaboration as very good, and hope to get more out of it than just transactions.

Analysis and discussion
For UCPH, the need for complementary capabilities has been critical in the partner selection process. This is in line with what Hitt et al. (2000) found about companies prioritisations in both emerging and developed markets. It can also be argued that UCPH have been looking for unique competences, another prioritisation for actors in developed markets. This is manifested in the need to have NMI as a partner because of their unique knowledge about microbiology assays needed in Cepan. This knowledge was developed in collaboration with UCPH in ENABLE, creating a strong activity link between UCPH and NMI. The importance of networks and interdependencies for business relationships and partner selection (Gulati 1995b; Håkansson & Snehota 1995) is also evident in the case. All three partners were part of UCPHs network, and the preference to collaborate with NMI is clear due to their assay expertise for these compounds classes. The build up of this expertise at another place is quite possible but would cause an undesired delay in the project. It might be too early to say that the collaboration have led to interdependencies between the two actors, as NMI do not depend as much on UCPH as UCPH depends on NMI.
The many interactions over the years between UCPH and LIOS have developed into a long-term business relationship (Håkansson & Snehota 1995) and led to trust between the two organizations (Gulati 1995a; Gulati & Sytch 2008). There is not enough data to see if UCPH and NMI have moved through their ambivalence period (Gulati & Sytch 2008) and started to build trust yet. It was mentioned by the NMI respondent that she thought that UCPH trusted in their ability to get good results. Trust in their ability is not the same as the kind of trust in them as an actor which develops in strong actor bonds (Håkansson & Snehota 1995). The building of trust, which is apparent in the UCPH – LIOS relationship and can be assumed exist between UCPH and SSI - due to their long history of

interaction – is in line with Shah and Swaminathan (2008). They argued that R&D alliances in nature have lower levels of process manageability and outcome interpretability and that partners then focus on building trust. The long history of interaction and collaboration between both UCPH and LIOS and UCPH and SSI points to that not only have trust been built, their earlier collaborations have also been successful. The UCPH respondent also stated this: "If we had not been satisfied with LIOS then we would not continue to collaborate with them". It can be assumed that the same goes for SSI.

Using the ARA-model (Håkansson & Snehota 1995) it seems that two (resource ties and actor bonds) connections are especially important in the partner selection process, but all three are important for the collaboration. First, when it comes to resource ties, it is clear that they are needed to hold the collaboration together. The most important resource, the compounds that are developed, becomes the glue that keeps Cepan together. Furthermore, if scientific competence is seen as a resource, that resource becomes a prerequisite in the partner selection process for this kind of collaboration.

Second, the decision to partner with both SSI and LIOS was much influenced by their former and long-term relationships. Especially for LIOS, where other alternatives could be found, their relationship with UCPH was crucial. For the *in vivo* expertise needed, which SSI has, alternatives seemed to be scarce. However, the UCPH respondent states that they were the obvious choice because they have worked together so much. This indicates that the deciding factor was their former relationship. Given this, the actor bonds developed between UCPH and SSI, and between UCPH and LIOS, seem to be very important in the partner selection process.

Third, it seems that the activity links created between UCPH and NMI in ENABLE were fundamental for their continued collaboration. When asked to describe their relationship the NMI respondent state "I think they simply trust in our work and how we are doing that". The respondent also mentions their prior collaboration in ENABLE where the NMI representative and UCPH representative co-led the UCPH program. However, it is clear that the actor bonds have not been developed as much between UCPH and NMI as with the other two project partners. This point to that actor bonds take longer time to develop to the extent that they become such an important factor in the partner selection process, compared to activity links.

There are several limitations in this study. The most crucial one is the low level of empirical data connected to Cepan and its partner selection process. First, no respondent from SSI have accepted an interview with focus on Cepan. Second, there were more people involved in the partner selection process, which should be interviewed. However, this paper describes a first step on the way to determine how activity links, resource ties and actor bonds influence the partner selection process, and if the links, ties and bonds are differently important dependent on the temporal stage of the relationship and type of collaboration.

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