The Extracellular Vesicles as a Hybrid: Life Science and its Object

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Abstract: Extracellular vesicles (EVs) are incredibly small vesicles found in the fluids of the body. Released by cells, they circulate in the body and carry different kinds of molecules as cargo; consequently, they are understood to play a significant role in cell-to- cell communication and are expected to offer potential as biomarkers and agents of drug delivery. The scientific work on them in molecular biology and biomedicine is cutting-edge, connecting production of new knowledge with expectations of new clinical applications and biotech products. This article is a case study of biomedical research-and-development collaboration on EVs in Finland. The subject of the article is the hybridity of EVs as an R&D object that is simultaneously thought of and enacted as an 'epistemic thing' and a 'technical object' (Rheinberger, 1997). In this context, EVs are a potential clinical tool, commercial product, and vehicle for upholding the continuity of research. The article argues that this kind of hybridization of research objects characterizes the practice of current life science and is closely linked to or even derived from the expectations attached to life science and biomedical research

Keywords: life sciences; objects of science; hybrid science; commercial collaboration; biomedical R&D.

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1. Introduction

In this paper, we study biomedical research collaboration on extracellular vesicles (EVs). These incredibly small vesicles – most of them are under 200 nanometres in size – are released by cells in their extracellular

environment (Raposo and Stoorvogel 2013; Palviainen et al. 2017). EVs can be found in the fluids of the body – for example, tears, sweat, urine, saliva, plasma, amniotic fluid, breast milk, and blood (Mateescu *et al.* 2017; Kalra *et al.* 2012). They carry different kinds of molecules, such as "proteins, nucleic acids, lipids and carbohydrates" (Mateescu et al. 2017, 2), as well as RNA (Raposo and Stoorvogel 2013). Several overlapping terms are used in connection with EVs – exosomes, prostasomes, oncosomes, ectosomes, outer membrane vesicles, membrane particles, and microvesicles (Palviainen et al. 2017) – but they can all be referred to as 'extracellular vesicles' (Palviainen et al. 2017, 76). Notably, "the contents, size and membrane composition of EVs are highly heterogeneous and dynamic and depend on the cellular source, state and environmental conditions" (Yáñez-Mó et al. 2015, 4).

EVs have been identified as potential biomarkers for diseases (Mateescu et al. 2017; Kalra et al. 2012). Furthermore, they are understood to contribute to "cell-to-cell communication" and are expected to have a role in disease progression – for example, in cancer or neurodegenerative diseases (Mateescu et al. 2017, 2). Their role in intercellular communication relies on their "capacity to transfer proteins, lipids, nucleic acids and sugars (…) even to sites remote to the vesicular origin", which is also why they are seen to influence "various physiological and pathological functions of both recipient and parent cells" (Yáñez-Mó et al. 2015, 2-3). In the past decade, EVs have become an actively studied subject in molecular biology and biomedicine[1]. They have been considered to offer medical potential not only as biomarkers but also, because of their ability to target very specific cells as part of cell-to-cell communication, as vaccines and 'delivery vehicles' for therapeutics (Raposo and Stoorvogel 2013; Mateescu et al. 2017; Saari et al. 2015).

In this study, we explore a research initiative on EVs in Finland in the 2010s that brought together experts and institutions from many special branches of biology and medicine, biobanks, public academic institutions, and private medical companies. The research endeavour was realized as part of a research program on personalized medicine funded by the main Finnish public innovation funding agency, Tekes. In this program, with the goal of combining scientific research with R&D (see below), funding was directed towards projects that were based on collaboration between public research institutions and private companies. Our analysis concentrates on the EVs as an object of life science in this context. We demonstrate that EVs are a hybrid object because of the way the research setting is organized and scientific work is practiced. Since the 1980s, the concept of 'hybridity' has been deployed to refer to many types of cultural mixtures in social sciences, especially in postcolonial and cultural studies (for an overview, see Frello 2012), and to assign a general cultural logic of globalization (e.g., Kraidy 2005). In addition, concepts such as 'hybrid practice' (Casper 1998) and 'epistemic hybridity' (Ning 2012) have figured in medical STS literature. We use the concept of hybridity in a nar-

rower and more specific sense to refer to the alignment and simultaneous presence of a scientific endeavour and the pursuits of clinical, social, and economic utility (see Hauskeller and Beltrame 2016a, 2016b; Beltrame and Hauskeller 2018). Such hybridity – or, rather, hybridization – can been seen to characterize the organization of research and its objectives as well as the object of research (see Cambrosio et al. 2009a). Our analysis emphasizes the collaboration of scientific, clinical, and commercial partners around a scientific object and the way such collaboration creates dependencies, constraints, and conditions for the research work, which make up EVs as an object that is shared yet manifold – i.e., a hybrid. Thus, our discussion on the 'hybridity' of the object of life science highlights the simultaneous presence of a variety of interests and objectives that are attached to the EVs and aligned through them.

Today, hybridization of organization, practice, and research objects is characteristic of many life science endeavours, which implies a profound blurring of the conventional distinction between basic and applied science (on the constructedness of this distinction, see Calvert, 2004; 2006). This can be seen, for example, in translational medicine, which does not acknowledge clear borders between clinics and labs or between research and care (Cambrosio et al. 2009b; Cambrosio et al. 2018; Tarkkala 2019). In this paper, we study this hybridity in the life sciences by focusing on expectations and manifold potentials associated with the object of science in terms of further research, innovations and applications, and future collaborations. Our approach to the EVs combines a view of the importance of expectations as a driver of biomedicine, realized in actions taken in the present (e.g., Brown 2003; Brown and Michael 2003; Sunder Rajan 2006; Tarkkala 2019; Morrison 2012), with the above concept of hybridity. Following this, our study focuses on hybridity by expectations. We ask first how the unknown and manifold potentialities in an object of life science summon a variety of actors together and modify research as collaboration. Second, we ask how hybridity by expectations influences what EVs are seen and defined to be and what trajectories and continuities of research it enables and encourages.

Our approach on EVs builds on discussions of objects of science as 'machines to make a future' (Jacob 1982; Rheinberger 1997; Rabinow and Dan-Cohen 2005). Obviously, 'future' here refers to scientific exploration of the 'unknown' in the life sciences and biomedical laboratories (Rheinberger 1997) as well as to the expected or promised applications of new knowledge (e.g., Brown 2003); it also refers to efforts to build continuity for research groups and their work (Miettinen 1998). Thus, in our article, hybridity is tied to the interplay of future making, expectations, and research tasks as they align around an object of science that is in many ways 'unknown'. Furthermore, our case of EV research is an example of a mode of biomedical science that ties academia, medical care, and the pharmaceutical industry more closely together, and our analysis highlights these intertwinements and alignments as part of knowledge production in

biomedicine (see e.g., Clarke et al. 2003; Fischer 2013; Vignola-Gagne et al. 2017). For example, social science studies on the development of cancer treatments have brought to the fore the dual role of medicines both in patient care and in producing knowledge about cancer as a disease and its pathways (Vignola-Gagne et al. 2017; Tarkkala 2019).

Rheinberger (1997) emphasizes that the emergence of scientific novelty in the laboratory requires a carefully orchestrated setting of researchers, previous knowledge, and suppliers of appropriate technologies and reagents. Extending this view, Cambrosio and colleagues have shown that novel developments and the consolidation of criteria for solid knowledge in biomedicine necessitate that work in laboratories and research sites can consistently follow specific patterns of activity, coordination, and regulation (Keating and Cambrosio 2003; Cambrosio et al. 2006, 2009b). These patterns form the basis both for the constitution of biomedical objects and knowledge production and for hybridization that blurs the boundaries of scientific and clinical work (Keating and Cambrosio 2003; Cambrosio et al. 2009a). The resulting biomedical platforms (Keating and Cambrosio 2003), with their epistemic, organizational, and regulatory patterns, enable the making of scientific futures in terms of scientific discovery and the application of new knowledge or inventions in clinical work. These futures have an additional dimension that Miettinen (1998) highlighted in discussing 'where-to' objects of research work. This concept refers to the future continuity of a research group or groups and partners of the group(s) through expanding, redirecting, and transforming their "basic activity" (Miettinen 1998, 446) while including "the societal use of results" (Miettinen 1998, 440) in their future visions and orientation. Thus, Miettinen's view of the futures in play for the objects of science is wider than that of Rheinberger, who focuses on the inherent dynamics of the practical pursuit of new knowledge in the life sciences.

In our analysis of EV research, we discuss both dimensions and also expand our scope of research objects beyond an internalistic understanding of laboratory work, in a manner that parallels Tuunainen's (2001) case study of R&D on virus-resistant potatoes. He suggested expanding on Rheinberger's work (1997), underlining that "both basic scientific concerns and societally significant applications" are at play in research work in the life sciences (Tuunainen 2001, 98); he also employed the concept of a 'dual object' to address the presence of both an epistemic and an application object in research. Similarly, Saari and Miettinen (2001, 315) have described application objects as addressing "industrial or other practical problems, in the solution of which the phenomenon studied is used", in contrast to the object proper as a phenomenon "to be understood and modeled".

These twofold concepts and analyses based on them are the basis for the discussion in this paper; however, we do not want to incorporate further dualisms to grasp the object in today's hybrid life sciences. For this reason, we discuss the EV as a hybrid research object and analyse the hybridization

of EVs in research practice, in which scientific exploration and the pursuit of clinical, social, and economic utility of biomedical innovations are simultaneous and aligned. This approach matches with that of Tuunainen and Miettinen, as they precisely address such simultaneity and overlap. All in all, our conceptual approach builds on Rheinberger (1997) and analyses that have complemented his view on objects of science and their dynamics (Tuunainen 2001; Miettinen 1998).

In sum, we study a case of EV research collaboration through 'partnership' as an example of hybridized life science research, highlighting especially the expectations involved. Collaborations are seen as the modus operandi of research work in current life sciences (Penders et al. 2015, 5), and many studies have identified and addressed an amalgamation of scientific, clinical, and commercial interests in biomedical collaborations (e.g., Cooper 2008; Cambrosio et al. 2009a; Sunder Rajan 2012; Ong 2016; Gardner, Webster and Mittra 2017; Aarden, 2017; Sun 2017; Beltrame and Hauskeller 2018). Research has shown that the partners in such collaboration are dependent on each other in terms of technical devices, finance, and epistemic authority. Moreover, Star and Griesemer (1989) have, with the concept of a boundary object, addressed how such collaboration is possible through cooperation by actors in creating a sense of a shared object, even when local flexibility and incorporation of actors' different viewpoints remain. However, as we root our analysis on Rheinberger's thinking and concepts that extend his view, our focus is slightly different. We examine collaborative R&D through paying attention to its object –in our case, the EVs. We claim that collaboration that crosses academia/commerce and scientific/clinical boundaries is essentially actualized on the level of mundane research practices. We demonstrate this by analysing how the research object is modified along with the unfolding of R&D work, as different scientific, clinical, and commercial interests and objectives are attached to the EVs. Moreover, we analyse accommodation of diverse interests and objectives in the research consortium, in which formation of the EVs as a hybrid object attached to multiple expectations and prospects is crucial[2].The novelty of our study is showing that hybridization of biomedical research (Hauskeller and Beltrame 2016a, 2016b; Beltrame and Hauskeller 2018) – i.e., the amalgamation of scientific, clinical, commercial, and social aspects – is aligned with the hybridization of the R&D object because expectations and assumptions of its potential greatly affect the coordination of research practices (see also Tarkkala, Helén and Snell 2019; Borup et al. 2006; Brown 2003; Brown and Michael 2003; van Lente 2012; Tamminen and Vermeulen 2012).

In what follows, we present our research data and the methods applied. We then move on to present the context of collaborative science in relation to our case, followed by analytical sections that highlight the EV and its hybridity as a research object.

2. Data and methods

This article discusses a case in which scientific and commercial partners came together in a research-and-development program; all partners shared an interest in extracellular vesicles and an "aim for applicability", meaning that developing personalized medicine was in their interest. The SalWe EV consortium and the partners involved form our case and site, which we will comprehensively introduce in the following section. In this section, we introduce how we ourselves approached our site and conducted our research.

The research data utilized in this article were collected between 2015 and 2017, when the working of the consortium was most intense. The data are of three types. First, there are 11 interviews with 10 informants connected in different ways with the SalWe program. Most were participants in a work package representing both industry (n=4) and academic partners (n=4), while two informants were interviewed due to their expertise in managing SalWe and SHOK programs. Because of the low number of participants interviewed, we only detail whether the quoted informant is a commercial or university partner. Some key informants were interviewed twice to get follow-up information. Second, our analysis is based on fieldnotes of observations in two public conferences where EVs were presented and discussed and in seven meetings in which project participants discussed the undertaking: how it was proceeding, what the findings suggested, the way forward, and so on. Finally, we incorporate scientific articles on EVs that contextualize, describe, and discuss the developing, technology-intensive domain of research.

We applied systematic content analysis to the research data, also utilizing the case study approach and STS ethnography in our analysis. The latter approaches helped us to contextualize the textual data of the interviews and articles, guiding us to employ different types of research data to triangulate the findings of our analysis. Comparison of interviews, fieldnotes of observations, and published research papers as well as our navigation between them allowed us to locate our findings in their context and test their accuracy.

Our content analysis of the data was fundamentally inductive, in keeping with our aspiration to 'let the data speak for itself'; however, we conducted our analysis in dialogue with literature on the objects of the life sciences: the hybridization of scientific practices, role of expectations, and organization of the life sciences into research platforms. Given this approach, we first read systematically through the interviews and other material, focusing on participants' descriptions of the EVs, of what they themselves were doing in research, and of the workings and objectives of the consortium. Three thematic framings came to the fore during this reading: 'basic science', with an emphasis on technology and methodological development, antibody development, and the EV Core facility service. During our second systematic reading of the data, we focused on what was said about EVs within these three framings, paying particular attention to two issues: first,

what the participants said they know and do not know about EVs, and second, how they characterized the EVs as an object and the potential of EVs and EV research.

In the analytical section, we organize our analysis of the EVs as a hybrid object according to the aforementioned three framings. Before that, we describe the SalWe program and the context of the Finnish EV consortium that is the site of our case study. More generally, the program is an example of a societal framework that facilitates the hybridization of life sciences.

3. Conducting collaborative science

The EV research consortium forms the site of our study. It was initiated in 2012-2013 when people from two university institutions (one biomedical, one molecular biology unit) and three companies (one producing blood products, one antibodies, and one pharmaceuticals) came together to plan a joint research effort. This consortium was summoned in the context of the public innovation promotion framework called Centres for Strategic Excellence (SHOK), administered by the Finnish innovation funding agency Tekes and funded by the Finnish government. The SHOKs were relatively independent funding bodies, and one of them, SalWe, launched a 30-million-euro biomedical program focusing on personalized medicine, of which the EV consortium was a major part. EV research was seen as a rising field in international molecular biology and biomedicine, and the participants shared the view that their main purpose was to diminish organizational and technological dispersion of EV research in Finland. Yet the initial aims of the joint effort were manifold:

> The major objective of the partners in the program is to create standardized technology platforms for extracellular vesicle studies. The novel tools and platforms can then be applied on the basic research and R&D of extracellular vesicles and the identification of EV-derived biomarkers. In the end of the project, there will be novel tools for monitoring the quality of blood products and novel sensitive biomarker methods for development of cancer diagnostics. In addition to research tools, the utmost objective of the partners is to create an active and intense national public-private network around the extracellular vesicles that will have link to international public-private researchers. (SalWe, 2013)

The work of the Get it Done (GiD) research program with SHOK funding was carried out between 2014 and 2018 and was indispensable to building up and consolidating the Finnish EV research milieu.

Within this framework, work on EVs constituted an assemblage of biomedical science focused on new knowledge and scientific methods and of R&D for seeking new medical products. The borders between public institutions and private business were blurred because the SHOKs' imperative

goal was to encourage such collaboration. Indeed, there were two conditions for funding: first, projects were to involve both public research institutions and independent companies, and second, companies had to provide half of the funding devoted to research. Furthermore, R&D priorities and the interests of the private company partners were supposed to orientate research work in the SHOK projects. This collaborative tie was not only formal; rather, it saturated the working of the EV consortium as a whole, as we will show in this article.

The Finnish EV consortium exemplifies a contemporary mode of operations for the life sciences and biomedicine. As many studies have shown (e.g., Gardner, Webster and Mittra 2017; Vallas and Kleinman 2008; Owen-Smith and Powell 2001), research on medicine, molecular biology, and the life sciences is often conducted in or closely related to settings in which science and R&D are intertwined. The two serve each other through collaboration between experts and technologies in academic or public research institutions, small and specialized innovative companies, and large multinational corporations. Research endeavours in these settings are usually embedded in a 'partnership' between public institutions and private companies for organizing, financing, and appropriating research. These are also the main features of the Finnish EV consortium.

One can often see another manifestation of the same phenomenon in the promotion of public-private collaborations in knowledge societies. In the research literature, this mode of science and its organization are referenced with terms such as 'collaborative' (Powell, Koput and Smith-Doerr 1996; Powell et al., 2005), 'mode 2' (Gibbons et al. 1994), 'entrepreneurial' (Johnston and Edwards 1987; Etzkowitz 1998), or 'marketized' (Wedlin 2008); other labels are 'triple helix' knowledge production (Etzkowitz 2008) and 'academic capitalism' (Slaughter and Rhoades 2004; Cantwell and Kauppinen 2014). Many studies (e.g., Pavone and Goven 2017; Kleinman and Vallas 2001) have suggested that the life sciences' mainstream has adopted this mode of 'knowledge production'; it has also been shown that biomedicine has become quite extensively subject to marketization and commercialization efforts in this context (Gardner, Webster and Mittra 2017; Mittra 2016; Powell and Owen-Smith 1998). Facilitated by two trends, this has developed and spread globally during the past half-century. Since the late 1960s, big corporations such as multinational pharmaceutical companies have made their R&D activities more open, seeking collaboration with academic research groups and smaller, innovative, high-tech companies (Mittra 2016; Mittra and Milne, 2013; Etzkowitz, Webster and Healey 1998). This growing openness has been congruent with the efforts of international organizations, such as the OECD, and the governments of wealthy industrialized countries to establish policies promoting science and technological innovation as part of long-term economic and industrial planning (Miettinen 2002; Powell and Owen-Smith 1998). In the landscape of 'innovation policy', science was ultimately expected to result in products, methods, or 'solutions' that would be practically useful and commercially

profitable. In practice, innovation policy in different countries encouraged the organization of scientific research into 'public-private partnerships' with academia and private companies as well as the initiation of governmental programs and funding 'instruments' to speed up the utilization of new sciences and technologies (Miettinen 2002; Powell and Owen-Smith 1998). The SHOKs in Finland were an offspring of such policy.

A collaborative, R&D-oriented, commerce-affinitive organizational model of science affects actual research practices in biomedicine (see Tuunainen 2005 for an example from the field of biotechnology). In the case we present, science and business are aligned or even entangled in the actual settings, procedures, and practices of biomedical research. Accordingly, research design, protocols, and techniques simultaneously serve many purposes in scientific exploration and in the further development of research technology, clinical applications, and commercial products. Data collection, analyses, and experiments take place in a framework of multiple definitions of objectives, results, and criteria for success or failure. In our analysis of Finnish EV research, our main interest lies in this multiplicity at work in research practice, building on a line of STS research that stresses the local practices of university research in striving for knowledge, applications, business, collaboration, and social utility (e.g., Rheinberger 1997; Tuunainen 2005; Miettinen 1998).

We argue that intensive future orientation facilitates the hybridization of research. As policymakers and funding bodies encourage and even oblige science and the scientist to be practical, productive, and receptive to economic appropriation, much or even most of the sphere has responded by becoming overtly *promissory* (Helén 2013; Petersen and Kristjansen 2015; Fortun 2008; Brown 2003; Brown Kraft and Martin 2006; Morrison 2012; Martin 2015). This response is notable especially in the life sciences and biomedicine with emerging technologies. For scientists, research laboratories, and institutions working in these fields, there are few chances to get research projects funded without augmenting proposals by promising ample prospects of solutions to grand medical problems and giving assurances of clinical and commercial applications. These expectations imply certain futures that are crucial for making and sustaining alignments between science and business and between science and medical treatments in biomedical R&D. Business and clinical rationales become entangled in experiments, and research seems to be conducted on the basis of the *potential* for profits and clinical applications inherent in biomedical exploration.

The researchers working in the EV consortium appeared to have a positive view of the hybridity – the simultaneous presence of multiple objectives – of their research. Projects that conjoin public biomedical research institutions and private companies, in which basic life science is entangled with practical objectives of developing biotechnology or applications to serve a medical diagnosis or treatment, were mostly seen as 'natural' or 'necessary' by the researchers, although they acknowledged

that EV research is not likely to produce 'medically useful' results in the near future. Nonetheless, in both public labs and private companies, researchers emphasized the collaborative aspect of the work; for them, the expansion of opportunities for collaboration is an asset of this endeavour:

> Well, it is a win-win. Synergy. Like when people have different viewpoints, different angles, and different needs … then we just get more done. There are more people with a joint interest in doing things and, on the other hand, knowledge and other resources. So we are stronger than we would be as a single group or, what is worse, as competing groups that just fiddle around with their own thing and jealously look around at what others are doing. (Research partner)

> This is purely about networking. We are a company partner, and yet it is very important for us that we have contacts with basic research, and this is a very good way to create a wider network we would otherwise not necessarily come into contact with. (Commercial partner)

Such a sentiment of 'joining forces for future gains' was widespread in research practices and settings of the EV consortium, as we will show in the following analysis. Perhaps this is why a somewhat surprising finding of ours is that tensions or disagreement between academic and commercial partners were not salient enough to hamper the work of the consortium. In this particular setting, the future orientation both in building networks and in conducting actual research tasks seemed to have the power to suspend possible controversies to the future, and allowed partners to acknowledge that their interests and objectives were diverted, although they shared expectations about the EVs.

4. The EV hybridized

The EV research consortium's objective was "to build up an internationally competitive research network in Finland to ensure high quality research and innovations in monitoring health and disease" (SalWe,2013, 99). Under this definition, a variety of scientific, medical, organizational, and commercial tasks, including the building and continuation of research work and collaboration (see also Miettinen 1998), are drawn together. Consequently, EVs are an object of multitasking. In this context, they carry the *potential* to generate discoveries in the life sciences, new tools for biomedical R&D, and new biotech products for clinical use, building research infrastructures, and sale. Nonetheless, in practice, an ethos of basic research was eminent in the consortium, as all participants seemed to acknowledge that certain scientific and technical thresholds have to be reached before any of the EVs' potential can be actualized. This had already been emphasized in the research plan:

> For solid and reliable diagnostic and clinical applications, the base of the EV technology and characteristics must be developed and established before biomarker development or novel EV-based therapies and drug delivery technologies can be developed. (SalWe 2013, 99)

In what follows, we analyse the work carried out and based on EVs. We begin by underlining the prospect of scientific novelty and the need for basic research and then address simultaneous knowledge-production and development goals before moving on to the way future continuity of research is embedded in the working with EVs.

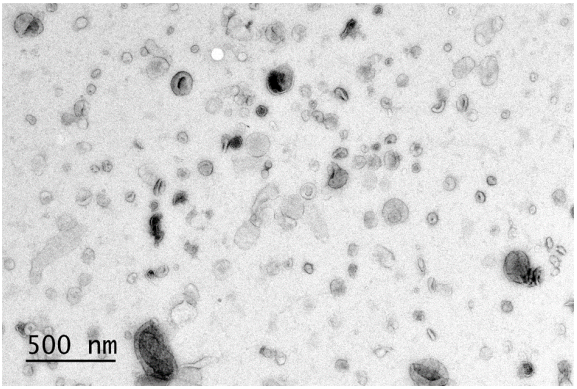

Figure 1. A picture of urine vesicles taken as part of the storage study with an electron microscope[3]. Image source: Maija Puhka.

4.1 Basic research, scientific novelty, and collaborative science

In a public lecture at the University of Helsinki, researcher Rienk Nieuwland described EVs as the "sleeping beauties of science" that contain "clinically relevant but unexplored information" (Fieldnotes, 18.6.2016). This characterization exemplifies how EVs are charged with expectations of medical applications while they simultaneously stand for scientific exploration and discovery and thus are an 'epistemic thing' (Rheinberger 1997). Epistemic things are both "material entities … that constitute the objects of inquiry" and entities characterized by vagueness, since they "embody what one does not yet know" (Rheinberger 1997, 28). In the words of Rheinberger (1997, 27), a researcher works "with a whole experimental arrangement designed to produce knowledge that is not yet

at his disposal". Finnish researchers also highlighted this aspect:

> We just had a meeting of the International Society of Extracellular Vesicles at Rotterdam. You could see there that there is hype about the utilization and application of EVs. But there is still so much we do not understand about what they are and what they do and how they work and where they go… So it is important to do basic research so that we understand what we are utilizing. (Research partner)

For Finnish researchers, conducting 'basic' work with EVs means working in a technology-intensive research field. Accordingly, a lot of their expectations focus on development work in terms of standardization, reference materials, and technology (e.g., Palviainen et al. 2017, 78). When talking about their work with EVs as 'basic research' or 'basic science', researchers emphasize the need for technologies that enable advances in scientific exploration with EVs, ultimately making discovery possible.

In Finland and elsewhere, EV research is considered a developing field. The researchers still have significant tasks ahead in terms of standardization, validation, and development of methods and techniques – for example, in the purification and characterization of EVs (Kalra, Drummen, and Mathivanan 2016; Mateescu et al. 2017; Théry et al. 2018). EV preparations become easily contaminated (Mateescu et al. 2017; Théry et al. 2018), and it is not known "how many functionally distinct subtypes [of EVs] there may be" (Mateescu et al. 2017, 2) or in how many ways they differ (Kalra, Drummen, and Mathivanan 2016, 2, 18-19). Indeed, even being sure that one has vesicles in a sample is a challenge. Thus, working with EVs incorporates the classic experimental dynamics of science, as presented by Rheinberger (1997). When describing their work, Finnish EV researchers emphasize the quest for a variety of elements that Rheinberger (1997) calls technical objects, "characteristically determined within the given standards of purity and precision". Technical objects are a precondition for experiments that might produce epistemic things, and therefore they "determine the realm of possible representations" of what is under study (Rheinberger 1997, 29). Similarly, Miettinen (1998, 431) has pointed out that "an object (a microbe, an instrument, a theoretical model, a sample of cellulose substrate) can be either a means or an object in research activity".

The consortium's scientific efforts were mainly oriented towards developing and improving technical objects in Rheinberger's sense (1997) – or the means of research activity, as suggested by Miettinen (1998) – and an EV as an epistemic thing is also necessarily implied in this view. By a focus on the improvement of methods and techniques of detection, measurement, and classification of EVs and by the setting of standards, both scientific discovery and practical applications became possible to consider

and reach for. Thus, concentration on technical objects was a priority, despite the promise EVs carry – for example, in "how they contribute to metastasis in cancer" (research partner). EV scientists in Finland were inclined to evaluate research in this field as tending to be ahead of itself, even when "basics… like storage life, measuring, and standardization [were] missing – or not missing, but deficient" (research partner). However, this tendency is simultaneously the beauty of the field.

> This is a new and developing scientific field; everything is still in development, which is rare. And that excites me; everything is new and surprising, and it's almost like whatever you find or don't find you can report as a scientific outcome. (Research partner)

The emphasis on technical objects was especially prominent in the consortium sector called 'the storage study'. This R&D work package concentrated on studying how EVs behave – that is, their quality and functionality, for example in red blood cells and platelets and in urine (see Figure 1.) – during and after storage at certain time points. The prior objectives of the study were rather practical, as a commercial partner set the task of searching for "advanced indicators of the functionality of blood products" and testing "how much information EVs can give of the condition of the blood products" (SalWe 2013, 100). This, however, was simultaneously considered basic research, essential to furthering the field. For example, rather than searching for a new blood product per se, a commercial partner wanted to learn whether vesicles could yield new information about already-existing items:

> We are trying to find out and clarify what really happens in the bag [of blood product] from the perspective of the vesicle. Quite the basics, that's what this has been all about, and then whether there is the possibility of finding a specific vesicle or certain vesicle classes – or their content – that could serve as markers. (Commercial partner)

The storage study highlighted that basic knowledge and standardization are needed in this field, in terms both of potential epistemic things and of developing and stabilizing technical objects. Even though the commercial goals in life science research are often seen as leading to more 'applied' and 'utility-oriented' science (see e.g., Glenna et al. 2011 for a discussion on the commercialization of university research), this EV project was always framed and described as predominantly 'basic research' by the interviewees. This view is congruent with the findings of social science research about scientists' different uses of the term. Calvert (2004; 2006) argues that scientists tend to describe their work as 'basic research' flexibly and with a considerable amount of ambiguity. According to Calvert (2006, 200), "scientists can use the term to protect themselves from evaluation and demands for applicability, and in this way use it to protect their interests." One way to use the term 'basic research' that Calvert (2004,

256-257) identifies is related precisely to underlining the epistemic goal of producing new knowledge on something yet unknown. Thus, 'basic research' as a description may be used flexibly depending on the context, for alleviation of pressures or creation of shared understanding about the state of the research. In the interviews we conducted, it was even suggested that given the funders' expectations of the life sciences, the kind of basic work done in this consortium would probably not have received funding in more 'scientific' funding calls. A common understanding among participants was that life science research proposals need to be 'future-oriented' (research partner) and show novelty, yet plans of further research building on the work done in the storage study seemingly lacked both elements.

> This field still needs a lot of basic research … We tried to get continued funding [for work] related to this study; the funding application proceeded pretty far, but in the end we received a rejection because it was said there was not enough novelty in this. And here we have a true misconception, because we truly have something new in it. Yet people just think that, yeah, the vesicles have been studied, but they do not realize what exactly about them has been studied. (Research partner)

R&D collaboration between academic and commercial partners provided the necessary resources for the storage study, although one research partner had the opinion that even research groups would probably not undertake it as their primary task because they "hardly consider[ed] it that exciting". Moreover, the storage study required time, and 'partnership' funding within the SalWe program was able to provide just that. Concretely, this meant, for example, continuation of employment, as the project was able to hire the people who actually conducted the analyses for the duration of the study. The data collection itself took more than two years because the samples were followed up to the two-year time point. On top of that, there were the analytical and reporting phases. Normally, "a research group does not have so much time to wait for the results", concluded a research partner.

Due to profound work in the storage study, the participants expected that the published article based on the results of the study would be scientifically valuable. They believed that this kind of research paper could be widely cited, as it would establish a common reference in the field.

> It is then a generally applicable reference that we stored our vesicles in a freezer for two years, and as has previously been shown, the vesicles survived. It is actually quite bizarre that no one has done such persevering work before, since it is the case that, for many labs, samples are kept a few years in a freezer. So everyone just assumes that the vesicles survive, but we can show that they really do. It is an important cornerstone for research. (Research partner)

However, this project was not just a safe haven for doing something that could be characterized as basic research. All the academic partners agreed that the involvement of commercial partners had an impact on the way the project was targeted and on the work carried out. The hybridization of the research object comes to the fore in the parallel necessities for an "industry-orientation" and production of "basic understanding and knowledge" (Miettinen 1998, 436). The academic partners also felt that the company partners had a different mindset, which the academics became familiar with and learned from during collaboration. Meanwhile, the company partners also acknowledged the need to create basic building blocks and undertake a both technical and epistemic groundwork for further knowledge production and utilization in the field of EV R&D. A discussion between two commercial partners exemplifies this:

> Partner A: By approaching this from a basic research perspective, we cannot go wrong. … In any case, we have displayed unequivocally that the vesicles are there – for instance, in the preparations – and they are increasing. They have significance.
>
> Partner B: This is not just in our heads!
>
> Partner A: But whether it makes any difference and whether it brings any utility in an applied or medical sense, that we do not know. But one of our goals is to find out what happens there.
>
> (Commercial partner)

In general, Finnish EV research consortium partners talked a lot about the focus on the 'basic'. However, they also saw their basic work – both scientific exploration and development of research technology – as inseparably attached to a more practical quest for EVs' usability and commercial potential. One way to understand this relationship is to think of the basic research as creating conditions for further utilization and future collaborations. In this context, the EVs appear as technical object:

> If we use vesicles as biomarkers, then that is what we are looking at right now, this aging, aging of the product: can we somehow define that with the help of the vesicles? Through either their content or the number of the vesicles? (Research partner)

The researchers also approached their work from more of an overview perspective. From this angle, they aligned the utility potential of EVs, the importance of technical objects in R&D on EVs, and the meaning of the EVs as an epistemic thing. As Tuunainen (2005, 287) wrote in his study on a biotechnology case, "theoretical, experimental and applied concerns" ran throughout the whole EV project. This involved more than just describing the same research as 'basic' here and 'applied' there depending on the audience (see e.g., Calvert 2006). An academic researcher reasoned over the manifold interests rooted in their efforts:

> At the same time as we produce utility or try to search for something the companies could utilize, we have to set up certain things so that we understand, methodologically, what we have. We cannot just take something and say that this is how it is; we have to know it exactly. And as these methods are very much in their early stages, at the same time, we have been interested in EVs in general: what they are and what they do and why. All of this knowledge has been valuable to us. (Research partner)

4.2 Biomarkers and antibodies for the clinics and for research

One of the working packages in the EV consortium was related to identifying possible biomarkers and developing an antibody[4] that could become a new product for a commercial partner. Scientific interest lay in discovering simultaneously whether EVs could be a source of biomarkers for prostate cancer and whether certain sources of biomarkers work better for the different stages of cancer: for example, whether urine is a better source for early stages and plasma a better source for later stages (SalWe 2013). Thus, an objective of the project was to study "EVs in different body fluids" to see if there was the potential to "differentiate between slow-growing and aggressive" prostate cancers by the source of the EVs (SalWe 2013, 101).

Exploring the development of an antibody, a commercial partner started to work on vesicle pools derived from the scientific partners. Some of the derived antibodies showed promise from the beginning, and one of the first tasks was to choose which antibodies would be chosen for further testing and development. As some of the antibodies seemed to recognize *something*, the task became to identify what exactly the 'something' was which was recognized.

This illustrates the hybridization of the EVs as a research object. It was approached both as a potential scientific novelty and as a possible commercial product. At the same time, the goal is indicative of the loop between epistemic things and technical objects (Rheinberger 1997). When an epistemic object becomes known and stabilized – as an antibody potentially could, once identified and standardized – it is possible for the same antibody to become part of the basic equipment on which further research and scientific exploration are built: that is, a technical object (Rheinberger 1997).

Simultaneous commercial and academic pursuits mean, in practice, that the same potential results concerning antibodies and what they recognize have a different significance for different partners. For example, a commercial partner developing and selling antibodies is not interested solely in markers for specific types of cancer or specific diseases, even if those markers were the program's initial focus. For the company, an antibody that "sticks fast and never let's go" could be optimal for development into a new product, regardless of whether it strictly relates to pros-

tate cancer. For academic partners, a good result could also be identifying an antibody and what it recognizes. In addition, an interest in these antibodies from outside the joint project raised concern over whether someone else might publish scientifically relevant results prior to the scientific partners involved in the project doing so. Concern also arose over whether further collaboration with the SalWe partners would occur. However, the company sees more data and information on the substance as greater validation in terms of developing the substance into an actual product.

A research partner suggested that the antibodies could have twofold uses. For example, no good antibodies currently exist that would widely recognize vesicles, so this kind of substance would enhance practical work in research laboratories, even if it does not make it to clinical use.

> If we found one [that recognizes antigens from the vesicle's surface], we could use it to characterize the concentration or number of vesicles or [use it] in the purification [of samples]. … But, yes, originally the idea was that the antibodies would recognize prostate cancer, and there can still be such antibodies, but we just are not there yet. (Research partner)

Thus, for diagnostic potential, the antibodies could become technical objects in the orchestration of scientific experiments. A research partner reflecting on this twofold quality said:

> I have been interested in whether something for the researchers would come up, but of course we should know what [the antibodies] recognize. And then the diagnostics is a separate thing: what can be discovered in terms of the cancer. We have two prospects here. (Research partner)

Chronologically, scientific and commercial fields do not necessarily proceed with results at the same pace. For example, commercial partners focus on patents first, which may take a long time. Scientific partners, however, must publish results as soon as possible to gain academic merit. Furthermore, what exactly the scientific partners could publish in this case – for example, regarding the antibody development – was under negotiation. As mentioned earlier, a highlight would have been actually identifying what the antibody recognizes. Even without that knowledge, however, a technically oriented publication could simply report on "how-to-do" vesicle antibodies because, as a research partner observed, "now we have shown that there are quite a lot of methods by which vesicles may be recognized". This situation also relates to working methods in a collaborative R&D project; the scientists were expected to wrap up data the project had collected so far instead of answering further questions the results presented.

Additionally, the GiD program's funding was reduced, and its duration was cut by a year in 2016. Thus, the EV consortium needed to narrow its focus. One element that was dropped was identifying a potential

diagnostic prostate cancer biomarker by sequencing cancer tissue vesicles' RNA or miRNA. The idea was to isolate specific prostate cancer vesicles from the prostate cancer tissue because other vesicles in this project originated from blood or urea. This work was abandoned, and the whole work package's prospect slightly changed because time was running out. Nonetheless, the situation evolved similarly to how the project had proceeded: the work's paths and directions were always based on results from earlier analyses, followed by an agreement on the necessary ensuing steps. This way, the object of study nudged the research interests in certain directions:

> Largely, we conduct experiments, see what kind of results we got, and then consider how to move forward with them. It is sort of like hand to mouth, the result dictates which way to go. (Commercial partner)

Identifying an antibody and its possible uses was one task that remained after the cuts in funding and project duration. It was hoped that the academics could eventually continue with the topics of academic interest to them, but, at the same time, realities had to be faced: the funds to continue might not exist outside of this work package because the "pipetting budget" of the SalWe project enabled university partners to continue without "having to think every time whether or not to do [something]" because of the price of reagents and other necessities in the work (research partner). Furthermore, funds for salaries might not exist, which would mean the expertise could disappear as people moved to other organizations and labs (research partner). The commercial partners also might be unable to continue their work on EVs because they depended on their research partners for things such as procuring vesicles. If identifying what an antibody recognizes requires vesicles, then gaining a supply while outside the joint program could become a challenge (commercial partner).

4.3 The Core facility and continuity

As noted in the storage study's context, even researchers have trouble being certain they are dealing with EVs. Multiple tests are often done to verify the analysis really studies what it is supposed to study (e.g., Puhka et al. 2017). Consequently, one result of the GiD program's work package on EVs was founding the EV Core. This continued work from other projects, but realizing a centralized facility became possible as the GiD intensified connections between involved partners. Based on the expertise of scientific partners, the Core was to be launched in 2016. In short, the idea was to help "people know whether they have vesicles in their samples or not". The Core was planned to offer expertise, isolation, quantification, analysis services, RNA isolation and sequencing, and consultation on EV studies. Equipment and machines were crucial. For example, "the espe-

cially sensitive flow cytometry" was obtained for researchers at the university and could now be utilized via the Core's service. A research partner summarized: "There are so many research groups nowadays who need concentration analysis, but do not have money nor willingness to buy the device."

Knowledge, expertise, and the ability to use devices like the Apogee A50-Micro flow cytometry or electron microscope had engendered suggestions about collaboration, so founding the Core facility service seemed a logical response in this situation. This response meant that "one could do small business and, perhaps, guarantee oneself a more stable income", instead of trying to collaborate with everyone (research partner).

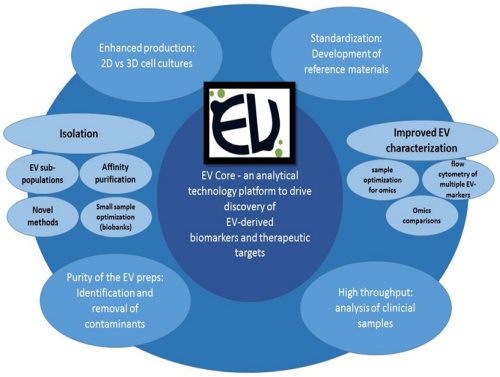

Figure 2. The EV Core as presented on their web page[5].

The EV Core started operation in 2016 (Palviainen et al. 2017) as "the world's first EV Core" providing "infrastructure, state-of-the-art and emerging EV-technologies for research groups, hospitals, companies and authorities in the EV-field" as well as "diverse EV isolation, purification and characterization services and […] contacts to various downstream analyses in other core facilities"[5]. On its web page, the Core appeared as an analytical technology platform for EV research (Figure 2). The SalWe program's participants saw the Core as a result that, according to a commercial partner, "stabilizes this field in Finland" and "internationally brings awareness that we have such a centre of expertise here". Simultaneously, the EV Core is also a space to develop, for example, isolation methods (Palviainen et al. 2017), to participate in standardization and validation work, and to gain insights into current events in the field. Along with the instruments at hand, the Core provides a chance to do research and, hopefully, to build personal career continuity inside the home institution. It also offers an opportunity to "stay abreast of what sort of things people are doing" with EVs (research partner) while simultaneously offering services that meet their

needs (research partner). In a sense, founding the Core service is simultaneously an inevitable part of *doing* research and *ensuring* the research's continuation, again illustrating the EV's hybridization. Conceptually, the EV and the EV Core include the dimension of a 'where-to' artefact. Miettinen (1998) introduced this conceptualization precisely to describe how research groups build continuation and intentionality into their work.

The Core's main goal is not to make a profit per se (Palviainen et al. 2017, 78) as long as it can "sustain itself" (research partner). Moreover, the Core's technological intensiveness is inseparable from expertise intensiveness. The Core connects specific expertise with specific technologies and devices as it aligns partners to collaborate with each other:

> There are vesicles. But since we still do not specifically know precisely what they are, this EV Core is unquestionably important […]. It should be developed and invested in because, as said, this field is so difficult, requiring specific equipment and instruments, the development of the instruments, of analytic software, everything like that for us to [make it work] […]. We cannot distribute this to many different places in a country this small. (Commercial partner)

At the end of the SalWe program, the continuation of the EV Core facility service faced a challenging situation. Continued funding was not guaranteed for researchers who had been hands-on during the analyses. Thus, how to move forward was uncertain, even though laying the foundations for continuity was one prime goal for establishing the EV Core in the first place. Additionally, the key researchers' expertise with the equipment and with hands-on work with vesicles proved to be the Core's actual asset.

> This Core, certain devices are connected to it. But, first and foremost, we, the researchers, have the expertise, which cannot be taken away from us [even] if we give the devices to someone who knows how they work but not how this is related to vesicles. … There have to be the people who know what to do with them, and both of those instruments are really challenging, not easy to automate, like press this button and the answer comes. Instead, you have to understand how you adjust them, how you put the settings, and what you get out of it, and then there is still a lot of tuning up. And then, for example, how to purify them [vesicles] so that contamination will not become a source of error. We measure really small particles that contaminate if your buffers are, for example, not filtered. Yeah, we cannot, for instance, take people here to measure with those devices without first educating them extensively about how to do it. (Research partner)

The urgency related to funding was especially connected to expertise. Funding cuts tend to yield a situation in which personnel are no longer available when funding returns; such a situation "would require us to get

the same people back; we cannot start this all again from nothing" (research partner). The above block quote emphasizes that expertise combining technical and scientific matters with craft cannot be adopted overnight (see Meskus 2018). A research partner explained that, even with someone eager to learn EV techniques and interested in joining the EV Core's crew, considerable time is needed to master the devices and the craft.

> You learn with your eyes and you learn from different samples. I am also learning all the time while I work, but I have a lot of grounding with which I can compare. So it is a bit… I might have time to educate a new person on some level, but in order to offer someone's work as a Core service, that requires time and careful consideration. (Research partner)

Along with the availability of expertise and skilled personnel, the fast pace of technological development posed a challenge – technological development makes instruments and devices outdated eventually. In this sense, a research partner stated a need to "step on the gas", because the interest in the EV Core has been promising, but more efficient and better equipment will enter the field at some point. To progress and stay relevant, one must follow developments, receive funding, and keep skilled persons on board. These issues are crucial for the EV Core to stabilize itself as a long-term, meaningful, well-known, and high-quality service.

5. Conclusions

Our analysis of EV research in Finland shows that, because science and R&D are entangled in the financing, organization, and everyday practices of EV research, the EVs are simultaneously thought of and enacted as many kinds of objects. Therefore, they are a *hybrid by expectations*. The EVs act as a genuine scientific object, 'an epistemic thing' (Rheinberger 1997). Their physiological functions and the biological mechanisms in which they are involved are not fully known; consequently, scientists think pursuing 'basic' research on EVs may lead to scientific discoveries in molecular biology and biomedicine when technology and research methods allow for new knowledge to be crafted. At the same time, researchers are working on stabilizing EVs and on the methods to observe and manipulate them, so EVs can serve as a tool for scientific research, 'a technical object' (Rheinberger 1997) enabling new knowledge and discovery. Technical and epistemic stabilization, or even standardization, of EVs also has a clinical arm. The expectation of EVs becoming biomarkers for detection of, for example, cancer and EV-related biotechnology becoming clinically useful are central to the research of the Finnish EV consortium. The clinical aspect closely relates to the commercial one: for company partners, research on EVs allows the development of EV-related products

for biomedical research and for the clinical market. From their perspective, EVs as biomarkers associate with a future biomedical commodity[6].

Finally, the EVs as research object are enacted in the Finnish consortium as something upon which to build the continuity and sustainability of this life science specialty (Miettinen 1998). By developing and maintaining the EV Core as a SalWe project spin-off, EV scientists believe they can strengthen their research's financial and scientific foundations. They reason that providing technical services and expertise in research methods for 'EV issues' to other biomedical research groups can sustain research collaboration, help them follow developments in the field, and even gain revenue. This would enable further development of the SalWe project's work and reinforce the position and capabilities of Finnish scholars in emerging life sciences and biotechnology fields.

The EV object has prospects in all these fields. Within biomedical R&D, the EV's promise includes various modalities. Epistemically, the EVs are unknown and have potential for scientific novelty; as prospective biomarkers, they offer promise or even a 'dream' of clinical and commercial utilization; as a stimulus for developing research techniques and methods, they support sustainability. EVs exist and are worked upon primarily through their potential, reflecting an overall orientation towards choreographed 'future making' (see Rheinberger 1997) in EV research and in biomedical R&D. Academic and commercial partners both repeatedly emphasized this collaboration's predominant 'basic research orientation', but the rhetoric of future uses and benefits brought focus to diagnostic and clinical utilization in a life science project. The current work simultaneously performs the expectation of eventual translation even while the work concerns taking the first steps in the domain. A research partner of the Finnish EV consortium pointed out this configuration:

> When thinking about applying for funding and so on, the applications must be very future-oriented, and so when the grant applications are written the potential usability of the results [in the future] must be very thoroughly thought through. One always tries to consider the potential usability of the results, but especially when it comes to the specificity of this field in which even the very basics are still part of the search, the preservation of samples is extremely important to know and explore. (Research partner)

Notably, the aspect of future-making also seems to have the power to prevent tensions regarding hybrid practices and alliances in EV research from escalating and thus paralyzing the project. As researchers share an idea that they are working upon something in a state of becoming, the EVs can simultaneously exist as many kinds of objects (scientific, technical, clinical, and commercial), which does not cause a problem with R&D activities because potential controversies or mismatching goals need not be resolved now. In other words, looking forward allows the suspension of such matters.

In a parallel way, the focus on the technicality of EV research facilitated the maintenance of unity and the solidity of the consortium's work, which had multiple directions. It included and aligned scientific pursuits, efforts to develop items or methods for clinical or commercial use, and the organization of a facility providing biomedical research services. According to the researchers, the EV is predominantly a technical matter in these three areas. They emphasized that work on EVs primarily concerns technology and methods. Consequently, the crucial question concerns what is allowed by research techniques and devices, whether expertise exists in certain analyses and methods, how EV preparations were crafted, the available reagents, and how to validate the results. Technicality provided a common ground for the consortium partners' diverse pursuits.

> B: We all have our own [focus], but then we share the object of study…
>
> A: In this work package, there has been a good situation because it is so clear that we all have our own interests, so we do not have worry. We can share the whole technology topic. We can share many things...
>
> B: … and all the results we get.
>
> A: Yes, because we know that we all have our own domains, but then there is also the intersecting zone. (Commercial partners)

To conclude, the hybridity that characterizes much of contemporary life science results from the amalgamation of elements and domains usually considered distinct: academic and corporate elements, public and private elements, scientific quests, clinical utility, and commercial pursuit. This subverting of traditional boundaries concerns the financing and organization of research and its concrete practices and objects. As our analysis of Finnish EV research shows, hybrid research practices simultaneously pursue various objectives, and the object of the research is manifold. Therefore, the practice and the object of life science again show the conventional distinction between basic and applied science is less apt to describe the actual undertaking.

Two of our observations on such entanglements are particularly important. First, the promissory ethos with which EV research was imprinted and the emphasis on its technical character were crucial for unifying the heterogeneous elements and objectives of EV research and mostly prevented epistemic and other tensions. Second, subverting the demarcation between basic (academic) and applied (clinical and/or commercial) research did not subsume the scientific quest to clinical or commercial utility. On the contrary, research and commercial partners saw EV research as an emerging and immature life sciences field, so they emphasized that the consortium's work was predominantly 'basic science'. The rationale was that biomedical companies need basic knowledge of EV science, and the academics were there to provide such knowledge. A bit surprisingly, academic partners were very content with the financing and

collaboration the hybrid formation provided. This arrangement allowed them to do 'basic science' via investigation and experiments focused on the basic biology of the EV and via basic research techniques and methods. According to them, such research 'lacks novelty' and is therefore unlikely to attract public research funding. However, this work also provides the only route to the expected innovations.

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[1] A search in PubMed reveals that there were 219 matches for the term 'extracellular vesicles' in 2008, whereas in 2018 there were 2,333 matches (https://www.ncbi.nlm.nih.gov/pubmed/?term=extracellular+vesicle, 22 May 2019). A search in Web of Science points in a similar direction, with matches rising from 209 in 2008 to 2,462 in 2018 (https://apps.webof-knowledge.com-/RAMore.do?product=WOS&search_mode=GeneralSearch&SID=F6To3PL5pRKjctlbHze&qid=1&ra_mode=more&ra_–name=PublicationYear&colName=WOS&viewType=raMore, 22 May 2019).

[2] Studies on bio-objects have also discussed the hybridity of objects in the life sciences (e.g., Vermeulen et al. 2012). This work has underlined that bio-objects "tend to disrupt the conventional boundaries and identities of biological forms and categories" (Metzler and Webster 2011 649), such as animal and human or viable and non-viable; thus, the concept helps to show the openness of "boundaries around "the living" (Holmberg, Schwennesen and Webster 2011, 742) and the movements "backwards and forwards between different life-statuses" (Webster 2012, 2). This discussion emphasizes that bio-objects are also characterized by their status as "contested socio-technical objects" (Holmberg, Schwennesen and Webster 2011, 741) and highlights processes of bio-objectification that engender such status and contestation in actual settings of research and usage. Our approach to the hybrid character of life science objects is in many ways affinitive to the ideas of bio-objectification, especially where organization of science is transformed (Vermeulen 2012). In this paper, we highlight the *practical* hybridity of the R&D object derived from the amalgamation – or hybridization – of scientific, clinical, commercial, and social objectives in the work of the life sciences.

[3] Electron microscopy is a characterization technique used in EV studies that also allows researchers to visualize and quantify the EVs present in a preparation. The scale of the image is in nanometres, which are one billionth of a metre.

[4] Antibodies are produced by the body in response to, for example, disease, and in this way their presence can be used for diagnostic purposes and to indicate the composition of certain samples.

[5] Available at https://www.helsinki.fi/en/research-groups/extracellular-vesi-

cles/ev-core (retrieved 17.9.2018)

[6] Despite apparent similarities, the research object's 'hybridity' discussed in this paper differs from Annemarie Mol's (2002) idea of multiple ontology of diseases. She claims that a disease as a medical object is multiple or "more than one and less than many" (Mol 2002, 82) because of various enactments upon a disease in different medical practices and sites via different devices. This specific kind of ontology is not our focus. Our analysis of the EVs' hybridization emphasizes the collaboration of scientific, clinical, and commercial partners around a scientific object, and we focus on how the collaboration creates dependencies, constraints, and conditions for the research. This moulds the EVs as an object that is shared yet manifold, i.e., a hybrid. Our discussion about the hybridity of the research object highlights the simultaneous presence of various interests and objectives aligned through the EVs.