Transitions in the vaccine innovation system: analysis of changing innovation barriers

Linda van de Burgwal[1*], David Stubbs[2], Hannes Kempter[2], Manuel Gadau[2], Tom van der Valk[1,2]
[1] Vrije Universiteit, Athena Institute, Amsterdam
[2] Raymond James Corporate Finance, Health Care, London

* l.h.m.vande.burgwal@vu.nl

Introduction

The productivity of research and development (R&D) in the vaccine development industry is declining (1-3). Timelines have consistently increased, development costs have risen and market values for vaccines have dropped (4-6). These developments translate into a "productivity gap", with insufficient release of new products, the hampering of current research practices, and ultimately failure to solve unmet medical needs (7-9).

The existence of market failure for R&D, and specifically for R&D in the context of emerging infectious diseases, has long been acknowledged. These diseases have insufficient market size and ability to pay and therefore the return on investment is limited (10). As a result, many large pharmaceutical companies have abandoned their development programs against infectious diseases (11).

In sum, these developments threaten the ability to respond quickly to emerging pathogens. (12-14). Currently the world is facing one such emerging pathogen; SARS-CoV-2. Considering the immense societal damage it is causing globally, the need for quick vaccine development is higher than ever before (15, 16). Rethinking the mechanisms through which to engage public and private stakeholders is thus of the essence (17).

The basis for many calls for reform is the ambition to strengthen collaboration between different stakeholders, based on the core principles of open innovation (18-20). This openness, however, is difficult to establish in a system that is rooted in inherently conflicting institutional norms and incentives, as well as legislative restrictions and ambiguities in regulatory frameworks that hamper stakeholders from engaging in an open manner (17, 21-24).

Since persistent problems are embedded in the system, addressing these problems cannot occur without system innovations (25). Here we build upon the theory of transitions research to understand how persistent barriers are embedded in the system of vaccine development. We adopt a root-cause analysis approach to distinguish symptomatic from systemic barriers (26), and use data collection at three time points to understand the transitions occurring in this system.

Theoretical framework

Building upon the multi-level perspective (27), the socio-technical regime of pharmaceutical innovation is characterized by large, incumbent pharmaceutical companies who take the lead

in the final development steps and marketing of new medical innovations (28). This regime has been effective in addressing the issues of the past, resulting in the development and market introduction of many vaccines that address previously unmet medical needs.

However, as evidenced by the appearance of a range of persistent problems, the configuration of subsystems is not well suited to address current challenges. Society calls for the availability of effective countermeasures, and is at the same time increasingly hesitant to accept vaccines (29, 30), developers experience a productivity gap, while at the same time feeling responsibility for addressing society's most unmet needs (31), governments contemplate compulsory licensing to ensure access to medical countermeasures developed in their territories (32), and regulators are pressured to ensure rigorous evaluation of clinical trial dossiers in a timely manner (33).

Crises are driving forces for transitions and transformations (34), and destabilization of a socio-technical regime generates windows of opportunity for niche-innovations (27). And indeed, the current covid-19 crisis can be seen as a driving force from the exogenous context for the adoption of practices and structures that are different from the dominant socio-technical regime. Moreover, innovation policies that support the development of covid-19 medical countermeasures are in line with efforts previously made in niche experiments: large-scale governmental funding (35), engagement of public and private stakeholders (36) calls for equitable access and distributive justice (37-39) and reciprocity (40).

Building upon the radical nature of the reform introduced by the pandemic (41), we might see that the dominant culture of the regime will change as well, unlike in earlier reforms to the health system (42). Also, previous emerging infectious disease outbreaks show that familiar barriers remain hard to overcome (43). The current pressure on the innovation ecosystem is thus an exquisite opportunity to study the intricacies of this complex problem, as such problems are best understood when changes are made to the system (27).

Innovation barriers are key to defining the limitations of socio-technical regimes, as they result from structural properties of social systems (44). This study therefore investigates how innovation barriers changed pre-covid and during covid to understand whether the system is indeed in transition.

Methods

This mixed-method study builds on a uniquely compiled dataset of vaccine innovation barriers identified before the onset of the COVID-19 pandemic (April-June 2019), a quantitative prioritization of those barriers at the top of the crisis (April-June 2020) and a qualitative identification of innovation barriers that are likely to persist beyond the covid-19 pandemic (March-May 2021).

Vaccine innovation consists of a number of distinct but closely interrelated sub processes that need to align for successful innovation (45). Typically, different actors are active in each of those sub processes, and thus identified obstacles can be external or internal to each actor (46). Data collection therefore draws from actor perspectives across the vaccine innovation cycle, to gain insight into which barriers are related to institutional arrangements, and which are a result of interfering actions of other stakeholders. Distinguishing between systemic barriers and their underlying causes through a root cause analysis, then facilitates insight into whether the system is indeed transitioning to a state better adapted to future challenges, or whether the underlying problems are not addressed (26, 47).

Qualitative interviews with 21 Key Opinion Leaders, influential and knowledgeable individuals within the extensive and rapidly changing field of vaccine development, took place between April-June 2019. The semi-structured interview design consisted of a topic list containing four sets of questions: 1) experiences on development timelines in the last 10-15 years, 2) identifying delaying steps in the vaccine development process, 3) possible solutions to the described bottlenecks and 4) confirmation of all perceived barriers and additional comments. For each identified barrier follow-up questions were asked to establish cause and effect and determine if the KOL could identify any opportunities that could address the barrier.

After thematic analysis of transcribed interview recordings, a root-cause analysis was performed to identify causal links were identified between innovation barriers (7, 48-50). This resulted in the deduction of key barriers and their causal factors.

92 responses to an online questionnaire (response rate 15%, after data cleaning 11%) provided insight in the impact of the barriers on vaccine development timelines (7-point Likert scale), and on the three most impactful barriers on general, and on covid-19 vaccine development in particular. Mean scores of the Likert-scale impact-ratings across all barriers for the non-pandemic vs. covid-19 situation were computed and tested against each other in a paired samples t-test.

The post-covid dataset compiles of 20-25 semi-structured interviews (in progress) with KOLs between March and May 2021. The aim of the interviews was to gain insight into which changes are likely to continue post-covid, as a means to understand whether interventions in innovation policy incorporated during the covid-19 pandemic to stimulate innovation, are likely to become embedded into the socio-technical regime of pharmaceutical innovation.The interview design consists of the topics: 1) identification of innovation barriers that will persists after the pandemic, 2) identification of innovation barriers that will arise or arose during the pandemic, 3) interviewees' experience on the development of possible solutions to these barriers and 4) confirmation of all identified barriers and additional commentary.

Interview data on anticipated post-covid innovation barriers was analyzed in a similar manner as the pre-covid interviews. Subsequently, a comparative analysis between pre- and post-covid innovation barriers was made, and viewed in light of proposed innovation and transition policies.

Results

The root cause analysis of pre-covid barriers resulted in the identification of 20 key barriers. Key barriers impact nearly all phases of vaccine development. The area that is impacted by most barriers starts at late stage preclinical and ends at the phase 3 clinical trials.

Innovation barriers identified pre-COVID-19 related to 'Limited ROI for vaccines addressing disease with limited market size', 'Limited ROI for vaccines compared to non-vaccine projects', 'Academia not being able to progress beyond proof of principal'. Importantly, many of such barriers relate to difficulties in collaboration networks.

Prioritization of barriers in comparison to those relevant during COVID-19 showed that the aforementioned barriers as well as the required knowledge base was lacking, due to lack of investments in earlier outbreaks. The two most impactful barriers during general vaccine development, that relate to a limited ROI, were barely mentioned as one of three most impactful

during covid-19. Also, the barrier 'High risk to upscale manufacturing of yet unlicensed vaccine' was prioritized by respondents.

Initial interviews for the post-covid dataset highlight the increased attention for onshoring of manufacturing capacity as well as a reduction in dependency on foreign supply chains. In addition, solutions to 'Limited ROI for vaccines addressing disease with limited market size', 'Limited ROI for vaccines compared to non-vaccine project', and 'Academia not being able to progress beyond proof of principal' are proposed as well as measures to counteract the lack of required knowledge base.

Discussion

This study shows a clear difference in KOL perception of barriers hampering timelines in general vaccine development in contrast to a markedly different set of barriers being specific for covid-19 vaccine development. By linking the findings of this study to the theoretical framework of transitions, the covid-19 pandemic provided a unique opportunity to see this transition of the system in action, as indicated by a shift in both symptomatic and systemic innovation barriers.

The covid-19 pandemic is expected to lead to increased interest and expected implemented policy changes in digital technologies for medical innovation, organizational collaboration while simultaneously sparking a trend towards self-dependency on vaccine development, manufacturing and deployment through supply chains. At the same time, Key Opinion Leaders see an increased trend towards collaboration, supported by novel technologies (16).

While innovation policies and transition policies are not always compatible (51), alignment can occur when innovation policies contribute to larger system transitions, especially when regime changes do not require phasing out of existing industries (52). Such is the case in the current covid-crisis, where actors engaging in this changed approach are not only those that have been supporting novel approaches before, but explicitly also large incumbents (36).

Despite these clear changes and alignment, it remains to be seen whether these changes will remain in place after the covid-19 pandemic. Proposed measures to embed the changes into a transitioned socio-technical regime will be discussed. The paper thereby informs transition and innovation policy.

By focusing on Key Opinion Leaders and building upon data saturation, the current study provides a clear overview of the main issues in the transitioning landscape of vaccine innovation. Nevertheless, niche actors can have diverging opinions or perceptions which are not necessarily included in this research. Future action-guided research should therefore focus on the implementation of the identified changes and lessons from this research.

References

1. DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: New estimates of R&D costs. J Health Econ. 2016;47:20-33.
2. Pronker ES, Weenen TC, Commandeur H, Claassen EH, Osterhaus AD. Risk in vaccine research and development quantified. PLoS One. 2013;8(3):e57755.
3. Sams-Dodd F. Is poor research the cause of the declining productivity of the pharmaceutical industry? An industry in need of a paradigm shift. Drug Discov Today. 2013;18(5-6):211-7.
4. Liu M, Li Q, Lin J, Lin Y, Hoffman E. Innovative trial designs and analyses for vaccine clinical development. Contemporary Clinical Trials. 2021;100:106225.
5. Black S, Bloom DE, Kaslow DC, Pecetta S, Rappuoli R, editors. Transforming vaccine development. Seminars in immunology; 2020: Elsevier.
6. Thakor RT, Anaya N, Zhang Y, Vilanilam C, Siah KW, Wong CH, et al. Just how good an investment is the biopharmaceutical sector? Nature biotechnology. 2017;35(12):1149-57.
7. Pronker ES, Weenen TC, Commandeur H, Claassen EH, Osterhaus AD. Risk in vaccine research and development quantified. PloS one. 2013;8(3).
8. Rappuoli R, Hanon E. Sustainable vaccine development: a vaccine manufacturer's perspective. Current opinion in immunology. 2018;53:111-8.
9. Ho ZJM, Hwang YFJ, Lee JMV. Emerging and re-emerging infectious diseases: challenges and opportunities for militaries. Military Medical Research. 2014;1(1):21.
10. Darrow JJ, Sinha MS, Kesselheim AS. When Markets Fail: Patents and Infectious Disease Products. Food & Drug LJ. 2018;73:361.
11. Rex JH, Lynch HF, Cohen IG, Darrow JJ, Outterson K. Designing development programs for non-traditional antibacterial agents. Nature communications. 2019;10(1):1-10.
12. Koff WC, Burton DR, Johnson PR, Walker BD, King CR, Nabel GJ, et al. Accelerating next-generation vaccine development for global disease prevention. Science. 2013;340(6136):1232910.
13. Organization WH. The world health report 2007: a safer future: global public health security in the 21st century: World Health Organization; 2007.
14. Zimmermann KF, Karabulut G, Huseyin Bilgin M, Cansin Doker A. Inter-country Distancing, Globalization and the Coronavirus Pandemic. The World Economy. 2020.
15. Bonaccorsi G, Pierri F, Cinelli M, Flori A, Galeazzi A, Porcelli F, et al. Economic and social consequences of human mobility restrictions under COVID-19. Proceedings of the National Academy of Sciences. 2020;117(27):15530-5.
16. van der Waal MB, Ribeiro CdS, Ma M, Haringhuizen GB, Claassen E, van de Burgwal LH. Blockchain-facilitated sharing to advance outbreak R&D. Science. 2020;368(6492):719-21.
17. Reperant LA, van de Burgwal LHM, Claassen E, Osterhaus AD. Ebola: public-private partnerships. Science. 2014;346(6208):433-4.
18. Gristwood A. Fresh approaches to vaccine development. EMBO reports. 2018;19(8):e46675.
19. Chesbrough H. To recover faster from Covid-19, open up: Managerial implications from an open innovation perspective. Industrial Marketing Management. 2020;88:410-3.
20. Lezaun J, Montgomery CM. The Pharmaceutical Commons: Sharing and Exclusion in Global Health Drug Development. Science, technology & human values. 2015;40(1):3-29.
21. Ribeiro CdS, van Roode MY, Haringhuizen GB, Koopmans MP, Claassen E, van de Burgwal LHM. How ownership rights over microorganisms affect infectious disease control and innovation: A root-cause analysis of barriers to data sharing as experienced by key stakeholders. PLOS ONE. 2018;13(5):e0195885.
22. Ribeiro CdS, Koopmans MP, Haringhuizen GB. Threats to timely sharing of pathogen sequence data. Science. 2018;362(6413):404.
23. Flach J, dos S. Ribeiro C, van der Waal MB, van der Waal RX, Claassen E, van de Burgwal LHM. The Nagoya Protocol on Access to Genetic Resources and Benefit Sharing: Best practices for users of Lactic Acid Bacteria. PharmaNutrition. 2019;9:100158.
24. Heymann DL, Liu J, Lillywhite L. Partnerships, Not Parachutists, for Zika Research. New England Journal of Medicine. 2016;374(16):1504-5.
25. Grin J, Weterings R, editors. Reflexive monitoring of system innovative projects: strategic nature and relevant competences. Paper for the session 'Reflexive governance for sustainable development'at the 6th Open Meeting of the Human Dimensions of Global Environmental Change Research Communicate; 2005.
26. De Cock Buning T, Regeer B, Bunders J. Biotechnology and food: towards a societal agenda in 10 steps. The Hague: RMNO. 2008.
27. Geels FW. Technological transitions as evolutionary reconfiguration processes: a multi-level perspective and a case-study. Research policy. 2002;31(8):1257-74.
28. Fernald KDS, Weenen TC, Sibley KJ, Claassen E. Limits of Biotechnological Innovation. Technology and Investment. 2013;04(03):168-78.

29. Salmon DA, Dudley MZ, Glanz JM, Omer SB. Vaccine hesitancy: causes, consequences, and a call to action. Vaccine. 2015;33:D66-D71.
30. Dror AA, Eisenbach N, Taiber S, Morozov NG, Mizrachi M, Zigron A, et al. Vaccine hesitancy: the next challenge in the fight against COVID-19. Eur J Epidemiol. 2020;35(8):775-9.
31. Piot P, Larson HJ, O'Brien KL, N'kengasong J, Ng E, Sow S, et al. Immunization: vital progress, unfinished agenda. Nature. 2019;575(7781):119-29.
32. Wong H. The case for compulsory licensing during COVID-19. Journal of Global Health. 2020;10(1).
33. Kesselheim AS, Darrow JJ, Kulldorff M, Brown BL, Mitra-Majumdar M, Lee CC, et al. An Overview Of Vaccine Development, Approval, And Regulation, With Implications For COVID-19: Analysis reviews the Food and Drug Administration's critical vaccine approval role with implications for COVID-19 vaccines. Health Affairs. 2021:10.1377/hlthaff. 2020.01620.
34. George G, Lakhani KR, Puranam P. What has changed? The Impact of Covid Pandemic on the Technology and Innovation Management Research Agenda. Journal of Management Studies. 2020;57(8):1754-8.
35. Yamey G, Schäferhoff M, Hatchett R, Pate M, Zhao F, McDade KK. Ensuring global access to COVID-19 vaccines. The Lancet. 2020;395(10234):1405-6.
36. Ho RJ. Warp-speed Covid-19 Vaccine development: beneficiaries of maturation in biopharmaceutical technologies and public-private partnerships. Journal of Pharmaceutical Sciences. 2021;110(2):615-8.
37. Bollyky TJ, Gostin LO, Hamburg MA. The equitable distribution of COVID-19 therapeutics and vaccines. Jama. 2020;323(24):2462-3.
38. Nkengasong JN, Ndembi N, Tshangela A, Raji T. COVID-19 vaccines: how to ensure Africa has access. Nature Publishing Group; 2020.
39. Abbas MZ. Treatment of the novel COVID-19: why Costa Rica's proposal for the creation of a global pooling mechanism deserves serious consideration? J Law Biosci. 2020;7(1):lsaa049.
40. Jenek S, Celli-Bird K, Celli-Bird K, McCormack M, Guille D, Evans N, et al. Monday, December 15:: A team of World Health Organization scientists is finally assembling in the Chinese city of Wuhan on a mission to find the answer to that multibillion-dollar question-where the hell did COVID-19 actually come from? 2021.
41. Broerse J, Grin J. Toward sustainable transitions in healthcare systems: Taylor & Francis; 2017.
42. Essink DR. Sustainable health systems: the role of change agents in health system innovation. 2012.
43. Koopmans M, de Lamballerie X, Jaenisch T, Consortium ZI. Familiar barriers still unresolved-a perspective on the Zika virus outbreak research response. Lancet Infect Dis. 2019;19(2):e59-e62.
44. Giddens A. The constitution of society: Outline of the theory of structuration: Univ of California Press; 1984.
45. Van de Burgwal L, Ribeiro CDS, Van der Waal M, Claassen E. Towards improved process efficiency in vaccine innovation: The Vaccine Innovation Cycle as a validated, conceptual stage-gate model. Vaccine. 2018;36(49):7496-508.
46. Schuitmaker TJ. Identifying and unravelling persistent problems. Technological Forecasting and Social Change. 2012;79(6):1021-31.
47. Sondeijker S, Geurts J, Rotmans J, Tukker A. Imagining sustainability: the added value of transition scenarios in transition management. Foresight. 2006.
48. Corbin JM, Strauss A. Grounded theory methodology. Handbook of Qualitattive Research. 2011:273-85.
49. Van den Nieuwboer M, Van De Burgwal L, Claassen E. A quantitative key-opinion-leader analysis of innovation barriers in probiotic research and development: valorisation and improving the tech transfer cycle. PharmaNutrition. 2016;4(1):9-18.
50. Dehzad F, Hilhorst C, de Bie C, Claassen E. Adopting health apps, what's hindering doctors and patients? Health. 2014;2014.
51. Kern F, Smith A. Restructuring energy systems for sustainability? Energy transition policy in the Netherlands. Energy policy. 2008;36(11):4093-103.
52. Alkemade F, Hekkert MP, Negro SO. Transition policy and innovation policy: Friends or foes? Environmental Innovation and Societal Transitions. 2011;1(1):125-9.

Extended abstract submission, EU-SPRI Conference

THE EMERGENCE OF DEEP LEARNING IN COLLABORATIVE DIGITAL INNOVATION. A FRAMEWORK AND THE CASE OF MEDICAL IMAGING DIAGNOSIS OF COVID-19

David Barberá, INGENIO (CSIC-UPV), Spain, jobarto@ingenio.upv.es

Deep learning has the potential to transform fields such as genomics or materials science, where collaborations between experts and computer scientists may be altered by this emergent technology (Cockburn, Henderson and Stern, 2018). This paper proposes a framework for understanding the impact of deep learning in the field of digital medical imaging, where collaborations between radiologists and computer scientists from universities, companies and hospitals have raised high (and, so far, largely unsuccessful) expectations over the last three decades about the development of computational models that radically change diagnostic practice (de Jong et al., 2017). To illustrate the model we will use the case of the development of deep learning tools to detect Covid-19 and which have been implemented as a useful tool for patient triage and complementary support to PCR diagnosis in some countries such as China.

Our framework is based on the proposed concepts of logics of data control and deep learning affordances. The concept of logics of data control comes from the literature of institutional logics, defined as the set of values, practices and rules governing action in organizational fields (Friedland and Alford, 1991). Data control logics refer to the set of values, practices and rules that govern access to data in the field of digital innovation (Hinings et al., 2018; Hilgartner, 2017). Logics of data control can be "activated" by a new digital technology (such as deep learning) thanks to the "affordances" that emerge from the interaction between humans and technologies (Faik et al., 2021). The concept of affordances has been developed by Information Systems literature and refers to the "possibilities for goal-oriented action that an actor or group of actors perceive in a technology as they engage with the materiality of its artifacts" (Marcus and Silver, 2008; Leonardi, 2011). We adapt this concept from information systems to account for the affordances related with the emergence of deep learning. The relationship between affordances and logics is non-deterministic: logics may not be activated if the affordances are not consistent with the actors' goals.

We will illustrate the model with the case of the emergence of deep learning in digital medical imaging. Digital medical imaging has been developing since the 1990s, without much impact on clinical practice. In this field, radiologists from various specialties and computer scientists working in universities, hospitals and start-ups (sometimes of academic origin) collaborate to design algorithms capable of diagnosing and predicting the evolution of various diseases. Until the advent of deep learning, radiologists have played a key role in the collaborative process, both in data acquisition and analysis: acquisition and analysis were part of the same data stream (Hilgartner and Brand-Rauf, 1991). The logic of data control in this organisational environment is that of expert control: data are not commercialised or openly distributed but are shared in collaborative projects between consortiums of hospitals, universities and companies, usually led by radiologists.

The emergence of deep learning in this field has revealed two interrelated affordances: the elimination of the need for radiological expertise in data analysis and the simplification of radiologists' intervention in data acquisition, which now only needs to be "labelled", a task that is often part of routine radiological practice. These affordances can activate data control logics other than expert control, as the case of Covid-19 shows. Since the beginning of the pandemic, numerous groups of computer scientists have taken advantage of these affordances to activate the logic of open access to data. Instead of creating collaborative projects, these groups simply had to use the numerous open databases tagged according to the existence and degree of infection created by various institutions during the crisis to train and test their algorithms, which have proven to be highly accurate.

Research groups and companies that were previously part of the organisational fields built around innovation in medical imaging have also used deep learning to develop algorithms to identify Covid-19. But these other initiatives have not taken advantage of the affordances of deep learning and have maintained the pre-existing expert control logic in this field: these projects are organised around consortia of hospitals and companies, where data is shared among consortium members but not open to the general public. We conclude discussing general propositions from our model which could be tested using quantitative analysis of co-authorship of scientific articles and patents published collaboratively by groups in hospitals, companies and universities in this field.

Propositions will compare patterns of collaboration before and after the emergence of deep learning in the field.

References:

Cockburn, I. M., Henderson, R., & Stern, S. (2018). The impact of artificial intelli-gence on innovation (No. w24449). National bureau of economic research.

de Jong, I. M., Kupper, F., Arentshorst, M., & Broerse, J. (2016). Responsible reporting: neuroimaging news in the age of responsible research and innovation. Science and engineering ethics, 22(4), 1107-1130.

Leonardi, P. M. (2011). When flexible routines meet flexible technologies: Affordance, constraint, and the imbrication of human and material agencies. *MIS quarterly*, 147-167.Friedland, Roger and Alford, R. Robert. 1991. 'Bringing society back in: Symbols, practices, and institutional contradictions,' in *The New Institutionalism in Organizational Analysis*, ed. Walter W. Powell and Paul J. DiMaggio, pp. 232–263. Chicago: University of Chicago Press.

Faik, I., Barrett, M. and Oborn, F. (2020). How information technology matters in soci-etal change: an affordance-based institutional logics perspective. Mis quarterly, 44(3).

Hilgartner, S. (2017). Reordering life: knowledge and control in the genomics revolution. MIT Press.

Hilgartner, S., & Brandt-Rauf, S. I. (1994). Data access, ownership, and control: Toward empirical studies of access practices. *Knowledge*, *15*(4), 355-372.

Hinings, B., Gegenhuber, T., & Greenwood, R. (2018). Digital innovation and transformation: An institutional perspective. Information and Organization, 28(1), 52-61.

Markus, M. L., & Silver, M. S. (2008). A foundation for the study of IT effects: A new look at DeSanctis and Poole's concepts of structural features and spirit. *Journal of the Association for Information systems*, *9*(10), 5.

Title: Mobilizing knowledge for science and innovation: a multi-criteria approach for the analysis of scientific impact of research collaboration processes through biomedical research networks

Hannia Gonzalez-Urango; Pablo D'Este; Rocío Poveda Bautista; O. Llopis, A. Arias Díaz-Faes.

There is increasing evidence that the search for solutions to technological, social and economic problems requires collaborative ties between different type of actors: scientists, technology and business practitioners, civil society (among others). Analysis of these types of networks and collaboration processes represents a line of strategic research in current science and innovation studies (EC, 2012; Owen et al., 2012).

Hence, we draw on the argument that greater network cohesion is crucial to elicit effective learning processes in research networks consisting of highly diverse actors. We argue that there is a poor understanding about the specific type of mechanisms that promote effective exploitation of the complementarities of network diversity, to jointly achieve considerable scientific and societal impact. This is particularly the case concerning research networks consisting of highly heterogeneous actors, when complementarities among partners as well as the coordination challenges involved might be greater. This discussion motivates our research.

The specific setting for our proposal is the biomedical research context. The biomedical context allows us to address the multiple dimensions of actor heterogeneity, and the analysis of processes that contribute to bridging translational gaps between knowledge generation and application.

The focus of this study is a research group participating in one of the most prominent support platforms for translational biomedical research in Spain: *Centros de Investigación Biomédica en Red (CIBER*). This is one of the main publicly funded initiatives to support research excellence and translational research in Spain (CIBER, 2006). This initiative embraces a wide range of research projects covering many different types of diseases and pathologies which are critical from the viewpoint of their impact on healthcare. The proposal aims to investigate how the scientific research network of this group operates to deliver both scientific discoveries and applicable results.

We propose the use of a multi-criteria approach (Saaty, 2010) to model the interaction processes of this group with relevant and diverse actors. These interaction processes will be grouped in components corresponding to distinct research phases from basic to clinical research stages. The approach will be used to analyze the influences that exist between these processes of interaction within and among applicable research results.

This will allow complementarities to be identified between interaction processes that foster cohesion among network participants. The influence analysis will identify the mechanisms of scientific collaboration that contribute to greater network cohesion, and how much they should be encouraged to coordinate actor diversity in research networks.

The multi-criteria approach involves a decision model that comprises a selection of decision criteria (network elements) and their grouping into components, and analysis of the influences among the elements and components of the network.

The network elements will be derived from semi-structured interviews conducted in a previous phase of the research methodology. The interviews based on the research phases, will provide

information on the interaction processes that respondents (researchers and stakeholders) identified as relevant for strengthening cohesion in translational research collaborations. We use all the researchers and stakeholders involved in processes of interaction that contribute to network cohesion. These stakeholders will include researchers, physicians, patient groups, and representatives of companies or other organizations. For the influence analysis among the elements of the network, we will prepare a questionnaire comparing pairs of interaction processes with dependency relations. This questionnaire will be administered face-to-face to experts selected after analyzing the case studies interviews. The experts will be asked about the interdependence relationships among all the network elements, and to respond to the pairwise comparisons of interaction processes in order to assess the degree of influence of each interaction process on some other process in the context of knowledge generation performance.

The results seek to discuss the benefits and advantages of linkages between different actors in a biomedical network and how they can be usefully conceptualized to inform future and address current and future research that wishes to have a clear impact on societal challenges. This is particularly important in times of crises.