INTRODUCTION

The pathways between basic science, clinical practice and health outcomes are multifaceted and complex. Analysis of these pathways has attracted the interest of the biomedical research community and public health agencies. Researchers and funding agencies are concerned with the ways in which scientific breakthroughs and evidence-based clinical findings are converted into practices with beneficial health impacts, including, but not limited to, therapies and medical guidelines. This interest is driven largely by the perception that many promising results from basic biomedicine have not contributed systematically to medical treatments and, ultimately, health care improvements.[1] In response, a wide range of publicly-funded initiatives have been set up to address this problem. As the main aim of these initiatives is to facilitate the "translation" of scientific discoveries into beneficial applications and practices, many of these initiatives have been branded "Translational Research" (TR).

TR has become a very popular term and has been applied to large research programmes, research activities and, even, academic journals, and has attracted the interest of biomedical scholars and institutions (Marincola 2003; Woolf 2008; Zerhouni 2007). The origins of the concept can be traced back to the 1990s, when the US National Cancer Institute (NCI) developed the Specialized Programs of Research Excellence (SPORE) (Lander and Atkinson-Grosjean 2011). Starting in 1992, SPORE provided support for efforts to facilitate the "translation" of basic discoveries generated at academic centres, into new interventions aimed at preventing and treating various types of cancer. Since then, several policy initiatives have focused on the transformation of basic knowledge into health benefits. In the US, the

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[1] Some analysts estimate that less than 10% of the most promising biomedical discoveries resulted in any benefit to clinical practice two decades later (D.G. Contopoulos-Ioannidis, E.E. Ntzani, and J.P.A. Ioannidis, 'Translation of Highly Promising Basic Science Research into Clinical Applications', *The American Journal of Medicine,* 114/6 (2003), 477-84; J. Ioannidis, 'Materializing Research Promises: Opportunities, Priorities and Conflicts in Translational Medicine', *Journal of Translational Medicine,* 2/1 (2004), 5.)

National Institutes of Health (NIH) launched the Roadmap Initiative (Zerhouni 2003), the Clinical and Translational Science Awards (Heller and de Melo-Martín 2009), and, in December 2011, a $575 million National Center for Advancing Translational Sciences (NCATS).[2] TR initiatives have also been launched in the European Union and its Member States. Some are explicitly labelled TR programmes, others have similar objectives and rationales although they are labelled differently. For example, in 2006 the Spanish Ministry of Health launched the Networked Centres of Biomedical Research (CIBER)[3] together with other research initiatives to facilitate the relationship between basic scientists and healthcare practitioners (Rey-Rocha and Martín-Sempere 2012).

Often the more popular the policy concept, the more ambiguous it becomes. This clearly applies to TR and there is emerging debate on the models of research which are considered to be "translational" and the nature and characteristics of a putative TR discipline (Littman et al. 2004). Consequently, the ways in which TR should be analysed, and more specifically the approaches to the evaluation of TR programmes are similarly open to debate. Given the substantial investment in TR programmes, the definition of TR evaluation strategies has become important for policy definition and implementation. Given the ambiguity about the type of activities that can be considered TR, evaluation approaches and practices can play an important role in determining these activities thus shaping the nature of TR initiatives. This paper discusses the dominant approaches to TR evaluation and proposes an alternative evaluation framework, which may have implications for the way in which TR programmes may be defined in the future.

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[2] www.ncats.nih.gov
[3] CIBER is the Spanish acronym for "Centro de Investigación Biomédica en Red". http://www.isciii.es/ISCIII/es/contenidos/fd-investigacion/fd-ejecucion/fd-centros-participados/fd-consorcios2/cibers.shtml

First, we provide an overview of the different ways in which TR is conceptualised. Many approaches consider TR as activities that bridge gaps in a continuum stretching from basic research to health outcomes (Morris et al. 2011). Other views emphasize the research process, how different groups interact, and how their roles may be redefined by a TR initiative (Currie and White 2012).

Second, we discuss different evaluation approaches associated with these different views of TR. One of the dominant approaches focuses on the outputs generated at different points of the "translational research continuum" and estimates the time it takes to produce them. A focus on "what" and "when" implies a TR evaluation approach that attempts to identify results and how they differ from what would have been achieved in the absence of the initiatives being assessed. It should be emphasised that this focus on outputs may derive from an explicit view of TR as addressing "translational gaps" along a "TR continuum", or may emerge without any explicit "theory" of the processes and objectives of TR. TR then is measured against success criteria based on the generation of outputs that are no different from the outputs generated by traditional research. Note that, in the absence of a "programme theory" the objectives of TR will, de facto, be defined by the evaluation strategy chosen.

Our proposal is to focus, instead, on "how" research is carried out, on the processes of collaboration and exchange that can be attributed to TR initiatives. To this end, we develop an alternative TR evaluation framework that focuses on understanding the processes of change across the divides that hinder the application of the capabilities and knowledge generated by basic biomedicine to health care. The extant literature attributes the low level of practical application of biomedical research to a variety of causes, including: (i) the divide between the interests and skills of the different professional communities and disciplines, such as basic scientists, clinical scientists and clinical practitioners (Currie and White 2012);

(ii) the problem of communication among fields that are becoming more complex and specialised (Littman et al. 2004); and (iii) the existence of institutional barriers and occupational boundaries that hinder the effective flow of knowledge and interests (Lander and Atkinson-Grosjean 2011).

Third, following the conceptual framework proposed by Ron Boschma (2005) we suggest that TR initiatives can operate by generating "proximities" along five different analytical dimensions: cognitive, social, organisational, institutional and geographical. We define these dimensions and argue that a TR support activity can be defined by the type of proximity it targets. We illustrate this by referring to two Spanish biomedical research programmes, and conclude by exploring the implications of using this alternative way of framing TR evaluation.

TRANSLATIONAL RESEARCH: A VARIETY OF APPROACHES

The development of TR initiatives reflects the perceived need to increase the chances that scientific discoveries will lead to benefits for patients, and to improve the alignment between biomedical research in biomedicine and health needs. TR emerged at a time when other initiatives aimed at facilitating the "valorization" or uptake of research by socio-economic actors were flourishing (Bozeman and Boardman 2004). TR has become part of the policy discourse justifying many current research funding programmes. The inclusion of the TR discourse in the policy agenda has been accompanied by intense academic discussion among biomedical scholars. What policy or management measures are needed to speed up the process of application of biomedical research advances to clinical practice? How should we characterize TR and evaluate TR initiatives? The development of a conceptual framework to describe the TR process and evaluate TR initiatives has become a theme in the academic research literature (for a review of the discussion see Drolet and Lorenzi, 2011).

The linear model of TR

The most popular representations of TR assume a linear model of innovation (Rogers 2003), prioritizing basic research as the primary source of new discoveries, which subsequently are developed into therapeutic solutions and finally are diffused to patients and the wider society. In the medical field, the adoption of this approach sees basic scientists at the origin of the innovation process, producing a large amount of fundamental knowledge at the molecular or cell level, some of which will be relevant for the development of new drugs or therapies. The fundamental knowledge generated by basic scientists moves forward through the stages of a "translational continuum" until eventually it is translated into specific benefits for patients or the general population, in the form of new drugs, devices and new prevention and treatment options. Every step in this linear progression addresses a specific problem and is undertaken by a specialized group of researchers. In this view, the successful application of new knowledge is dependent on the successful completion of every one of the stages along the "translational continuum" (Van der Laan and Boenink 2012).

Insert Figure 1 about here

Indeed, the idea of moving forwards through stages, which has been described as going from "bench to bedside", is thoroughly ingrained in most of the existing conceptualisations of TR - in academia and among practitioners and policymakers (Khoury et al. 2007; Sung et al. 2003). This stage approach to TR does not differ substantially from the classic linear stage process which characterises all clinical research. What makes TR approaches different is the explicit identification of which steps in these processes are more problematic and slow the progression towards application and health benefits. Thus, TR models identify a series of

translational chasms, gaps or blocks that need to be bridged (Woolf 2008). These chasms are viewed as obstacles and typically are described using what has come to be known as a "T-terminology" (Dougherty and Heller 1994), which consists of a structured list of (T)ranslation gaps to be bridged. According to these models, the main objective of TR is to bridge these gaps so as to facilitate more rapid movement of knowledge through the successive steps from basic research to application.

One of the first models adopting a T-terminology was developed by the US Institute of Medicine's Clinical Research Roundtable, which identified two main gaps: T1 and T2. The first chasm (T1) is related to the transfer of basic discoveries into human clinical testing, the second, T2, refers to the dissemination and adoption of successful clinical discoveries into daily clinical practice. As TR research has developed, more detailed models have been proposed, which include more T-phases and more chasms to be bridged. Westfall et al. (2007) proposed a TR model beginning at T1, where knowledge coming from basic science moves to human clinical research through the development of Phase I and Phase II clinical trials. According to this model of TR the process starts at the "bench", with fundamental discoveries in molecular biology, genetics and other basic sciences which may be of interest for understanding human health. The T2 chasm comprises the activities related to the translation of initial human testing results into clinical practice. Activities such as Phase III and Phase IV clinical trials, and observational studies and survey research, are considered to occur at this stage. The final gap (T3) deals with the translation into practice, and the dissemination of the new clinical treatment (e.g. through the development of guidelines for clinical practice, patients and the general population). Other models break down the translational continuum even further by proposing an additional final gap (T4), which emerges in the effort to advance towards real-world health outcomes by promoting the adoption of evidence-based recommendations by health practitioners (Khoury et al. 2007).

Some of the proponents of these linear TR models acknowledge that knowledge can flow also from "bedside to bench". For instance, Marincola (2011) stresses that hypotheses tested in basic research experiments can be based on observational evidence from practitioners. Research based on clinical evidence is particularly important because it provides factual knowledge collected through practitioner observation (e.g. through direct contact with patients), which can be translated into specific hypotheses to be tested in the lab, or lead to ideas that open up new research avenues. However, although the bidirectional nature of TR is acknowledged in most TR models, the majority of TR policy initiatives pursue or are based implicitly on a unidirectional "bench to bedside" understanding of knowledge generation and application, as reflected in the terminology referring to consecutive gaps (T1, T2, T3,…) which need to be bridged.

This focus on the identification of T-gaps has posed a series of challenges that have framed much research on TR analysis and evaluation and some problems. In analysing TR to find solutions to different translational gaps, the identification of these gaps and the different views of stakeholders about how to address them, can lead to different understandings of what TR is about (Van der Laan and Boenink 2012) and what specific skills scientists should develop to support TR (Rubio et al. 2010). Littman et al. (2007) point out that, for academics, TR represents (1) a channel to test whether novel ideas generated by basic science have the potential to translate into practical applications, (2) an opportunity to gain observational insights and develop novel scientific hypotheses to be tested in the lab, and (3) a means to gain legitimacy and improved access to research funding. However, for clinical practitioners such as physicians or clinical staff, TR is viewed primarily as responding to the need to shorten the path between scientific evidence and actual practice (Davis et al. 2003). Business organizations view TR as a process to accelerate the development of a new drug or therapy and as an opportunity to make go/no go decisions at an early stage in the biomedical

innovation process – potentially resulting in major savings by avoiding unproductive investments. Also, the fact that public organizations conduct TR is seen by industry as an opportunity to save on research whose returns are very uncertain (Littman et al. 2007).

The interactive-process model of Translational Research

Although different stakeholders may hold different views on the objectives of TR, there is a consensus on specific "gaps" among the succession of translational gaps. This "gap-centred" perspective, implicitly or explicitly sees knowledge accumulating through different stages from fundamental to applied research. However, some scholars have expressed concern about the adequacy of a linear TR model to frame analysis and develop policy strategies (Graham et al. 2006; Littman et al. 2007; Marincola 2011). A linear TR model builds implicitly on the theoretical separation between basic and applied research. Although this separation is widely used when talking about science and technology policy, numerous studies show that it is problematic. In particular, fundamental knowledge can be sought in order to solve an applied problem, *à la* Pasteur. This arguably is a different form of research, "use-inspired basic research" (Stokes 1997), which fits well with the TR goal of generating knowledge with an explicit focus on patient applications and public health benefits. However, a TR model based on a linear progression from basic science to health applications cannot account for the existence of "user-inspired basic research". Also, a linear conceptualization of TR may clash with the evidence on how medical innovation processes emerge and develop in the health sector. The medical research process does not always proceed linearly. Rather, innovation scholars conceptualize it as an iterative process in which insights provided by one group of stakeholders spurs advancement in surrounding professional and epistemic groups (Consoli and Mina 2009; Hobin et al. 2012).

The idea that knowledge moves forwards and backwards along the unidimensional line of the TR continuum may partially capture the view of a dynamic relation between basic and applied research and the application of its results, but cannot account for the existence of a different type of research, involving scientists who carry out fundamental research while are also systematically considering potential health applications. In fact, the participants in TR can interact, playing different roles simultaneously. It has been argued that the progress of biomedical research depends increasingly on close collaboration between researchers, practitioners, medical institutions, patient communities and research sponsors (Meslin et al. 2013). Here, the role of "boundary spanners", that is, actors who facilitate communication across different communities, is particularly important (Lander and Atkinson-Grosjean 2011; Swann et al. 2007). Boundary spanners are individuals who engage in significant transactions with members of other communities, facilitate knowledge exchange between groups, and manage intergroup conflicts (Richter et al. 2006).

From this perspective, clinical scientists working at the interface between basic scientists and health practitioners could play a crucial "boundary spanning" role, intermediating between the needs and objectives of the different actors, and conveying knowledge in a fast and timely manner (Kelley et al. 2012). To be effective, clinical scientists need management and coordination skills and knowledge of the different "languages" used by the diverse "epistemic cultures" of basic scientists and clinicians (Roberts et al. 2012). This is more easily achieved if individual researchers engage in both basic and clinical work. It has been suggested that clinicians working at the interface between basic scientists and the final beneficiaries of the research (e.g. patients) can contribute to the establishment of new partnering mechanisms with patients, with the objective of assessing therapies and performing observational studies (Kelley et al. 2012). However, the links among the diverse groups of actors involved in the development of new drugs and therapies can be problematic.

From this perspective, the main objective of TR can be redefined. Rather than focusing on bridging the gaps between successive stages in the TR process, the emphasis is placed on the roles and interactions of different actors who traditionally have fulfilled very specialized and compartmentalized roles. For instance, basic scientists may become involved in TR when conducting "user-inspired research" in close contact with, among others, clinicians and patients. Another form of TR can emerge when patient organizations collaborate with researchers to identify research problems. Clinicians can act as "boundary spanners" helping others make connections. There are many different ways to establish much closer working interactions among the different actors in the research process. Instead of seeing TR as addressing the problems that appear at specific points in a traditional, staged, linear research system, in our approach, TR addresses the separation between different groups of researchers and stakeholders throughout the process linking research to the development and application of solutions to health problems. To do so, TR focuses on processes -on how the sharing, exchange and acquisition of knowledge are articulated and how different actors get involved in this process.

TR EVALUATION: GAPS AND LAGS VS PROXIMITIES

Different ways of understanding the notion of TR open the way to a variety of translational policies and initiatives with different objectives and logics. These various notions are associated also with different ways of evaluating TR initiatives. In the preceding section we defined two main, contrasting, views of TR. Tlead to different approaches to the evaluation of TR.

Gaps and lags: evaluating the translational continuum

If TR is seen as the attempt to bridge a series of sequential gaps that hamper the translation of research results into socially beneficial applications, its evaluation should focus

on the specific gaps that TR is supposed to address rather than the whole R&D process. The success of a TR programme can then be defined by the extent to which it has reduced or bridged these gaps. The diversity of evaluation techniques that have been proposed reflects the different definitions of these gaps and the different indicators used to measure how well they have been bridged. Morris et al. reviewed 23 TR evaluation papers and concluded that "different studies use different measures, of different things, at different time points." The authors argue further that "understanding lags first requires agreeing models, definitions and measures, which can be applied in practice" (Morris et al. 2011).

This perspective assumes that the key indicator to assess TR initiatives is the time it takes for the different translational gaps to be bridged and, therefore, for the research to be translated into treatments and other health improving measures. Time lags are used also by Trochim et al. (2011). They develop a generic approach to TR evaluation and propose a flexible solution focusing on what they consider to be the final objective of TR: the reduction in the time needed to develop new clinical practices and drugs patients. They adopt a generic linear TR model to identify "markers" in the translation process and to assess the time that it takes for outputs to move across these markers. The identification of these markers is flexible and does not require a choice between one or another model of TR. There is flexibility also in the direction of the activity across markers, allowing for both "bench to bedside", and "bedside to bench" movements. The approach suggested by Trochim et al. focuses on the outputs of TR, and on the time it takes for the output of a specific activity to be translated into a different type of output identified by another marker. In other words, this form of evaluation is concerned with TR outputs rather than how these outputs are achieved.

Several TR evaluations have adopted this procedure. Even when the TR programmes themselves are unclear in the definition of their goals, time lag studies have become an

increasingly dominant approach to their evaluation. In these evaluations, the gap between the different research phases and the outputs they generate ceases to be an indicator of success and is converted into the objective of TR: shortening the time between different research stages becomes what TR is about. It could be argued that there is a risk of the tail of evaluation wagging the dog of TR. In other words, how success is measured may define the nature of the research objectives being pursued. Further, TR evaluations that focus on measuring the time lags between different research stages pay little attention to the standardization of such lag measurements and to understanding the factors underlying the measured lags (Morris et al. 2011). This presents problems for evaluation practice; for instance, time lags may be poorly assessed if the differences between scientific domains are not considered in the estimation (Contopoulos-Ioannidis et al. 2003).

A focus on outputs and time lags has some advantages. For instance, it allows the use of traditional indicators, such as scientific publications, by linking them to a "marker". This may be convenient since traditional indicators are easily available, but their application may reinforce some of the processes and practices that TR is supposed to combat. For instance, basic scientists can be assessed according to their published output, particularly the time it takes for publication to take place; however, this takes no account of how the outputs weregenerated, how the different research steps were defined and the roles of the different actors involved in the process. An understanding of TR that takes account of how the research and innovation processes are organized calls for a different evaluation approach. In the next section, we formulate an evaluation framework, which we argue is better suited to addressing the ways in which TR initiatives affect the research and application processes.

Proximities: evaluating interaction processes

Our proposal is to focus on how TR programmes affect the ways in which research objectives are defined, research is conducted, and its results applied in practice. We posit that TR initiatives attempt to address problems in the organization and management of biomedical research by bridging the divide between different actors involved in the development of new drugs, therapies, diagnostics or public health practices. These actors include the doctors and patients involved in the identification and definition of therapeutic and health problems, the researchers defining and addressing the relevant fundamental research challenges, and the clinicians and doctors developing and testing solutions. These different groups belong to different organizations, follow different implicit and explicit rules, and respond to different sets of incentives and performance criteria. These conflicting logics (Sauermann and Stephan 2013) and different epistemic cultures (Knorr-Cetina 1999) can make it difficult to align objectives and establish information flows. Stakeholders separated by institutional and organizational boundaries find it difficult to communicate needs and results. For instance, Ferlie et al. (2005) show that maintaining institutional separation among different medical professions is a major barrier to the development of medical innovations.

Thus, TR initiatives can seek to reduce some of the divides among biomedical researchers, clinical doctors, general practitioners, regulators, etc. It is important to emphasize the networked and non-linear nature of these social interactions: for instance, basic research can be influenced by insights from general practitioners and regulators, without the mediation of clinical doctors. We would suggest that these interactions may be difficult to operationalize due to the various types of distance between these different groups. Following Boschma (2005), learning processes and knowledge exchange interactions are facilitated and strengthened by five forms of proximity: cognitive, social, organizational, institutional and spatial.

Cognitive proximity reflects similarities in the way people perceive, interpret, understand and evaluate the world (Wuyts et al. 2005). A certain degree of cognitive proximity, that is, the extent to which the actors share a similar knowledge base, is a prerequisite for interactive learning, as it facilitates effective communication and a common reference space to process and transfer complex information and knowledge. However, as Nooteboom (2000) and Boschma (2005) point out, both too much or too little cognitive proximity can be detrimental to innovation and learning processes. A high level of cognitive proximity can result in the exchange of redundant knowledge due to the similarity in the knowledge sources. Too little cognitive proximity can lead to the exchange of information that is not fully understood by the actors, rendering the communication ineffective. Thus, research on cognitive proximity claims that there is an optimal level of cognitive proximity for interactions between actors to be productive (Boschma and Frenken 2011).

Social proximity refers to relations built on common experience, friendship and kinship, which can facilitate interaction and communication based on mutual trust and reciprocity. As social proximity between the actors increases, they know one another better communication becomes easier.

Organizational proximity refers to the governance structure shaping the interactions between actors. High organizational proximity is often associated with a hierarchical structure governing the actors' interactions, while low organizational proximity is generally associated with a flat governance structure or arms' length interactions among the actors.

Institutional proximity refers to the norms, rules and values that influence how actors behave. Large institutional distance, promoting behaviour that responds to different, potentially conflicting, sets of incentives or values, may impose serious impediments to fruitful learning interactions among the actors. For example, the institutional distance

between universities and firms is considerable because their incentives and norms differ significantly. Institutional proximity contributes to reducing uncertainty among the actors, even in the absence of previous social interaction (Lagendijk and Lorentzen 2007). In the biomedical field, the institutional distance between different occupational and professional boundaries represents a major barrier to the exchange of knowledge and the spread of innovations (Currie and White 2012; Ferlie et al. 2005).

Finally, *geographical proximity* refers to the spatial or physical distance between actors. This matters in knowledge dynamics because spatial co-location favours the exchange of knowledge that is complex or difficult to transfer (i.e. tacit knowledge) (D'Este et al. 2013; Frenken et al. 2012; Ponds et al. 2007).

All these types of proximity are inter-related. Some may be complementary; others may act as substitutes. For instance, Harrison (1992) and Howells (2002) argue that geographical proximity facilitates face-to-face interactions, favouring trust-based relationships and knowledge exchange, suggesting a reinforcing effect of spatial proximity on social proximity. In contrast, some proximity dimensions may be substitutes for each other: barriers to knowledge exchange posed by geographic distance might be overcome if the interacting partners share a well-defined division of labour (i.e. organizational proximity) (Rallet and Torre 1999).

The main challenge for TR programmes is developing interventions that generate a configuration of distances between actors that is appropriate for the specific goals of the programmes. Distance problems can be addressed along one or more of the dimensions reviewed above. For instance, initiatives can be designed to improve communication and understanding between patients, clinicians and researchers (addressing cognitive distance), to introduce coordination mechanisms across different organizations involved in the research

and application processes (addressing organizational distance), to align their incentives and norms (addressing institutional distance), or to improve trust and cohesion among actors (addressing social distance). In other words, different TR initiatives may be aimed at reducing the different distances among the actors involved in biomedical research and the application of its results.

TR EVALUATION: INCREASING PROXIMITIES AND "PROGRAMME THEORIES"

The first step of an alternative TR evaluation strategy is to determine the, implicit or explicit, "programme theory" underpinning the TR initiative under study. In other words, we need to define the policy goals in terms of the proximities that are to be improved and the process by which such improvements are expected to occur. As argued above, while the "gaps and lags" approach to evaluation focuses on outputs and the time it takes to progress from one output to another, in a proximities approach, the attention is on the research and knowledge utilization processes. This is in line with current proposals to focus research impact evaluations on the processes by which impacts are generated (Kok and Schuit 2012).

How TR programmes pursue their goals will vary across initiatives. For example, a TR project may be aimed at facilitating TR by merging two laboratories. In this case, the TR programme logic is focused on geographical and organizational proximity. In other cases, laboratories (e.g. in a university and a hospital) are expected to interact, but to remain separate, with joint activities organized to foster knowledge exchange. In this case, the logic focuses on overcoming institutional distance through social and cognitive proximities. Drawing on two contrasting Spanish examples, the IDIBAPS centre and the CIBER networks initiative, we show how the dimensions of proximity can be used to describe the different "programme theories" of TR initiatives.

Collaborative centres seeking to enhance interaction via spatial proximity: the case of IDIBAPS

IDIBAPS is a TR centre which is located opposite to the Clinic Hospital of Barcelona. It houses some 460 researchers with diverse institutional affiliations: the Clinic Hospital, the University of Barcelona, Spanish and Catalan research establishments (CSIC and ICREA), and its own staff. It provides a space for researchers with different affiliations and expertise to work together on different themes (e.g. biomarkers for oncology), using common facilities (e.g. bioinformatics, biobanks, imaging instrumentation). IDIBAPS can be described as a TR initiative primarily acting mainly upon spatial proximity through the co-location of laboratories and shared access to research facilities. This spatial proximity is expected to generate other forms of proximity; for instance, IDIBAPS work practices are expected to enhance trust and collaboration among the actors (thus increasing social proximity). Ultimately, these proximities should facilitate knowledge flows (increasing cognitive proximity) among different cognitive areas. Therefore, the evaluation of an organization like IDIBAPS should seek to determine whether and how expectations about interactions and cross-fertilization are being met.

Collaboration networks seeking to enhance interaction via organizational proximity: the CIBERs

The CIBERs were established in 2006 by the Spanish Government to promote excellence in biomedical research through the establishment of stable cooperative research arrangements which could be defined as loosely-coupled networks.[4] The CIBERs were selected based on an open call to biomedical research groups. Applicants had to propose broad networks of research groups including universities, public research organizations, hospitals, clinics and

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[4] Loosely coupled networks are organizational structures that may help coordinate transactions among highly heterogeneous partners, providing a balance between the mechanisms of control and flexibility. Loosely coupled networks lie somewhere between highly hierarchical organizational structures which impose a strong degree of control and bureaucracy on learning-related activities, and weakly articulated governance structures that provide a fragile setting for building trust-based and sustainable relationships.

research foundations. Nine CIBER research networks[5] were founded between 2006 and 2007, each focused on a specific pathology or disease, in line with the strategic goals of the Instituto Carlos III (equivalent to the US National Institutes of Health), and with the explicit task of conducting TR.

Since members of the CIBERs continued to work in their own organizations, increasing spatial proximity was clearly not the objective of the initiative. It was aimed at coordinating, through the common legal and economic framework provided by the CIBER platform, diverse biomedical groups within universities, hospitals and public research organizations. The CIBER platform provides an articulated governance structure to catalyse coordinated actions among the actors involved in the TR process. By connecting these research groups through mechanisms and common practices and decision making processes agreed among all partners, the CIBER platform aims to increase organizational proximity among a group of heterogeneous research actors.

Although the groups belonging to a CIBER are only "loosely coupled" we can expect that, by setting some basic conditions for the creation of common rules and shared expectations, the CIBERs may provide the means to generate social proximity and through it increase cognitive proximity. In other words, the CIBER networks can be understood as an organizational arrangement, aimed primarily at increasing the organizational proximity among the actors (basic researchers, doctors, patient groups), who tend to be distant in all dimensions. This greater organizational proximity should enhance social proximity, which should facilitate cognitive flows.

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[5] Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Epidemiology and Public Health (CIBER-ESP), Obesity and Nutrition (CIBER-OBN), Hepatic and Digestive Diseases (CIBER-EHD), Neurodegenerative Diseases (CIBER-NED), Respiratory Diseases (CIBER-ES), Rare Diseases (CIBER-ER), Mental Health (CIBER-SAM) and Diabetes and Metabolic Associated Diseases (CIBER-DEM).

ANALYSING PROXIMITIES AND THE IMPLICATIONS FOR EVALUATING TRANSLATIONAL RESEARCH

The need for a programme theory

TR addresses a problem that has organizational, social and cognitive roots: different communities with different practices and values are involved in a process that is complex and difficult (Currie and White 2012). The above two cases illustrate how two different initiatives, both labelled translational, have taken different approaches and implicitly draw on different programme theories. The forms of collaboration and interaction that we can expect from these initiatives are very different, and we suggest that when evaluating them we should aim at understanding these differences. We are interested in investigating how research objectives and projects are designed, how the research is conducted, and how the application of research results is and carried out. In other words, we need to understand the variety of the processes involved in TR initiatives.

We argue that a process-based approach to evaluation has advantages over an evaluation focusing on outputs. First, focusing on outputs provides no information on why an output has or has not been generated according to the initial, implicit or explicit, expectations of stakeholders. Second, existing practices could be relabelled "translational" if TR policies and their evaluation were concerned only with the generation of outputs and their identification. In the case of TR, where there is ambiguity about what differentiates it from other research forms, understanding how interventions operate in practice and what processes they trigger is particularly important. If TR initiatives are to be transformative, they must implement changes in the way research and the development of clinical practices and therapies are conducted. This calls for an approach that goes beyond "linear evaluation" of TR. It requires an evaluation approach that focuses on these processes. Third, evaluation frameworks are not

neutral in relation to the objectives of an initiative. The way in which a project is evaluated will affect how it is conducted and how its performers conceive their objectives. Focusing on specific outputs can implicitly suggest an intervention rationale that is not concerned with the organization of the research or how specific "translational gaps" are addressed.

The proximities framework we have proposed helps to focus attention on the way the research is conducted and the specific aspects that the initiative is intended to address. These aspects may sometimes be made explicit in the definition of the intervention, but they may also only be implied in relation to how the initiative is implemented. In this latter case, the framework could be used to explore and develop a "programme theory" for a TR initiative; in other words, help policymakers to reflect on and explore the initiative's rationale. The cases described show how the framework can be used to describe both the goals of a TR initiative and how these goals can be achieved.

In adopting this approach, we are proposing that the immediate goal of a TR initiative is to address the problem of the distances separating the different groups involved in medical research. The "translational gaps" are due to excessive distance in one or more significant dimensions. The groups involved in the translational process have cognitive differences, are institutionally separate and, therefore, follow different rules, are faced with different types of incentives, and often are geographically dispersed. The definition of an initiative and its evaluation must be flexible and allow for the fact that too much proximity is not always desirable. For instance, too large a cognitive distance can be problematic, but so can too much cognitive overlap; cognitive proximity is positive only up to a certain level. A specific programme theory must reflect this problem of balance, and the interpretation of evaluation results must be sensitive to this potential problem if there is a possibility that it may become relevant.

The programme theory of a TR initiative should define expectations about whether and how changes in proximity in one or more dimensions caused by the intervention, will trigger shifts in the other dimensions, and the effects of these changes on the development and application of beneficial goods and services. These effects will be mediated by changes to the way research is carried out. Increased proximity can result in increased collaboration among the groups involved in the various tasks that constitute the TR process (the definition of fundamental and clinical research objectives, research, and the application of its results). We can expect changes in proximity to generate new interactions across groups, for instance, between research performers and the diverse users and beneficiaries of the research results, where knowledge moves back and forth along various channels, and within networks, rather than along a linear bedside to bench continuum.

We can identify other building blocks of a TR programme theory. An intermediate outcome of increased proximities may be the generation of complex interactions among the different groups involved in the TR process. Although this may vary across initiatives, it is important to take into account the broad variety of potential stakeholders: basic researchers, clinical researchers, technologists, practitioners (doctors, nurses, etc.) public health and private industry managers, and patients. The ways in which stakeholder groups interact can be traced and analysed using instruments developed for the evaluation of the socio-economic impact of research, such as those developed by the EU-funded SIAMPI project (Molas-Gallart and Tang 2011; Spaapen and van Drooge 2011), which focuses on the processes of collaboration that can be linked to an initiative.

Moving forward: the operationalization of a proximities approach to TR evaluation

This paper has argued that a different approach to the evaluation of TR is both possible and desirable and has shown that it will rely on programme theories which will need to be developed for each different TR initiative. The next step will be to operationalize the approach. While an output-based gaps and lags evaluation provides easily measureable and potentially comparable results, a proximities approach to evaluation will yield a description of the contextual conditions in which the initiative was implemented and its effects on the relevant processes. Narratives built on qualitative research techniques could describe how the different proximities evolve throughout an intervention. The narratives could be accompanied by quantitative indicators; there are numerous examples from the innovation studies, economic geography and management literatures of attempts to measure different proximity dimensions. The main approaches to developing proximity measures draw heavily on two alternative sources: primary data mainly from surveys and fieldwork research, and secondary data relying mainly on bibliographic and patent information. Cognitive proximity has been measured as the degree of overlap among the knowledge bases of potentially interacting actors. This overlap can be captured at the individual level by analysing the similarity between scientists' publications or patents profiles (Kotha et al. 2013). The cognitive distance between actors can be captured by focusing on the patent subcategories in which their discoveries are classified (Tzabbar 2009). Finally, science maps offer a visualization of the overlap between actors across scientific fields (Rafols et al. 2010) or patent categories (Kay et al. 2014). Geographical proximity can be operationalized by measuring the physical distance between the interacting partners, based on their physical addresses (Laursen et al. 2011). Geographical information based on postcodes allows the calculation of the "great circle" distances between any two partners, while relative measures of distance, such as travel times between any two location points, have also been used (Ejermo and Karlsson 2006). Institutional proximity refers to whether actors belong to similar or distinct types of

institutions (e.g., universities, hospitals, public research organizations, etc.). Bibliometric analysis may be useful to explore actors affiliated to more than one institution (e.g. a hospital and a university). Organizational proximity is often measured by whether actors belong to the same organizational structure and, thus, answer to the same authority. A more detailed approximation of organizational proximity can be obtained by measuring the degree to which the organization is characterized by a flatter or more vertical chain of command (Ponds et al. 2007), and the relative position of actors in these "hierarchies". Social proximity can be proxied by the extent to which actors have interacted in the past, for instance, via co-authorship or co-inventorship, and the duration of such linkages (McFayden et al. 2009). Softer measures based on social network research can be captured through surveys enquiring about the extent to which actors have developed strong ties with each other, reflecting a relationship of kinship, trust and reciprocity (McFayden and Cannella 2004).

Thus, there is a variety of techniques that can be adapted for use in evaluation research. Use of a proximities framework does not determine the research techniques to be employed; these need to fit the specific circumstances of the individual initiative being assessed. The activities supported by a TR initiative will be different, be implemented in different contexts and will have different targets and objectives. For instance, the research techniques applied to an initiative that focuses mainly on cognitive issues, will be different from those applied to one that addresses institutional differences.

Since the adequacy of a specific research technique will depend on the specific TR evaluation problem and its context, it follows that the outputs of TR evaluations will not and should not be directly comparable. Calls for an approach based on a single set of research techniques, yielding measurable and comparable indicators of TR "output", from our perspective, are out of place. An evaluation approach that focuses on processes will seek to

provide detailed information on the effects of an initiative starting at the level of those groups directly involved in it. However, the way that this information is shaped, and the indicators on which it is based will depend on the type of initiative, its objectives, and the types of proximities the programme is designed to address.

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