Translational Research: An Imperative Shaping the Spaces in Biomedicine

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Abstract In this paper we recapitulate the history of the conceptual entwinement of biomedicine and translation and argue that a translational imperative has come to dominate public and institutional perceptions of biomedical research that is still peripheral to the practices that order the fields unified under the term biomedicine. We show this by first delineating a brief history of the conceptual developments in the sociology of science and technology in particular in relation to translation and the complex multi-agent social interactions contributing to the structure of this field. We then report the findings from our studies of translational spaces and how the actors in them conceive of the imperatives. The push toward translational research from funding and science policy institutions seems, however, at least in the field of cell therapy research, not to have altered greatly the established practices of validation and merit that organise the disciplinary complexes that form cell therapy biomedical research today.

Keywords: Translational research; biomedicine; translational space; translational imperative; cell therapy.

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1. Introduction

We were invited to contribute a discussion of the concept of translational research and its emergence in biomedicine on the basis of our work on this topic. The history of the intersection of biomedicine and translational research is complicated, and therefore we discuss in this article the changing relationship between both, how they influence and grow together in what is a current translational imperative in which biological

and medical research give direction and set restrictions for one another. We use examples from cell therapy research, an area we conducted extensive empirical research on, assuming that whilst the configuration of biomedicine through translation may play out differently in detail in different fields of biomedicine, the degree and influence of the translational imperative has similar structural effects.

1. Concepts of Biomedicine and Translational Research

That medicine relates to biology is a trivial notion. That increasingly medical diagnosis has come to rely on biological/tissue tests, and that therapies intervene into biochemically well-defined physiological or metabolic processes, is a product of the 20th century. In this context the emergence of the concept of biomedicine has occurred. Biomedicine has changed medicine and constitutes a whole set of new practices and localities of research, including multidisciplinary laboratories, new journals and the grammar of research ethics and clinical trials. Viviane Quirke and Jean-Paul Gaudillière date the rise of biomedicine to after the Second Word War and characterize it as a "step change in the scale of investment in research, a new role for the state as scientific entrepreneur, an increasingly fundamental level of investigation in biology and medicine, and a closer relationship between the laboratory and the clinic", accompanied by the idea of "the therapeutic miracle" and the "search for magic bullets against tuberculosis, cancer, and cardiovascular disease" (Quirke and Gaudillière 2008: 442-3). Cell therapy research developed in this period as studies into the effects of nuclear radiation on the body and how destroyed cell systems could be repaired. The stem cell in the bone marrow and its regenerative function for the blood system, and with it the leukaemia patient, were determined as biomedical cell therapy research (Kraft 2009).

1.1 The Translational Imperative

Translation between the laboratory and the clinic may therefore seem to be at the core of the activity we call biomedicine. In its Funding guide the UK's largest medical research funder, the Wellcome Trust, explains that, 'Translational research helps turn early-stage innovations into new health products, advancing the innovation to the point where it becomes attractive for further development by the medical industry or healthcare agencies'1. This present-day definition suggests a one-directional flow of information, from the laboratory into general medical care, identifying

1 http://www.wellcome.ac.uk/funding/Innovations/wtd027704.htm

the envisioned gaps between the different stages of such innovation. The imperative, therefore, of what funding bodies and science policy managers have introduced as translational research lies on the concept of 'pulling through'; the problem is how to effectively turn new biological knowledge into widely used medical treatments. The 2014 overview for the UK NIHR Biomedical Research Centres (BRC) stresses that all projects and project leaders must have a track record 'in translating advances in basic biomedical research into clinical research, and pulling through basic biomedical research findings into benefits for patients, the public and the NHS'.2

1.2 Biomedicine and Translation in Sociology

The one-directional model stressed in the above notions of translation is simplistic compared to the ways in which the sociology of science and technology has been using the concept of translation since the 1960s. The scientists' use of the metaphor translation for flows of knowledge and information across disciplines and their peculiar languages and practices was followed by the emergence of the sociology of translation. A name commonly attributed to Bruno Latour (1979), Michel Callon (1986) and others who worked in this field in the 1980s. Translation is a key concept in actor-network theory. Applied to the field of biomedicine it presents its main actors as attempting to create a central network of interactions that each actor has an interest in building and defending.

> The first is that of the reduction of the big world (the macrocosm) to the small world (the microcosm) of the laboratory. The second stage is that of the formation and setting to work of a restricted research group that, relying on a strong concentration of instruments and abilities, devises and explores simplified objects. The third stage is that of the always perilous return to the big world: ... (Callon et al. 2009: 48).

This description points out that the flow of information and what is needed to achieve biomedical innovation is not from the bench to the bedside but a more complex interweaving of stages in which complexity is reduced and then reintroduced again. The emphasis is on interactive practices that produce translation as a reconfiguration of the macrocosm (ibid: 68).

2 http://www.nihr.ac.uk/files/pdfs/Briefing%20documents/4.2%20Biomedical%20Research%20Centres.pdf)

1.3 Science as Social Practice

This focus on the performance of science also dates back to the 1960s when the knoweldge practices of science became a study object for sociologists and, as Sheila Jasanoff recapitulates, sociologists began to "carry out science on science" (Jasanoff 1994: 6), a turn of attention aimed at rational policy decisions on science and technology innovation in the future. Proponents of the Sociology of Scientific Knowledge (SSK) studied science as a social practice and consequently scientific knowledge as a social product (Barnes 1974 and 1977; Bloor 1976, Collins 1985; Shapin 1982). In policy contexts this was taken up as a new imperative to understand the developments in the sciences in their relationship to technology and economic growth and, above all, how "to get returns on the money we spend on science" (op. cit.: 6).

SSK and its precursors, especially Ludwik Fleck (1979[1935]) and Thomas Kuhn (1970[1962]), began to understand science as the product of social processes and negotiations, which mediate scientists' accounts of the natural world, raising fundamental questions about taken-for-granted divisions between "social versus cognitive, or natural, factors" (Shapin 1995: 289). The 'truth' or 'falsity' of scientific claims derives from the interpretations, actions and practices of scientists rather than residing in nature as a separate world of facts that exists objectively for the scientists, independent of the methods and practices they employ to study it. Understanding science as a social practice includes not only studying its methods but also its social structures and the vested interests and social objectives that operate on and within the activity of making scientific knowledge.

This perspective presents translation as a process in which the knowledge practices of different fields in the macro-and-microcosms in biomedicine cooperate with social practices that influence the epistemic and internal stratification processes in complex webs of interactions. Scientists and clinicians balance many and often conflicting expectations of what counts as achievement as set out by funding organisations, the scientific community, publics, patients, industries and policy makers. The art of translation is to balance these expectations across disciplines and turn them into individual and institutional successes and desirable medical innovations. Biomedicine and translation thus is multi-layered, an interweaving of interests and activities. From 2000s onward, the concept was further expanded in sociological studies on cell therapy research to different concepts of intersecting social spheres.

2. Cell Therapy Research: New Understandings of Translation

From its beginnings in bone marrow repair, research on cell therapies

has taken several forms over the past decades, diversifying into many expert areas. Thus the term cell therapy research now ties together a range of types of specialist expertise in both biology and medicine, strongly influenced by ethical and political factors (Hauskeller 2004). Paul Martin, Nik Brown and Alison Kraft (2008) chart the development of haematopoietic stem cell research over a fifty-year period and describe the relationship between basic science and clinical research communities as a two-way flow of knowledge in which clinical innovation has played a key role. They emphasize the communities of promise that form around emerging cell therapies and that national governments incentivize the exploitation of basic research and the creation of new policies and institutions to ensure that scientific findings can be applied in the clinic.

The large body of social science work on the external societal influences on cell therapy research from the past 15 years is accompanied by a number of studies on the translational processes within scientific communities. For example, Steven Wainwright, Clare Williams, Mike Michael, Bobbie Farsides and Alan Cribb describe a distinction between the "warp of discourses which enact the improbability of collaborations between 'bench' and 'bedside', and the weft of other discursive strategies which enact the possibility of collaboration between the lab and the clinic" (2006: 2062). Steven Wainwright and Clare Williams (2008:165) draw on Livingstone's metaphor of geographies of science, which he described as "sites of speech and locations of locution" (2003:23) to explore the spatial shaping of science and the scientific shaping of conceptual, social and political spaces.

2.1. Platforms and Trading Zones

The metaphor of the platform is moved from being applied to biomedicine to being used to characterize processes of translation. Peter Keating and Alberto Cambrosio describe biomedicine as a 'hybrid-practice' and their notion of the biomedical platform draws together panoply of diverse actors from technicians, physicians, and researchers, policy makers and regulators, with material objects (Keating and Cambrosio 2003). They argue that in the 1990s biomedicine itself had become an independent actor in cancer research, alongside basic and clinical research (Cambrosio et al. 2006). Joelle M. Abi-Rached, Nikolas Rose and Andrei Mogoutov re-configure the translational platform as an array of heterogeneous actors including technologies, practices and techniques and enabling multiple transactions between the clinic, the laboratory and society. They stress that the products of translational research, be they specific applications (drugs, neurodevices, etc.) or practical guidelines (systematic reviews, meta-analyses etc.) allow a change in both clinical practice and population behaviour, as identified by Steven Woolf (2008). In the context of their study on the new brain sciences, Abi-Rached et al.

distinguish areas of research that act as vectors between the laboratory, the clinic and society and argue that each specialized community is centred around its own journals, institutes and organizations. These are connected in trading zones, a notion they develop following Peter Galison (1997), to capture not merely zones of passive exchange and flow of information, but

"Zones which facilitate the active transactions and transmutations of diverse devices, practices, techniques, and perhaps above all styles of thought. They are platforms which allow the emergence of new disciplines and discursive practices and along with them a reorganization of their objects of study". (Abi-Rached et al. 2010: 13)

This notion of trading zones where translational activity is enacted is helpful to identify agency. However, engagement in the translational trading zone is not always deliberate, but affected by targeted policy decisions. Whether we prefer the image of interconnected platforms or of the webs woven through multiple centres of agency, a social and political imperative to be translational acts upon biomedicine as shown across the range of social science studies. To illustrate this we provide a brief summary of findings from empirical research concerning the scientists' view of, and practical engagement with, this imperative.

2.2. The Utility Imperative in the Translational Space of Cell Therapy Research

Between 2006 and 2011 the authors carried out ethnographic studies on stem cell research for the heart in laboratories, clinical environments and at networking events. Analysis drew on observation and semi-structured interviews with laboratory scientists, clinicians and focussed on the regulatory, disciplinary and ethical tensions that shape the 'translational space' (Harrington 2011). In addition, we studied from its inception in 2004 the British Cardiovascular Collaborative for Stem Cell Repair of the Heart (Collaborative), a clinician-led multi-disciplinary group of top UK biomedical researchers who aimed at developing stem cell treatments together instead of competitively in order to achieve fast clinical implementation. One of the aims of our research was to explore the motivations and attitudes of the stakeholders working in this field. The data on practices, networks of interactions and interdisciplinary exchanges show that differently positioned participants in the field employed different strategies to negotiate the translational imperative. The quotes below exemplify opposite views on translational research. And what we call the translational imperative. First a molecular biologist working in a laboratory funded for translational research:

So I have to play the game, I have to play the rules of the game because in the end what I want is to be funded and to be in a lab working and doing research. [...] There are many things you can do with the cells I

work on. They are not necessarily going to translate into something useful, but you can do the research and that research will be useful anyway. It may not be translated, but the point is, in a paper when I send my project to the funders, it's like, yeah, stem cells, a disease, a cure! So… it's more about, [pause] giving the people what they want to read, even if inside you know it's not necessarily achievable, or it's not your first priority, but again you have to combine all these things, basic research with translational research and get the money.

The scientist states that conforming to the translational imperative is necessary in order to get funded. Translational research is performed as an adjunct to the biological inquiry. The opposite perspective is presented by a clinical–scientist who states that biological research should be driven by medical needs and requirements, describing the purpose of the Collaborative and the view of the multidisciplinary group that met several times a year over a period of 7 years, as:

All agreed that clinical researchers had first to define which problems they would attempt to treat with transplanted cells (e.g. heart failure, dilated cardiomyopathy, or myocardial infarction) and by what route (e.g. intravenous, percutaneous, or surgical). Then the groups working on animal models would adapt their models to that clinical need […] The group working on cells and gene transfer to cells would define the best cells to transplant, or the best way of stimulating endogenous cells to activity.

The clinicians participated in the Collaborative in order to find new methods to change the function of the ailing heart and expected the scientists to provide them with the biological knowledge and cells to aid that goal without necessarily fully understanding the mechanisms by which the cells regenerate heart tissue. The clinical focus is on whether procedures are safe3 and in the long term prove to be efficacious4. Innovation pathways for new cell therapies from the laboratory into the clinic have been promoted and pre-planned by both funding organisations such as the Wellcome Trust and regulatory institutions such as the UK Human Tissue Authority5 and the scientific interest currently focuses on new ways of creating cells with regenerative potential. Some of the clinicians involved in the Collaborative have formed a significant European Network that won funding in 2011 for a large clinical trial with established stem cells, which they perceive as the ultimate test. The Collaborative as a

3 The Clinical Trials observed in this research were Phase 1 that is designed to 'assess safety' although often the conversations between clinicians were centred on 'efficacy'. This dilemma raises questions concerning the 'focus' of a clinical trial and the ethics surrounding this position.

4 When discussing this divide between the scientist and the practicing clinician reference was made to 'Aspirin' [acetylsalicylic acid (ASA)] and the fact that it's functioning mechanisms have only relatively recently been discovered although it has been in use since 1500BC when an infusion of dried myrtle leaves (which contain salicylic acid) was used to relieve back pain and since 1899 under the trade name 'Aspirin'.

5 http://www.hta.gov.uk/_db/_documents/Role_of_regulators_in_regenerative_medicine.pdf

group however ceased meeting in 2012. This may be interpreted as a case in which the tensions between biological and medical research could not be resolved and the translational imperative failed to pull through the new treatments originally envisaged.

The heteronomy of success indicators in the different fields of biomedicine seems still stronger than the commitment to translation, which is not directly one of them. Scientists and clinicians need to publish papers in top journals and the criteria which the translational imperative aims to introduce and add to the success stories of a particular biological or medical laboratory's achievements, are not aligned with the internal workings of the sciences that contribute to biomedicine. The platforms are not aligned and thus the difference between publicly accountable research and research excellence still overshadow compliance with this imperative of social and commercial utility.

This case of stem cell research for the heart offers a valuation of the imperative for translational research that so far has not been very successful. Research in other fields within biomedicine is likely to show equal levels of complexity, in which the justifications, initiatives, rhetoric, funding support, and other strategic mechanisms of facilitating translation may more successfully create the normative basis for science that translates into improved health.

Conclusion

Biomedicine and translational research as concepts have different historical origins, yet, the necessity for multidirectional and multi-actor engagement is inherent in both. Sociology has been analysing and reflecting on the social practices which shape the developments of translation and its penetration of more and more areas of biology and medicine which draws in a growing number of social sectors and agents. That research has to be oriented toward therapeutic application to deserve public funding and be of societal value is an imperative that contradicts and challenges to the point of denial the complexity of successful interactions and transfers between multiple agencies. Biomedicine is pregnant with translation. Implied in the use of the metaphor of translation is that exchanges are transformations in which the meaning, however well captured, shifts slightly between original text – be it the clinical or the laboratory's – and the new text. The narrow reins with which regulators try to predetermine with simplistic notions of translation and to-do lists the outcome of the science yet to be conducted and how its results ought to be implemented negate the potential that lies in biomedicine as an evolving project for many kinds of clinical innovations and understandings of biology.

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