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Translational biomedicine in action: Constructing biomarkers across laboratory and benchside

Stefano Crabu

Department of Philosophy, Sociology, Education and Applied Psychology (FISPPA), University of Padua, Via Cesarotti, Padova 10/12 35123, Italy.
E-mail: stefano.crabu@unipd.it

Abstract This article, based on ethnographic research conducted in a major Italian institution specialising in cancer care and research, provides insight into the clinical and basic research laboratory practices articulated around an experimental protocol designed to develop a biomarker. The article adopts an 'ecological' perspective matured in the field of science and technology studies of the translational process and suggests that biomedical activities are multi-directional, and cannot be understood in reductionist terms, that is, as a two-way linear transfer of bio-knowledge from the bench to bedside and back. I propose the notion of technomimicry, in its dual acceptation in the clinical and experimental sense, to understand the cognitive, social and material strategies involved in the circuit of migration of heterogeneous materials and information across scientific laboratories and clinics. Clinical and experimental technomimicry theoretically capture the multi-directional and multi-modal process of the re-location of materials and bio-knowledge from one site to another. These concepts also highlight how the epistemological boundaries of the clinic and laboratory are required to be mutually adjusted and continuously realigned in order to translate laboratory facts into clinical activities, and clinical evidence into researchable issues.
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Introduction

Contemporary life sciences are increasingly marked by the 'translational imperative' (Fischer, 2012; Rose, 2013; Lewis *et al*, 2014), which implies a close proximity between research and development (R&D) activities and clinical practice through the two-way transfer of information, materials and knowledge

between scientific laboratories and clinical settings. This close relationship implies the possibility for the latter to foster exploration of new scientific issues (Zerhouni, 2007; Goldblatt and Lee, 2010; Evans and Scarbrough, 2014).

Both on the policy level and in scientific debates, support for this research model has been increasingly justified through the argument that substantial investments of material and financial resources in basic laboratory research, while contributing to major scientific discoveries, have not immediately produced the expected new therapeutic and diagnostic devices or new life technologies that could significantly reduce the incidence of certain diseases in terms of morbidity and mortality (Perlstadt, 2009). From a scientific perspective, this argument has been justified by claiming the weakness of experimenting on animal models for the production of clinically relevant evidence (Contopoulos-Ioannidis *et al*, 2003; Butler, 2008; Shanks *et al*, 2009). From a socio-organisational perspective, some authors have insisted that the main factors hampering the construction of epistemological and institutional dialogue between bench and bedside are the divergent objectives, role expectations and different professional cultures that characterise physicians and scientists. (Hallowell *et al*, 2009a).

Conceptually speaking, translational research circumscribes an approach oriented to enhance the transformation of scientific evidences constructed in laboratories into new clinically actionable patient treatment protocols and technologies (Brown, 2007). Therefore, new research and funding programmes have revived the rhetoric of 'unity between care and scientific research' in order to develop treatments that are more effective, less invasive and personalised to the patient's genetic profile (Jones *et al*, 2011; Cox and Webster, 2013).

Assuming a sociological perspective, translational biomedicine brings a number of relevant issues pertaining to new configurations of disciplinary epistemologies, medical and scientific practices, and institutional arrangements to the attention of social studies of health and medicine (Cambrosio *et al*, 2006a; Wainwright *et al*, 2009; Cambrosio *et al*, 2012).

This article contributes to the on-going debate on the emergence of translational biomedicine by presenting data collected through ethnographic research conducted in a major Italian institution specialising in cancer care and research. The article focuses on the research and clinical practices articulated around an experimental protocol designed to develop a biomarker, which is a new clinical utility to support the personalisation of treatments for patients suffering from colorectal cancer. In particular, it pays special attention to how the patient's body is elaborated and re-configured as an 'experimental subject'. I argue that the experimental subject is constructed through an ensemble of sociomaterial practices – as an expression of the mutual entanglements between social actors

and technologies (Orlikowski, 2007) – which imply the coordination and epistemological congruence between laboratories and clinical settings.

The activities rooted in translational science and devoted to the development of biomarkers for personalised medicine are multi-directional and cannot be understood in reductionist terms: as merely the two-way linear transfer of bio-knowledge from the bench to bedside and back. The concept of *technomimicry*, in both the clinical and experimental sense, is crucial here. *Clinical* and *experimental technomimicry*, considered together, constitute a useful conceptual device to understand the cognitive, social and material strategies involved in the circulation of heterogeneous materials and information across scientific laboratories and clinics.

Clinical technomimicry highlights how the laboratory itself can be re-framed and adjusted to render laboratory facts and scientific phenomena congruent with the processes of care and the clinical management of patients. Similarly, *experimental technomimicry* helps to understand how the clinic itself can be re-framed as a research site where patients are enroled not only for care, but also as participants in biomedical research activities. In this sense, clinical and experimental technomimicry theoretically capture the multi-directional and multi-modal process of re-locating materials and bio-knowledge from one site to another. They also highlight how the epistemological boundaries of the clinic and laboratory are required to be mutually adjusted and continuously re-aligned in order to translate laboratory facts into clinical activities, and clinical evidences into researchable issues.

Scientific Background: Translations, Bodies, Biomarkers, and Personalised Treatments

Recent achievements by the Human Genome Project have led to changes in the way biomedical research and clinical practice are conceived and conducted. New alignments between 'normal' and 'pathological' (Keating and Cambrosio, 2003; Miller *et al*, 2006) have emerged and are redefining the overall scope of 'post-genomics'.

One of the major spin-offs concerning translational biomedicine is 'pharmacogenomics', which has become significant in molecular oncology and promises a new era in personalised medicine (Hedgecoe, 2004; Ginsburg and Willard, 2009). Personalised medicine identifies a specific segment of translational biomedicine that opens up new clinical strategies in the treatment of patients since it combines traditional drug administration evaluation factors (such as age, body mass index and sex) with the patient's genetic profile (Basik *et al*, 2011).

In molecular oncology, a growing number of medical institutions specialising in cancer care and research on both sides of the Atlantic have pursued new research programmes focusing on treatment personalisation (Webster *et al*, 2004; Keating and Cambrosio, 2012). The main objective of these research programmes is to identify, quantify and validate specific molecular devices (called biomarkers), which allow cancer patients to be stratified according to their genomic profile in order to design more effective clinical treatments (Kohli-Laven *et al*, 2011). Therefore, biomarkers may be clinically utilised to categorise and classify persons within sub-molecular populations who differ in their susceptibility to a particular disease or their response to a specific therapeutic compound (Tutton, 2012).

In analytical terms, biomarker development requires an extensive human molecular categorisation process. It is a medical-scientific activity of distinguishing, labelling and categorising biological phenomena by classes or categories (Bowker and Star, 1999). This means that a human subject is represented by a discrete and objectified genetic characteristic (such as a gene or protein) that may help predict the likely response to a specific drug. For this reason, biomarkers are not simply tools used for allocating human subjects to a set of predefined epidemiological labels but are also devices for naming and identifying specific patterns of inter-variable bio-physiological characteristics in the human genome.

Currently, identifying and validating biomarkers represents an area of great sociological interest for analysing production processes and materialisation of biomedical knowledge (Löwy, 2000; Lock, 2007). Despite the key role played by personalised medicine, social sciences have not fully explored biomarker discovery and validation. Instead, the vast majority of contributions have focused on genetic discrimination (Kahn, 2004, 2010; Abu El-Haj, 2007; Fitzgerald, 2014); the relationship between biomarkers and processes of patient subjectification (Rosser, 2000; Clarke and James, 2003; Clarke *et al*, 2009); and the importance of biomarkers in the management of biomedical risk and ambiguity in diagnostic decision making (Fosket, 2004, 2009; Sulik, 2009; Lock, 2013).

Notably, these works have largely omitted the practices of design and development of new molecular devices and have taken for granted the embedded technoscientific dimension. Theoretically, therefore, it would be useful to investigate the way in which patients, physicians, biological samples and researchers (supported by a number of technological devices) shape cooperative strategies to drive translational processes of knowledge across bench and bedside.

These cooperative strategies are articulated through practices allowing the conversion and abstraction of 'life in itself' into information (Clarke *et al*, 2010). I suggest that there are three main different levels of abstraction of the materiality

of the living body in information: (i) *in vivo*, in the form of direct intervention on the organism; (ii) *in vitro*, in the form of a biological sample; and (iii) *in silico*, as a form of computer-assisted elaboration of data and information. These three levels constitute the technoscientific modalities of producing knowledge in contemporary biomedicine (Thacker, 2005).

The next section outlines the theoretical framework elaborated to grasp the process of biomarker construction as an emerging outcome by the ecology of interactions between heterogeneous social actors, medical and scientific knowledge, and technologies.

Theoretical considerations

Facing the emergence of translational biomedicine, the most recent contributions arising from the dialogue between science and technology studies (STS) and social studies of health and medicine (Keating and Cambrosio, 2003; Atkinson *et al*, 2007; Epstein, 2007) suggest that the on-going reconfiguring of disciplinary epistemologies, biomedical work and institutional arrangements must be understood by starting from practices where scientific and clinical knowledge, standards, protocols and technological devices are related to each other through a relationship of mutual generation (Latimer *et al*, 2006; Cambrosio *et al*, 2009; Moreira, 2012).

A number of ethnographic studies in the field of STS have been conducted in research laboratories and have explored the social and technical dimensions of daily scientific activities (Latour and Woolgar, 1979; Knorr-Cetina, 1981; Lynch, 1985). Referring to the theoretical reflections surfaced by laboratory studies, STS invite to focus the analytical gaze not only on discursive practices or human interactions but also on the widespread network of relationships between human and non-human entities. Thus, this theoretical tradition emphasises the agency of heterogeneous materials (such as symbols, technologies and artefacts) that contribute, along with human subjects, to the construction of collective action and everyday life (Law, 2010).

Social sciences, paralleling laboratory studies, have a long tradition of qualitative research on the practical dimension of clinical medicine (Berg, 1992, 1997; Atkinson, 1995; Timmermans and Berg, 2003; Mol *et al*, 2010). However only a few contributions have explored the recurring interactions between the laboratory, bench and clinic (Löwy, 1996; Quirke and Gaudillière, 2008). Traditionally, scientific research and clinical practices have been understood to be profoundly different, and sometimes conflicting, activities because of their different epistemological, cultural and ethical orientations (Morgan *et al*, 2011). Although scientists and physicians are conceptually and theoretically associated with different professional communities (Snow, 1993) and epistemic cultures (Knorr-Cetina, 1999), the issue of boundaries and

demarcations (Gieryn, 1983, 1995) between scientific research and clinical practice seems to be overshadowed by the changes triggered by translational biomedicine and the scientific discourses mobilised in supporting it. In fact, the most interesting issue raised by personalised medicine is the central position that the patient's living body and its biomedical trajectory (in terms of information, biological material and clinical evidence) has assumed not only within activities exclusively concerned with care but also as a constitutive (and non-residual) element in scientific research.

Recent literature on translational research has addressed the issue of epistemic coordination between laboratory and clinic by framing translational biomedicine as promissory science, emphasising the performativity of technoscientific expectations in mediating laboratory and clinical practices (Wainwright *et al*, 2006; Martin *et al*, 2008; Brosnan and Michael, 2014; Crabu, 2014a).

Given this state of affairs, this article takes a different analytical approach towards translational biomedicine. I adopt an 'ecological' perspective rooted in social studies of the translational process (Star and Griesemer, 1989; Fujimura, 1995; Suchman, 2000) in order to investigate the sociomaterial relationships by which physicians, scientists and patients develop convergence strategies to support the circulation of materials and knowledge across research laboratories and clinical settings. Specifically, an 'ecological' sensitivity allows to take into account the 'distributed agency' (Star, 1989) between human subjects and non-human objects and the processual construction of their mutual interdependence. According to this ecological perspective, the concept of social action is not centred on an interpretative model, which sees human actors as the unique and dominant agent that organises social life, but instead emphasises the materiality of the context and the mutual relations, changes, and negotiations through which social actors, together with technological objects, elaborate the social order.

The present article attempts to follow this theoretical perspective by exploring how personalised medicine – as a specific subfield of translational biomedicine – and related technologies (for example, biomarkers) emerge through a dialogue between heterogeneous actors, expert knowledge, materials and technological devices that are extremely diversified and belong to domains, which are commonly considered as distinct fields of scientific and epistemological work (Lewis *et al*, 2014).

After presenting the empirical context and related methodology, the following sections will analyse empirical data in relation to the outlined theoretical framework. It will discuss, therefore, the concepts of clinical and experimental technomimicry as they pertain to the process of shaping the epistemological congruence between clinic and laboratory. The aim is to capture the socio-material practices of the translation of materials and knowledge between these two sites in order to build a biomarker as a new clinically actionable technology.

Methodology

Empirical field

Personalised medicine has played a central role in redefining cancer treatment and research practices. The field of oncology has recently increased efforts to define a number of therapeutic options for the personalisation of care. For this reason, as pointed out by previous studies, personalisation of care represents an emblematic context for gaining insight into translational biomedicine (Cambrosio *et al*, 2006b; Keating and Cambrosio, 2012).

The empirical material discussed here was collected through ethnographic research conducted by the author in a department of clinical and experimental pharmacology (which will be referred to by the pseudonym 'Human_Ph@rma') hosted by a major biomedical institute in Northern Italy specialising in cancer care and research. The department was carefully selected following several in-depth conversations with the scientific director and other key informants. The ethnographic research was carried out 4 days a week for a period of 6 months.

Human_Ph@rma is dedicated to conducting investigations in the pharmacogenomics field to determine the best way to utilise genetic information to personalise cancer therapy. The department's director has a strong international reputation in this research area. The laboratory team – including molecular biologists, pharmacologists, chemists, data managers and medical laboratory scientific officers – contributed, with the support of clinicians and research nurses, to the study of a single nucleotide polymorphism (a DNA sequence variation) of the gene 'UGT1A1'. From early descriptive studies, the UGT1A1 gene polymorphism has been a promising research object for translational biomedicine with the aim to personalising treatment for patients suffering from colorectal cancer.

When the ethnographic research was carried out, Human_Ph@rma's researchers were working on a research protocol devoted to validating the UGT1A1 gene polymorphism as a biomarker that would stratify colorectal cancer patients based on their likely response to chemotherapy by identifying a 'treatment-resistant' population (that can receive a higher dose of the drug) and a 'sensitive' or 'mutated' population (for whom the prescribed dose will be lower).

The ethnographic investigation focused mainly on the ensemble of socio-material practices articulated around this experimental protocol in order to reconstruct how personalised medicine is acted within an ecology of actions involving the patient's body, biomedical technologies, scientific knowledge and healthcare professionals.

The ethnographic method allows to perform the main methodological principle arising by the ecological perspective, or rather of directly following human and non-human actors and their actions (Star, 1999). In this way, both contextual and emergent entities involved in the 'local articulation' of the research protocol

(Crabu, 2014b), and that therefore contribute to the construction of the biomarker, are taken into account. In other words, ethnography inspired by an ecological sensitivity allows the exploration of the distributed agency and the mutual entanglements among human subjects and technical objects at stake in the mediation between laboratory and clinical practices (Star, 1999).

Data collection

Empirical data were primarily collected through the ethnographic observation of daily activities within laboratories and hospital wards. The observations closely followed all the Human_Ph@rma staff (three molecular biologists, two pharmacologists, two research nurses, one data manager, one clinician and one laboratory scientific officer) involved in a range of different protocol-related activities. Subsequently, 10 in-depth interviews were conducted with the scientific director and all the Human_Ph@rma staff. Participants gave consent for the interviews to be audio recorded; interviews were transcribed using the verbatim method. Finally, other Human_Ph@rma institutional documents such as the informed consent form, the form for clinical data collection, the experimental protocol and other informational materials relating to the management of the enroled patients were also consulted.

Analysis

Field notes and interviews transcriptions were coded using Atlas.ti software and followed constructivist grounded theory principles (Charmaz, 2009). Adopting a grounded theory data coding process allowed descriptive labels to emerge at an early stage. Subsequently, this coding process was accompanied by the development of theoretical labels, which were guided by an ecological perspective to social phenomena.

Findings

Enroling the patients: configuring the 'in vitro' experimental subject

> The potential patient (x) to be included in the protocol is normally selected by the physician, who starts the procedure [by] obtaining the informed consent by the patient. I normally give them oral and written information so that they can read it carefully at home and, when they come back, they can decide whether to participate in the study or not. In the meantime, we start with the patient screening, staging, monitoring, etc. [INT._1, data manager]

According to the protocol, the clinician is responsible for identifying potential human subjects for recruitment. Patients, by providing their 'biological self',

represent the key actors for the implementation of R&D activities localised between the clinic and the laboratory.

During experimental subject enrolment, the patient may physically enter Human_Ph@rma premises, answer a short questionnaire on general health conditions, consent to biometric and clinical tests, and provide biological samples. At this stage, informed consent plays an essential role: it is a device through which patients are formally configured as 'experimental subjects' that are aware that they are giving access to their biological self not only for therapeutic purposes but also for research objectives.

Patients selected for the experimental study donate a blood sample in order to assess and identify the genetic variation of the UGT1A1 gene polymorphism, which is responsible for metabolising a specific chemotherapy drug in colorectal cancer treatment:

> *In the bioanalytical laboratory, I meet Maria* [lab scientific officer]. *She is working on a set of biological samples. Maria explains to me:* 'You know, it is the same old story here! I need to do this genetic analysis. I'm processing the samples to analyse [the] "UGT" gene and its polymorphism. This helps us understand if the patient can be enrolled in the experimental protocol. As a rule, we use the extractor to extract DNA from the patient's blood. For [the] "UGT" polymorphism, there is an initial sequencing for assigning a molecular weight to your genetic material, and then you check if the mutation takes place'. *[ethnographic field notes]*

For patients included in the experimental study, the 'molecular make-up' involves a set of technologies and tools that transform and abstract a biological sample into genetic information. This activity manipulates *in vitro* blood samples in order to 'extract' and 'produce' patient-specific bio-knowledge relating to its own DNA. Here, the main disciplinary field is molecular biology, which activates a bio-molecular representation of the patient in terms of genes and polymorphisms specific to those genes. If the 'genotyping' excludes the mutation of UGT1A1 gene polymorphism, the patient may be included in the experimental protocol and receive a specific chemotherapy regimen. The genotyping of the patient – achieved using a standardised technology for molecular measurement (Derksen, 2000; Keating and Cambrosio, 2005) – enables the production of genetic parameters related to the specific molecular condition of the patient. This practice bestows 'genuine plasticity' on the sample (Taussig *et al*, 2013): biological material extracted from the patient is transformed into something completely different and immaterial (that is, genetic variables) but at the same time is able to represent the patient itself.

The *in vitro* activities at Human_Ph@rma, however, are not limited to patient genotyping. The enroled patient – through the material mediation of blood

plasma samples – crosses the boundaries of the laboratory after chemotherapy cycles administered in hospital:

> As you can see, plasma sampling is scheduled at specific times. What I do is quantify the drug and its metabolites within the samples and determine their concentration. […] In practical terms, I need to determine the concentrations of a given drug and its metabolites, which I then relate to time. On the basis of the concentration-time ratio, I use dedicated software to investigate all the pharmacokinetic properties of the compound, such as half-life values. In short, I assess drug metabolism. [INT._2, pharmacologist]

This excerpt highlights how the experimental subjects, through the research activities conducted on their biological samples, are easily mobilised, transported and rendered biologically intelligible in order to facilitate their migration from care to biomedical research. After the administration of the therapeutic compound and through the analysis of biological samples, the patient is represented by a set of drug metabolites. Producing an ensemble of biological parameters related to the metabolic processes of the patient, which is carried out using a specific technology for molecular quantification and standardised procedures (Keating and Cambrosio, 2003), transmutes the patient's sample into a bio-informational representation of his/her living body for developing a laboratory facts relevant for clinical care.

Moving from molecular biology to pharmacokinetics, next pharmacologists try to assess how a known bio-molecular condition – in this case, the absence of a mutation in the 'UGT' gene – may affect drug concentration and its metabolisation in the patient's body.

Overall, these laboratory activities configure the patient into a mere biological resource responsible for drug metabolism. According to Rose (2007), technologies for decomposing, manipulating and quantifying vitality at the molecular level enable 'the fragmentation of the body into transferable tissues which could, often with difficulty, be freed from their marks of origin and re-utilised in other bodies' (p. 14). By resorting to a specific technology for molecular quantification, the transformation of the biological sample into abstract biomedical information – or rather representing the patient solely in terms of a genetic variation responsible for drug metabolisation and metabolites – ruptures the specific affinity and idiosyncratic liaison between the individual patient and his/her biological sample and between the biological sample and the specific pathological singularities affecting it. For this reason, *in vitro* activities are oriented towards the biological samples in order to get information about the drug and its metabolism, rather than towards the relationship between the patient and the pathological condition.

In general, the centrality of the patient's living body recalls the methodological foundation of translational biomedicine, which is based on the assumption that using biological materials extracted from human beings should enable the production of knowledge and tools that may have an immediate and direct relevance on care practices:

> […] *even when you do experiments, you will always try to get the most reliable and accurate results, as accurate as possible, because the data that you are producing will have an impact on the patient: this is what translational research is all about*. This means that if you are analysing samples for the first time, you should always work in pairs, as you do in diagnostics. It is about patients, and you just can't get it wrong. [INT._3, laboratory technician – emphasis mine]

Handling *in vitro* biological samples focuses on the level of DNA and its variations, generating a source of knowledge and information to support the therapeutic intervention on the patient. Molecular biology, along with studies on drug metabolism, is oriented towards generating abstract information from the biological sample so that biomedical knowledge can be extended to a plurality of subjects categorised under the same molecular classification. In this sense, the scientific practices conducted on the biological samples are carried out in accordance with a number of procedures and adjustments that may help build reliable and clinically relevant evidence. For this reason, researchers tend to refer to clinical diagnostic routines as a repertoire of standardised activities that are sufficiently stable and reliable to be re-adapted and re-located into research laboratories. In this way, laboratory practices reduce a metabolic condition into quantitative biological variables that can be measured, thus allowing their migration to the clinic.

This multi-directional translation process implies an epistemological border-crossing between the clinic and laboratory research. In our example, the technological devices for molecular measurement and quantification shape a process of epistemological border-crossing of both bio-knowledge and biological material, enabling laboratory evidence to be translated into clinically actionable knowledge (Wainwright *et al*, 2006). This process can be expressed as *clinical technomimicry:* the set of sociomaterial practices distributed in the laboratory which shape the epistemological congruence between scientific research and clinical action (Lewis *et al*, 2014). This process occurs through a set of cognitive, material and technological resources performed by bio-researchers to accomplish the daily scientific work of analysing biological samples inside laboratory spaces. Theoretically, the concept of *clinical technomimicry* may help understand the relationship between research and clinic by focusing on the sociomaterial practices allowing laboratory science to incorporate clinical needs in its logic of

action and relocating laboratory evidence into clinically actionable knowledge that allows intervention in the patient's biomedicalisation trajectory.

Working 'in vivo': Body, molecules, and hospital wards

The previous section exploring laboratory practices showed how the relationship between the body and pathology is subsumed into abstract bio-molecular information pertaining to human metabolism of a chemotherapeutic compound. Contextually, the living body is also concerned with *in vivo* clinical work, which centres on the pathological dimension and its progression. Here, the patient is configured and represented as a biological resource that carries a specific disease.

In vivo practices aim to validate a specific gene polymorphism as a 'druggable' biomarker relevant to the personalisation of clinical care:

> We are evaluating how certain polymorphisms of "UGT" allow treatment with higher doses of the drug because they show a lower toxicity and a better clinical response. […] Patients are treated with different doses depending on their body surface and genotype. The amount of the drug should be assessed by a physician. […] At each treatment cycle, the clinician must decide whether we can proceed or not. [INT._2, pharmacologist]

Working *in vivo* requires research nurses, pharmacologists and medical oncologists to perform practices directly on the patient's body within the hospital. At this stage, the experimental subject receives drug infusion, blood testing, and monitoring of biochemical and physiological parameters to determine how their genetic profile may impact the correlation between chemotherapy and disease regression. The amount of drugs to be administered is gradually increased until the maximum dose tolerated by the patient has been identified.

> It is clear that a patient included in an experimental protocol should receive further monitoring compared to other patients. […] With this type of patient, you have to be much more accurate even on the clinical level. For example, if CAT [Computed Axial Tomography] is to be performed every two months, after two months and one day a CAT scan must be done. I mean, in a normal routine, if you do it after a week, it doesn't make much difference. Even if you do it after one month. However, when it comes to experimental protocols, you need to be as accurate as possible, especially with the sampling, because these data and samples will also be used by the laboratory researchers working downstairs. [INT._4, oncologist]

The 'molecular gaze' (Rose, 2001) (extended to the experimental subject through laboratory activities) is juxtaposed with the 'clinical gaze' (Foucault, 1994) (aimed at evaluating the course of the disease in relation to chemotherapy). Physicians are responsible for collecting clinical data on the patient while

administrating the therapeutic compound. Clinical oncology employs a number of monitoring activities – such as bio-physiological and blood chemistry information and CAT scans to evaluate tumour lesions – in order to represent the living body in term of a composite set of clinical records. The oncologist's emphasis on compliance with formal protocol requirements is also of particular interest for understanding the multi-localised and multi-disciplinary management of the experimental subject. During the ethnographic investigation, the timely implementation of the protocol (for example, the timing of examination and sampling procedures) was one of the main concerns expressed by the operators involved in the experimentation. In clinical routine, for the sole purpose of therapeutic relevance, it is possible for the oncologist to exercise discretion in the timing of patient monitoring. However, traditional physician autonomy in clinical patient management (Allsop and Mulcahy, 1996) ceases when the patient's treatment is also intended for data collection aimed at articulating experimental protocols across bench and bedside.

In translational research, the clinic is not a place where biomedical knowledge is exclusively 'consumed' to heal a patient (van den Hoonaard, 2009). Rather, clinical settings are reframed to advance scientific research. Here, an ensemble of procedures oriented towards producing scientific data and biological samples are re-located from the laboratory to the clinic in order to generate information and biological material epistemologically consistent with research laboratory needs.

Although physicians can assume that analyses conducted on a patient with a month's delay may not affect the management of cancer care, the coordination of scientific protocols with related experimental subjects requires coordination between clinicians and researchers. The clinical gaze must comply with standardised laboratory procedures so that the data obtained are epistemologically reliable for research purposes.

The process of coordinating between clinical gaze and laboratory procedures can be conceptualised by the notion of *experimental technomimicry*. This concept refers to how the clinic re-adapts its routines and care practices to establish epistemological congruence with the research laboratory's rules and methodological conventions. This process occurs when a research protocol is translated into the clinic, changing working medical practices in order to align the care setting to the laboratory research model. The concept particularly captures the multi-modal practices involved in translating clinical signs and symptoms into researchable issues or in a set of 'doable' scientific phenomena (Fujimura, 1987). As Clarke and colleagues have demonstrated (2010), in contemporary biomedicine, patients are increasingly involved in a range of research activities that may go beyond the requirements of a single therapeutic project. In this sense, the notion of *experimental technomimicry* undermines the

traditional dichotomy between the laboratory and the clinic and highlights how laboratory practices may shape the biomedicalisation experience.

Working 'in silico': Locating bio-representations in biomarkers

During clinical and experimental activities, the medical and scientific staff construct and collect a large amount of molecular and clinical information concerning the experimental subject's biomedicalisation trajectory. The patient's body is engaged at different levels in these activities and is represented by a set of discrete elements (specific to the biomedical disciplines involved in the protocol) aimed at biomarker validation.

In this cross-laboratory scenario, an additional aspect of *in vivo* and *in vitro* activities is centralised electronic data management. The information derived from the patient's body and biological samples is recorded on paper forms which are then re-processed *in silico* with IT tools:

> When medical visits, therapy, and pharmacokinetics have been completed, you should try to retrieve all the information available, including examinations performed, medical visits, and so on. […] To do this, we use CRFs [Case Report Form]. CRFs arise from a "fanciful" approach, and then we rely on the professional experience gained over the years. […] You would try to get the most relevant information out of each form and summarise it into the CRF that in your opinion is the most appropriate. Then, of course, we require the help of those who can extract data with statistical software to find the information that we are looking for. [INT._1, data manager]

The transformation of a genetic variation into a 'druggable' biomarker requires accurate management and data analysis throughout the entire experimental process and involves a diverse range of human actors, technologies, and biological entities. Generally, the CRFs provide an important tool for organising and managing clinical and biological information through which the patient's living body takes on an immaterial informational status.

In analytical terms, CRFs allow the research team to arrange a set of patient bio-representations and identify the patient as a statistical unit composed of a number of variables, such as nominal variable (sex, type of disease, peculiarities of the genetic profile), ordinal variable (staging of the disease) and cardinal variable (weight, number of polymorphonuclear leucocytes).

According to Lionelli (2012), digitally managing bio-data and building databases play a central role in contemporary biomedicine by fostering the interface of clinical and biological knowledge and thus supporting translational medicine into shaping new care options.

During *in silico* activities, the main disciplinary field is halfway between information science and biostatistics, which denotes the disciplinary infrastructure

where biological information about the patients is processed into alphanumeric strings and submitted for analysis.

Reducing the experimental human subject to a statistical unit is a process of abstraction where different multi-representations of the patient (as a longitudinal expression of his/her biomedicalisation trajectory) are isolated, processed and analysed within *in silico* contexts unrelated to the organism from which they were obtained. Using a statistical algorithm for assessing the correlation between genetic variation and clinical response to drug treatment suspends any similarities between the human subject and the related idiosyncratic medical/scientific information. In this way, the molecular and clinical representation of the patient's body may be reduced to an informative dimension no longer related to a specific patient. Thus, a genetic variation pertaining to a single body is configured into a 'druggable' biomarker that may be extended to other persons, thus providing a new therapeutic option.

As Nelson and colleagues have highlighted (2013), biomarker validation involves the transformation of a genetic variation into a single, clinically actionable, biological entity. This entity defines a new molecular class based on genetic variation by incorporating the knowledge obtained from the interfacing between clinic and laboratory. In this respect, through the notion of technomimicry – which put into light the 'heterogeneous engineering' (Law, 1987) of cognitive, material and social resources – it has been possible to theoretically capture the production of a new clinical tool that can be re-located from one organism to another, and can help categorise all the patients affected by a specific disease (colorectal cancer in this case) in relation to their genetic profile.

Discussion and Final Considerations

First, this article examined the variety of practices that are differently localised between the laboratory and the clinic. Then it focused on how the growing connections between patients' living bodies and biomedical innovation processes may reflect the breakdown, erosion and redefinition of the traditional boundaries between the patient's status as an object of research and an object of care, as well as between clinical practice and scientific research. Indeed, multiple works describe these processes as constituent elements of the main historical evolution of western biomedicine, which is based on the production of evidence through inter-laboratory studies (Cambrosio *et al*, 2006a).

Since the seminal text of Canguilhem (1989), social studies of health and medicine have emphasised the need to understand biomedicine considering the clinic in relation to the processes of scientific research (Keating and Cambrosio, 2003). These works have revealed how the alignment between normal and

pathological, or between health and disease, is shaped at the interface between laboratory and clinic, or between medicine and biology (Löwy, 1996).

This article explored the often-neglected sociomaterial practices by which the epistemic relations between these two domains are generated. In particular, I stressed how biomedical knowledge emerging from the laboratory and therapeutic practices are mutually reconfigured, defining the 'biomedical space' of translational research for the development of personalised treatments. The concepts of *clinical technomimicry* and *experimental technomimicry* were introduced to aid the investigation of the multi-dimensional relations between the scientific and medical levels, and may be useful for understanding the biomedical translational process. These process are conceptualised as the emerging outcome of an ensemble of sociomaterial practices whose main objective involves configuring patients as 'experimental subjects' in order to extract scientific knowledge that may potentially generate new therapeutic options.

From a theoretical standpoint, technomimicry represents a conceptual device for emphasising the sociomaterial practices through which life-related knowledge can be translated into therapeutic options through *in vivo, in vitro* and *in silico* activities. Further, technomimicry provides an account of translational research in the making, or a description of how information about biological processes is incorporated into material devices, thereby translating new institutional models of care and research into practice.

About the Author

Stefano Crabu is a sociologist of science, technology and medicine based at University of Padova with particular interest in study of processes of biomedical innovations. His doctoral research was an ethnographic study of biomedical organizations for oncological translational research. Recent publications have centred on sociomaterial and epistemological aspects of translational biomedicine, and laboratory practices.

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