



# The knowledge production model of the New Sciences: The case of Translational Medicine



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## ABSTRACT

The tremendous achievements of life sciences research in the last 40 years have brought relatively little improvements to medical practice, suggesting a deficiency of the medical innovation system in capitalizing on these fundamental advances. We argue that a major cause of the poor innovative performance is the slow adaption of the scientific system to the novel research technologies made available by the progress in the life sciences – rather than resistance of practitioners. We interpret the changes in the organization of medical research through the lenses of the theory of New Sciences, which puts forward that the application of novel research technologies promotes new epistemological and methodological approaches to the investigation of complex phenomena, increasing interdisciplinary intellectual exchanges. In oncology, Translational Research, that embodies the features of a new science, coexists with the standard model of knowledge production in clinical medicine. Our comparison of the two approaches finds that Translational Research allows investigations across diverse and cognitively distant knowledge bases, thanks to the intensive use of research technologies that emerge from fundamental research. Unlike standard studies, the scientific impact of translational studies benefits from the adoption of an interdisciplinary approach. However, translational studies have an overall lower impact than their counterpart.

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## 1. Introduction

An effective governance of medical innovation systems is a critical issue for policymakers in many countries – both in the developed and developing World – given the trends of increasing costs of healthcare provision, ageing population, escalation of technological interdependency, and intensification of science-industry linkages (Faulkner, 2009; Nicolini, 2010; Ryan, 2010; Peine et al., 2015). Indeed, medical innovations are the outcome of the co-evolution of different cognitive and institutional domains, such as fundamental biomedical science, clinical practice and medical technology (Gelijns and Rosenberg, 1999; Metcalfe et al., 2005; Morlacchi and Nelson, 2011; Nelson et al., 2011; Consoli and Ramlogan, 2012; Rafols et al., 2014; Kukk et al., 2015). Some studies have shown how advances in the treatment of specific diseases and the introduction of novel approaches, such as personalized medicine, have been based on novel combinations of medical technologies with clinical practices and fundamental research (Amir-Aslani and Mangematin, 2010; Tierney et al., 2013; Coccia and Wang, 2014; Faulkner, 2015). However, the great expectations brought by the so-called “biotechnology revolution” are still largely unmet. In the last four decades, basic life sciences have attained unprecedented achievements

and have generated an entirely new class of research technologies, i.e. novel tools and instrumentation to be used in the process of knowledge production, generating expectations for disruptive changes in a broad range of sciences and industries; despite these advances, the ability of the medical innovation system to generate new and more effective drugs, devices, diagnostics and therapies has been poor (Henderson et al., 1999; Moran, 2007; Hopkins et al., 2007).

One explanation for this disappointing performance rests in the delay of the biopharmaceutical industry in identifying suitable business models and in shaping innovation ecosystems favorable to the exploitation these new technologies (Sabatier et al., 2012; Lehoux et al., 2014; Kukk et al., 2015). We argue that an equally important reason why medical innovation has progressed relatively slowly – if compared to the great opportunities disclosed by fundamental advances – is to be found in the “science side” of the system.

The availability of novel and more powerful research technologies and the policy pressures demanding an increase in productivity of the medical innovation system, have brought to the emergence of the new field of Translational Medicine. Advocates of Translational Medicine claim that the medical innovation would benefit from insights brought by an intensification of interdisciplinary linkages, the systematic utilization of clinical insights in basic studies, and the prioritization of the solution of patients' problems – rather than disciplinary priorities – in the life sciences research agenda (Marincola, 2007; Sablinski, 2014).

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Translational Medicine attracts great interest both within the scientific community and among policymakers, who highlight it as a key strategy for scientific progress in the medical sciences (Grimes, 2011; McLeod et al., 2011; van der Valk et al., 2011; Douglas et al., 2014).

The aim of this paper is to gain insight in the model of knowledge production of Translational Medicine, compared to the “standard” approach that consists in clinically-driven studies that marginally rely on fundamental research; specifically, we compare the two approaches in terms of reliance on novel research technologies, creation of cognitive linkages across disciplines, and drivers of impact on the advance of medical sciences. We take as our case breast cancer research, where the translational approach is particularly prominent. However, also in this field, the “standard” model of research is widely employed and presents limited intellectual exchanges with the translational community (Cambrosio et al., 2006; Jones et al., 2011). For these reasons, breast cancer research is a case that allows the translational and the standard approaches to be rigorously compared. Our study is designed to capitalize on this methodological opportunity.

We address these issues taking the theory of the “new sciences” as conceptual reference. The “new sciences” that emerged during the last decades of the 20th century, such as life-, nano- and computer sciences, exploit new and powerful research technologies that allow scientists to investigate the elementary building blocks of extremely complex phenomena such as the human body and its diseases. Systematic application of these research technologies gives rise to a unique model of knowledge production (Bonaccorsi, 2008, 2010). The concept of “new science” is used increasingly to gain insights into the features of interdisciplinary fields (e.g. Jansen et al., 2010; Lepori, 2011; Heimeriks, 2012; Heimeriks and Leydesdorff, 2012; Horlings and Gurney, 2013).

We contribute to this debate by offering one of the first empirical tests of the theory based on fine-grained comparison of the research conducted in the same medical field according to the principles of new and established sciences. In this way, we bring to light some of the micro-level mechanisms producing tensions and delays in the acceptance of new scientific paradigms (Lakatos and Musgrave, 1970). In particular, our finding that translational studies are systematically penalized in terms of impact on subsequent research compared to standard studies adds insights on why scientific communities are slow in adopting interdisciplinary approaches. We suggest that science-internal hindrances represent a major cause of the scarce efficacy of the medical innovation system.

Furthermore, our study contributes to the more general literature on the economics of innovation and technological change, by giving new light on the effect of technological development on the dynamics of science. Studies on the effects of technology on science highlight that research technologies bridge scientific and industrial communities, underpin the emergence of new professional groups and shape new models of collaboration across existing disciplinary boundaries (De Solla Price, 1963; Rosenberg, 1992; Stokes, 1997; Joerges and Shinn, 2001; Shinn, 2005; Meyer, 2007). This paper relates the use of research technologies to the differences in the institutional and epistemological dynamics of science, as it shows that only translational studies make an extensive use and contribute to the development of knowledge in the fundamental fields that generate novel research technologies.

The remainder of this paper is organized as follows: we start by defining the theoretical framework from which we derive our hypotheses. After presenting our research design and data, we test the hypotheses, and then discuss our findings.

## 2. How research technologies stimulate scientific change

### 2.1. Research technologies and New Sciences

Scientific instrumentation plays a dual role in the process of knowledge production: first, it provides researchers with the technical tools to carry out investigations by enabling the collection and analysis of

empirical data; second, it opens up the possibility of investigating new phenomena, thus paving the way to epistemic change (Rosenberg, 1992; Collins, 1994). The literature on research technologies emphasizes the contribution to epistemic change brought by research tools that emerge from advances in fundamental research. Research technologies offer sets of methods, techniques, standards, and associated concepts that can find application in various settings across disciplinary boundaries. Furthermore, they offer substantial improvements in computing power, accuracy, and precision of research tools (Shinn, 2005). Research technologies have been studied mainly from a sociological perspective which looks at how they are invented, their circulation across geographic and institutional settings (primarily, industry and academia), and their contribution to the reconfiguration of occupational groups across disciplines (Joerges and Shinn, 2001). Recently, they have been proposed as a major factor underpinning the emergence of a class of “new sciences” representing a model of knowledge production that is radically different from that of the established sciences (Bonaccorsi and Thoma, 2007; Bonaccorsi, 2008, 2010; Bonaccorsi and Vargas, 2010).

The theory claims that, following an established tradition in the core disciplines of natural sciences, “new sciences” are predicated on reductionist reasoning, especially in terms of methodological stance; however the application of a reductionist approach to complex phenomena (such as the human body or diseases) leads, differently from established sciences, to the proliferation of theories, each addressing different levels of analysis of the phenomenon (e.g. the gene, the molecule, the organ) – typically corresponding to a scientific field. The New Sciences’ attempt to understand also the linkages between theories and observations developed within each of scientific fields. For this reason, a key feature of new sciences is the establishment of cognitive and institutional complementarities, defined respectively as the integration of knowledge developed in heterogeneous disciplinary areas or in multiple institutional settings, such as academia, industry and medical practice. The creation of systematic linkages among concepts and phenomena at the interface between different levels of analysis is a driver of the emergence of novel areas of research that does not imply a weakening of disciplinary boundaries, but rather an increase in the knowledge flows among disciplines (Bonaccorsi, 2008; Bonaccorsi and Vargas, 2010).

### 2.2. Translational Medicine as a new science

Translational Medicine can be regarded as an example of a new science because it relies on the exploitation of novel research technologies, embraces a reductionist research strategy, and progresses by establishing connections among concepts, methods and insights relative to different disciplines by means of research technologies based on fundamental life sciences and computer sciences (Bonaccorsi, 2010).

Traditionally, the cognitive exchange between clinical medicine and the fundamental life sciences has been limited; in fact, medical practice has advanced through cumulative learning on the functioning of specific organs or diseases, or through the systematization of empirical information on patients, without clear guidance from theoretical principles. One of the reasons for the limited reliance of clinical studies on fundamental theories is recognized in the organization of medicine around tight disciplinary specializations defined by diseases (Nelson et al., 2011; Thagard, 1999; Bonaccorsi, 2010). This applies also to the case of Oncology, which is organized in sub-disciplines defined by the different types of cancers.

However, the many interrelated factors affecting the objects of analysis of clinical research – the patient, the organism, the organ – impede the identification of causal explanations of phenomena addressed by distinct disciplines. For instance, in oncology, advances in our understanding of the disease may come from the integration on information on how social or environmental factors affect the mutation of the genes responsible for the occurrence of the disease, that is produced in distinct disciplinary domains – molecular biology, biochemistry,

genetics, clinics, epidemiology, and social and environmental studies (Bonaccorsi, 2010). Moreover, this organization of medical research has made it difficult to exploit the fundamental advances brought by the so-called “Molecular Biology revolution” from the mid-1970s. These advances paved the way for the development of research technologies – such as recombinant-DNA, monoclonal antibodies, sequencing, polymerase chain reaction, high throughput screening, combinatorial chemistry (Henderson et al., 1999; Judson, 1979; Morange, 1998; Coccia, 2014); furthermore, they gave rise to the ambition to connect clinical investigation to a theoretical framework.

Alone or in combination with information technologies and data-mining facilities, these technologies offered unprecedented opportunities to understand the biochemical causes of physiological and pathological phenomena, allowing laboratory analyses on human samples connected to large clinical datasets (Webb and Pass, 2004).

As a consequence of the poor exploitation of technology-enabled cross disciplinary explorations, medical research has demonstrated limited ability to translate fundamental advances into new drugs, diagnostics, and devices (Moran, 2007; Hopkins et al., 2007). In response to this dissatisfaction, towards the end of 1990s, science policy actively supported “translational” research programs aiming at creating systematic linkages among the different disciplines investigating diseases.

Empirical studies have demonstrated that during the last decades, biomedical research has increasingly relied on inputs generated outside disciplinary boundaries (Porter and Rafols, 2009; Rafols et al., 2014) and on the emergence of an interface between fundamental and clinical disciplines (Boyack, 2005; Jones et al., 2011). However, most medical studies are conducted according to the “standard”, clinically driven approach.

2.3. The drivers of scientific impact in the New Sciences

To compare the drivers of scientific impact between “new” and “established” sciences, we draw on the notion in Evolutionary Epistemology that knowledge accumulation is a two-step process consisting of the generation of competing explanations for a research problem, and their subsequent selection based on their fitness to resolve that problem (Bradie, 1986; Campbell, 1974). In this sense, scientific communities develop selection criteria that filter the relevance of theories, approaches, and contributions, and thanks to the positive feedback from the application of successful discoveries (Callon, 1994), control the direction of knowledge accumulation. These criteria are signaled through the reputational system of science (Dasgupta and David, 1994; Merton, 1957). In this system citations are the key informational device, since their signals combine priority for single discoveries with their impact on subsequent research. In this perspective, citations indicate the extent to which a given idea “fits” the criteria of selection set by a community (Gittelman and Kogut, 2003). Therefore, by identifying the cognitive characteristics of scientific contributions that receive a higher

number of citations, we may infer the criteria that a scientific community considers to be important for the accumulation of knowledge.

We conceptualize the characteristics of a given focal body of research using a simple three-stage sequential model of scientific knowledge production (Fig. 1). First, we consider its knowledge base, i.e. the way it draws on previous research as “buildings blocks” for its own contribution, particularly the disciplinary diversity of these inputs. Second, we characterize the focal body of research in terms of the disciplinary scope of its own subject matter. Third, we consider its impact on subsequent research in terms of forward citations.

Regarding the building blocks for Stage 1, the theory of new sciences highlights the formation of cognitive complementarities. They are expressed in the ability of a focal body of research to link together previously unrelated (cognitively distant) different tools and insights as inputs. A study that ties together previously disconnected inputs offers a search advantage for subsequent research by making it possible for scientists to invoke connections between elements that have been validated in one problem area, to aid the understanding of new findings in other areas (Schilling et al., 2003). According to the theory, establishing such cognitive complementarities is particularly pronounced for new sciences because their reliance on new and powerful research technologies provide them with empirics that can be fruitfully interpreted only by integrating different disciplines. Indeed, principles and standards of research technologies offer scientists operating in distant epistemic communities a shared cognitive platform enabling direct exchanges of theoretical insights, methods, and empirical findings (Shinn, 2005). This permits recognition, to a large extent, of analogies among concepts referring to different layers of reality, and the use of methodologies developed in distinct disciplinary traditions. In contrast, standard science relies on lower diversity of research inputs firstly because they are less driven by new research technologies, secondly because they do not receive insights and analogies which migrate across disciplines and domains using new research technologies as their vehicle. Therefore we expect that cognitive complementarities do not drive scientific impact in “standard” research.

**Hypothesis 1.** Cognitive complementarities are a driver of scientific impact in new sciences but not in “standard” science.

The second stage of knowledge production concerns the *scope* of the subject matter covered by the focal body of research. In standard science the relevance of new contributions is assessed by criteria that are principally internal to each discipline (Whitley, 2000), and there will often be reduced receptiveness to issues spanning several disciplines (Klein, 2008). By contrast, one of the defining characteristics of New Sciences is their reach across different and disciplines in their analysis. For example, in Translational Medicine, diseases are explained by reference to factors at the genetic, molecular, or cellular levels. At the same time, these levels have their own specialist disciplines (Bonaccorsi, 2010).

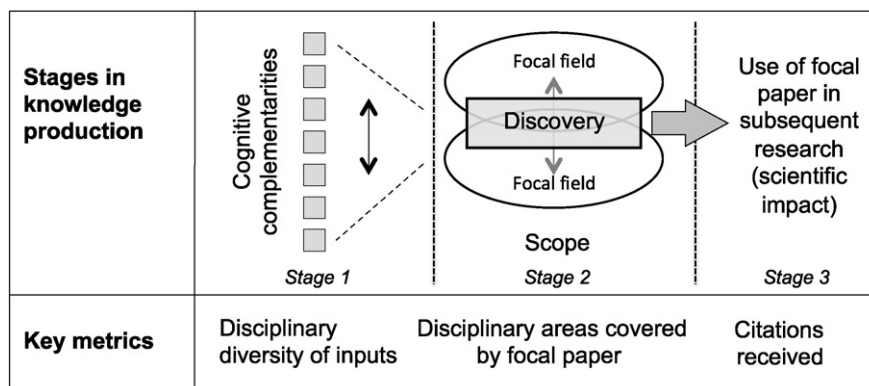


Fig. 1. Stages in knowledge production.

Hence, New Sciences have no intrinsic reservations about research issues transcending single disciplines, nor any systematic preferences.

**Hypothesis 2.** Increasing scope in the subject matter of a focal contribution detracts from the scientific impact on subsequent research in standard science but not in new sciences.

### 3. Research design

In our empirical analysis of the drivers of scientific impact in breast cancer research we utilize data on publications because they allow us to observe the dynamics of scientific change and relationships among scientific fields reducing the risk of subjective bias (Consoli and Ramlogan, 2008). In order to identify the relevant publications, we adopted multiple criteria since previous studies have not discovered any simple bibliometric markers distinguishing translational from “standard” medical research (Luwel and van Wijk, 2015). As described further in Appendix 1, our approach is based on the identification of two groups of Lab Leaders, one belonging to the translational and the other to the “standard” epistemic community. For each Lab Leader, we retrieved their articles published in 2003–2007 from the Institute for Scientific Information - Web of Science (ISI-WoS) database. We focused on this period because we want to capture the cognitive dynamics at the early stages of development of this field. We obtained 356 articles – 177 authored by Lab Leaders adopting a translational approach and 179 authored by those favoring the standard approach. The low numbers reflect the shortage of cases of Lab Leaders where the classification was unambiguous.

The dependent variable in our study is the impact of an article, based on number of citations received from “original research articles” and review articles up to December 2010. We cleaned the performance measure from self-citations, because, among the scientific community, these are not meaningful for impact (Aksnes and Rip, 2009). In order to take into account the time that a paper is available for citation (*Years from publication*), we adjusted the regression models using the “exposure” option (Long and Freese, 2006).

In order to capture the subject *Scope* of an article, we rely on the categorization of journals into the subject-categories used by ISI-WoS. ISI-WoS subject-categories indicate the research areas covered by journals; they can be considered proxies for the disciplinary specialization of the articles published in those journals. To examine the scope of a given article, we first associate it with the subject-categories describing the journal in which it was published. We then aggregate the subject-categories into four *Disciplinary Areas* (see Appendix II): *Oncology*, consisting only of the homonymous subject-category, i.e. the core discipline in breast cancer research; *Practice-Group*, which includes medical specialties defined by their main operational principle; *Disease-Fields*, which includes medical specialties defined by disease type or organ(-system); *RT-Fields*, which refers to the fundamental disciplines from which the research technologies applied in medical research originate. We use four dummies to characterize each *Disciplinary Area*. A fifth dummy, labeled *Multiple*, takes the value 1 if the focal article is associated with multiple *Disciplinary Areas*. This allows us to compare the impact of studies spanning multiple fields (*Multiple*) with mono-disciplinary studies addressing more fundamental issues (*RT-Fields*), applied medical research (*Oncology*, *Disease-Fields*), and clinical practices and techniques (*Practice-Group*).

We capture the role of cognitive complementarities in a focal paper by measuring the diversity of its inputs from previous research. We use the variable *Diversity Index* which builds on the methodology proposed by Porter et al. (2007) to measure the diversity found in sets of scientific journal publications. The *Diversity Index* takes value the 0 for papers where all references fall into a single subject-category, to a maximum of 1 for i) number of disciplines referenced, ii) their mutual cognitive distance, and iii) the heterogeneity of the distribution of references

across subject-categories. The last measure is derived from a “science matrix” based on the frequency of co-citations among subject-categories. Subsequently, we generated the categorical variable *Diversity* with three intervals (low, medium and high), defined at the cut-off points of the 33rd and 67th centiles of the distribution of the *Diversity Index*.

We distinguish between the standard and the translational approaches with a dummy that takes the value of 1 for publications produced by translational Labs and 0 for “standard science” Labs. We appreciate how the approaches differ in terms of cognitive complementarities and subject scope, by including two sets of dummy variables. The first set focuses on the differences between approaches in studies that span multiple *Disciplinary Areas* and those that are contained within one disciplinary area. To this purpose, first we create the variable *Monodisciplinary*, that characterizes papers classified exclusively in one of the following *Disciplinary Areas*: *RT-Fields*, *Oncology*, *Disease-Fields* and *Practice-Group*; then, we consider all the possible categories produced by the combination of *Approach* with *Multiple* and *Monodisciplinary*: *Translational-Multiple*, *Translational-Monodisciplinary*, *Standard-Multiple*, and *Standard-Monodisciplinary*. The second set is based on the six categories defined by combinations of *Approach* and *Diversity*, i.e. *Translational-Low Diversity*; *Translational-Medium Diversity*; *Translational-High Diversity*; *Standard-Low Diversity*; *Standard-Medium Diversity*; *Standard-High Diversity*.

We apply seven controls. Since theoretical breast cancer research studies tend to receive more citations (Lewison et al., 2010), we control for the focal paper's orientation towards more basic or more applied issues. We characterize this orientation by means of the CHI-classification<sup>1</sup> which distinguishes between: 1) clinical observation, 2) clinical mix, 3) clinical investigation, and 4) basic research (Narin et al., 1976). Following, Van Looy et al. (2006), we aggregate Levels-3 and 4 into a single category representing a basic orientation, and refer to Levels-1 and 2 as clinical orientation. The variable *Orientation* takes the value 1 for basic orientation and 0 otherwise.

Within a Lab Leader's research program, there may be synergies among individual projects: a later article building on earlier investigations might exploit synergies and cumulateness; on the other hand, subsequent contributions might be unrelated to the author's previous work. In order to account for these effects, we considered the dummy *Cumulative* which takes the value 1 if the focal article cites the Lab-Leader's previous production in the period considered.

We control for the extent to which a paper builds on a novel vs. mature knowledge base. We avoid the distorting effect of citation of “classical” contributions, considering the age of the most recent quartile of its references. The dummy (*Age*) identifies articles that are based on a mature knowledge base: it takes the value 1 for papers whose age of the most recent quartile of their references is higher than the average for the sample, i.e. three years.

Collaborative research is known to have greater impact than individual research (e.g. Adams et al., 2005), so we control for research team size. A set of dummies is used to distinguish among “*Small collaborations*” with less than 9 co-authors, “*Medium-sized collaborations*” with 9 to 11 co-authors, and “*Large collaborations*” with more than 11 authors. The cut-off points used to define the classes are the 33rd and 67th percentile of the distribution of the size of the research team.

We use a dummy to identify each *Lab Leader* to capture individual factors - e.g. individual talent, organization of the team of inner collaborators, age of the team.

We employ negative binomial regression models since our dependent variable - number of citations received by each article - is a non-

<sup>1</sup> We are aware of the limits the CHI-classification for measuring “basicness” (Tijssen, 2010), and the limits of subject-categories to define disciplines (Pudovkin and Garfield, 2002). We base our variables on these tools because of their widespread diffusion in studies of scientists' productivity. The former is used by e.g. Van Looy et al. (2006); the latter by e.g. Ponomarev and Boardman (2010).

**Table 1**  
Descriptive statistics.

Variable	Total		Translational		Standard		Test
	Mean (std. dev.)	Median	Mean (std. dev.)	Median	Mean (std. dev.)	Median	
Total n. of articles	356		177		179		
N. of Citations	26.736 (55.489)	11	27.395 (54.443)	12	26.084 (56.650)	11	– 1.659*
Diversity Index	0.449 (0.151)	0.471	0.508 (0.110)	0.500	0.391 (0.164)	0.413	– 6.798***
	n.	%	n.	%	n.	%	<sup>b</sup>
Diversity							
Low	117	32.87	31	17.51	86	48.04	<i>p</i> = 0.000
Medium	122	34.27	70	39.54	52	29.05	<i>p</i> = 0.044
High	117	32.87	76	42.94	41	22.90	<i>p</i> = 0.000
Disciplinary Areas							
Oncology	198	55.62	94	53.11	104	58.10	<i>p</i> = 0.393
Disease-Fields	17	4.78	12	6.78	5	2.79	<i>p</i> = 0.087
Practice-Group	45	12.64	13	7.34	32	17.88	<i>p</i> = 0.004
RT-Fields	18	5.06	17	9.60	1	0.56	<i>p</i> = 0.000
Multiple	78	21.91	41	23.16	37	20.67	<i>p</i> = 0.609
of which							
RT-Fields + other	25	32.05	22	53.66	3	8.11	<i>p</i> = 0.000
Other combinations	53	67.95	19	46.34	34	91.89	<i>p</i> = 0.000
Orientation	111	31.18	90	50.85	21	11.73	<i>p</i> = 0.000
Cumulative	196	55.06	117	66.10	79	44.13	<i>p</i> = 0.328
Team-Size							
Small	130	36.52	62	35.03	68	37.99	<i>p</i> = 0.583
Medium	95	26.69	50	28.25	45	25.14	<i>p</i> = 0.550
Large	131	36.80	65	36.72	66	36.87	<i>p</i> = 0.999
Age	123	34.55	65	36.72	58	32.40	<i>p</i> = 0.496
Publication Year							
2003	80	22.47	38	21.47	42	23.46	<i>p</i> = 0.704
2004	60	16.85	31	17.51	29	16.20	<i>p</i> = 0.778
2005	70	19.66	35	19.77	35	19.55	<i>p</i> = 0.999
2006	64	17.98	31	17.51	33	18.44	<i>p</i> = 0.890
2007	82	23.03	42	23.73	40	22.35	<i>p</i> = 0.802

Significance at 0.10, 0.05 and 0.01 levels is indicated by \*, \*\*, and \*\*\* respectively.

<sup>a</sup> Wilcoxon-Mann-Whitney test.

<sup>b</sup> Fisher-test.

negative count with over-dispersed distribution. For ease of interpretation, we display Incidence Rate Ratios (IRR). An IRR greater than 1 indicates a positive contribution to citations, while an IRR between 0 and 1 indicates a negative effect. We checked for heteroskedasticity with graphical and numerical techniques. We used robust standard errors. We can exclude that the results of the regressions are substantially biased by multi-collinearity since the maximum Variance Inflation Factor is below the threshold of 10 in all the models. All models include 356 observations.

## 4. Results

### 4.1. Descriptive statistics

The descriptive statistics presented in Table 1 suggest that translational and standard medical research involve distinct patterns regarding both disciplinary specialization and input diversity. In both approaches, more than half of the production is represented by mono-disciplinary studies in oncology. Differences emerge outside the core disciplinary domain, and in the way this core is addressed: translational studies often address the areas of RT-Fields and Disease-Fields, which instead account for a negligible share of Standard research. Standard research includes comparatively more investigations of Practice-Group. The share of articles covering multiple Disciplinary Areas is similar, indicating that “standard” research also regularly addresses issues referring to different disciplinary domains; however, there is a substantial qualitative difference between the two approaches in this regard. In fact, 54% of the translational studies characterized by broad scope, combine RT-Fields with other areas, while “standard” research rarely makes contributions that matter for both RT-Fields and other Disciplinary Areas. This result underscores the substantial difference between the model

of knowledge production in Translational Medicine and “standard” medical research.

The average of the *Diversity Index* is 30% higher for translational than “standard” research; the majority (43%) of translational studies show high levels of Diversity, while standard studies show low levels of Diversity (48%). Translational Medicine shows a clear orientation towards more basic issues, but this is to be expected based on the procedure used to build the sample. As for the other controls, there are no significant differences between the approaches.

We deepen our examination of the *Diversity Index* by looking at its components, i.e. we analyze the distribution of references cited by focal papers across Disciplinary Areas. For each focal paper we calculate the share of references to four *Disciplinary Areas*<sup>2</sup>; we summarize the mean and median values in Table 2 which presents the results for the entire set of articles and the results disaggregated by level of *Diversity*. This highlights the type of knowledge bases associated with low, medium, and high levels of cognitive diversity.

The knowledge base in “standard” research is focused heavily on oncology: in the median article we find 50% of references draw on this Disciplinary Area. Studies in Oncology offer a major contribution also to Translational Research, although the approach is significantly less reliant on this kind of input (the median share of references to oncology is 40%). There are important differences between the two approaches in relation to the weight of the other Disciplinary Areas and levels of *Diversity*.

In the standard approach, an increase in the level of *Diversity* corresponds to a decrease in the inputs from Oncology: in the case of highly integrative articles, we find that the difference between the two approaches is no longer significant (on average, 32.8% vs. 29.5%). What are the other knowledge bases utilized by these two approaches when they pursue

<sup>2</sup> If a reference refers to multiple Disciplinary Areas, we attribute it to each of them. Thus, the category “Multiple” is not considered in this analysis.

**Table 2**Mean and median (in parentheses) share of cited references by disciplinary area, disaggregated by level of *Diversity* of the focal paper.

Approach	Disciplinary Area of references	Total	Diversity		
			Low	Medium	High
Standard	Oncology	0.512*** (0.500)	0.640*** (0.689)	0.445* (0.461)	0.328 (0.333)
	Disease-Fields	0.115*** (0.053)	0.062 (0.032)	0.161 (0.054)	0.236 (0.188)
	RT-Fields	0.059*** (0.018)	0.024*** (0.000)	0.089*** (0.589)	0.102*** (0.091)
	Practice	0.314*** (0.276)	0.277 (0.208)	0.360*** (0.350)	0.334*** (0.313)
Translational	Oncology	0.392 (0.403)	0.552 (0.591)	0.427 (0.442)	0.295 (0.300)
	Disease-Field	0.140 (0.090)	0.059 (0.032)	0.081 (0.045)	0.227 (0.172)
	RT-Fields	0.273 (0.259)	0.171 (0.100)	0.278 (0.260)	0.388 (0.315)
	Practice	0.195 (0.143)	0.212 (0.143)	0.213 (0.128)	0.169 (0.153)

Note: Asterisks indicate the level of significance of difference between the distributions of the share of references in each disciplinary area of translational and standard studies. Differences are tested with Wilcoxon-Mann-Whitney test.

Significance at 0.10, 0.05 and 0.01 levels is indicated by \*, \*\*, and \*\*\* respectively.

cognitive diversity? Table 2 shows that the knowledge base in the standard approach is characterized by a strong presence of inputs from the Practice-Group at each level of *Diversity*, and that Disease Fields are an important source of knowledge for highly integrative papers. RT-Fields represent marginal knowledge at each level of *Diversity*.

The knowledge base is substantially different for Translational Research. RT-Fields are an important source of inputs at each level of diversity, and are the most important source, at the expense of oncology, for highly integrative work. In contrast to what we observe in “standard” research, the contribution of Practice-Group declines as research becomes more integrative. The pattern for Disease-Fields inputs is similar for both areas.

This evidence indicates that the disciplinary diversity of the inputs to the two approaches is the result of substantially different patterns of knowledge production: Standard research tends to combine knowledge on oncology, or other diseases, with practical knowledge produced in the Practice-Group, with little or no contribution from RT-Fields. By contrast, Translational Medicine relies heavily on RT-Fields at each level of diversity. It is useful to consider these different input-profiles when interpreting the *Diversity Index*. For the standard approach, high diversity refers primarily to rare combinations of building blocks from Oncology and Practice-Group. For the translational approach, high diversity refers to a much greater extent to combinations of RT-Fields with Oncology and Practice-Group. These results provide evidence to the theoretical expectation that a new science will utilize research technologies in order to establish cognitive complementarities.

We next examine the drivers of scientific performance by looking at the mean and median citation level of translational and “standard” research for the two key cognitive drivers: *Diversity Index* and *Disciplinary Areas* (Table 3).

The relationship between *Diversity Index* and level of performance seems to differ between the approaches: In the “standard” approach we find an increase in the mean number of citations as we move from low to high *Diversity*, while the median number of citations received by papers with low and high *Diversity* is respectively similar and higher than for those with medium *Diversity*. This indicates that, even in the “standard” approach there are gains deriving from knowledge diversity; however, they are not systematic, but rather are driven by few highly integrative papers that receive a high number of citations. Translational studies, by contrast, show higher citation rates than “standard” ones only for a medium level of *Diversity*, at other levels standard studies have a higher impact.

In relation to *Disciplinary Areas*, we find that the median citation level of translational studies is similar across areas, while there are large differences among means. Again, these differences are due to a few highly cited papers. In the standard approach, the median articles in *Oncology* and *Practice Group* show similar performance, which is slightly higher than their translational counterparts, while studies across multiple disciplines have considerably lower mean and median impact.

Overall, these results indicate the strength of “standard” science in *Oncology* and *Practice Group*, while translational studies achieve a

substantially similar level of performance in all *Disciplinary Areas*. The “standard” approach presents too few observations in RT-Fields and Disease-Fields for meaningful comparison with translational research.

#### 4.2. Regression analysis

In order to validate the descriptive findings by using more robust econometric tools, we employ a series of negative binomial regression models to test the hypotheses about the effect of cognitive factors on the scientific impact of discoveries emerging from translational and standard approaches.

Our dependent variable is the number of citations obtained by an article. After presenting the controls-only Model 1, in Model 2 we introduce the key explanatory variables: *Disciplinary Areas*, *Diversity*, and *Approach*. In Models 3 and 4 we include the categorical variables expressing, respectively, the joint effect of *Approach* and *Diversity*, and *Approach* and *Multiple*. These variables allow us to assess whether the two approaches differ significantly for drivers of scientific impact.

Based on calculations on the coefficients in these regression models, we can gauge the effect of the key explanatory variables in each approach as well as the difference between approaches, at every level of the key explanatory variables. We test the significance of these estimates with a Wald test. The results are reported in Table 5.

Model-1 shows that only the control for large size of co-author team has a positive and strongly significant impact on citations. All the subsequent models confirm this effect and show also that basic-oriented papers are expected to receive about 30% more citations than those with a clinical orientation.

Model-2 shows that adoption of a translational approach is highly penalizing in terms of scientific impact; all other things being equal, a translational paper receives about one quarter of the citations received by a paper based on “standard” research. We find also that *Disciplinary Area* strongly affects the acceptance and diffusion of the work in the scientific community. Compared to contributions specialized in *Oncology*, papers

**Table 3**

Scientific impact across key cognitive dimensions in translational and standard research.

	Translational		Standard	
	Mean (std. dev.)	Median	Mean (std. dev.)	Median
<i>Diversity</i>				
Low	18.68 (17.20)	12	24.86 (42.00)	12.5
Medium	40.57 (77.86)	17.5	26.13 (67.87)	9
High	18.82 (31.50)	8.5	28.59 (68.19)	12
<i>Disciplinary Area</i>				
Oncology	24.65 (30.21)	11	24.93 (38.27)	13.5
Disease-Fields	13.67 (8.52)	13	7.60 (7.33)	3
Practice-Group	77.08 (167.03)	12	54.53 (110.41)	13
RT-Fields	32.94 (54.54)	11	4.00 (—)	4
Multiple	19.66 (19.75)	14	7.81 (6.88)	5

addressing issues related to *Practice-Group* have an expected citation rate more than two times higher while articles on *Disease-Field* and *Multiple Disciplinary Areas* are penalized compared to contributions to *Oncology*.

In Model-3 we examine *Hypothesis 1* by comparing the two approaches in terms of the effect of input complementarities (the three levels of *Diversity* derived from the *Diversity Index*) on subsequent scientific impact. To make this comparison we draw on the Wald tests of differences between the estimates presented in *Table 4*.

For the translational approach, these tests show that studies with medium *Diversity* are expected to receive 65% more citations than low *Diversity* papers; this citation rate is not significantly different from that of high *Diversity* studies – which are expected to receive 62% more citations than low *Diversity* studies. By contrast, in the standard approach, higher diversity does not mean a stronger impact. Indeed, medium and higher levels of diversity show *lower* impact compared to low level diversity, but this penalizing effect is significant only for the medium level where a 40% decrease is observed. Hence, confirming *Hypothesis 1*, exploitation of cognitive complementarities does increase the scientific impact in a new science, whereas a similar effect is not found for standard science.

*Hypothesis 2* refers to differences between the two approaches in the relationship between subject scope and scientific impact. To understand whether the penalizing effect of broad scope investigations is specific to one of the approaches, the interaction in Model 4 between *Multiple* and *Approach* shows that articles based on the standard approach covering multiple *Disciplinary Areas* are expected to receive about 55% fewer citations than articles specialized in oncology. The Wald test reported in *Table 4* shows that, in translational research

**Table 5**

Effect of interacted variables in the translational and the standard approaches. Results of Wald tests.

Model	Relationship Diversity × Approach	IRR (std. err.)
Model 3	Medium, Translational vs. Low, Translational	1.650** (0.348)
Model 3	High, Translational vs. Low, Translational	1.626** (0.397)
Model 3	High, Translational vs. Medium, Translational	0.985 (0.184)
Model 3	High, Standard vs. Medium, Standard	1.426 (0.365)
	Multiple (disciplinary area) × Approach	
Model 4	Multiple, Translational vs. Oncology, Translational	0.919 (0.166)

Significance at 0.10, 0.05 and 0.01 levels is indicated by \*, \*\*, and \*\*\* respectively.

there is no penalty associated with explorations outside *Disciplinary Areas*. *Table 1* showed that the nature of studies with broad *Scope* differs between the translational and the “standard” approaches, in the former case representing a form of RT-driven research, and in the latter exploration of issues spanning several disease areas and clinical practices. The model indicates that, in the translational approach, both studies focused on oncology and those covering multiple areas are expected to receive almost 80% fewer citations than a standard study specialized in oncology. These results provide support for *Hypothesis 2*, of a negative effect of broad subject scope in the standard approach compared to Translational Medicine which appears to be able to accommodate broad scope subjects in its research agenda. It emerges that translational scientists can move out the core domain of oncology towards multiple fields without compromising their expected citation impact. Absence

**Table 4**  
Regression models.

	Model 1 IRR (std. err.)	Model 2 IRR (std. err.)	Model 3 IRR (std. err.)	Model 4 IRR (std. err.)
Approach		0.239*** (0.088)		
Baseline: Standard				
Diversity				
Baseline: Low				
Medium		0.897 (0.139)		0.916 (0.142)
High		1.002 (0.174)		0.975 (0.167)
Disciplinary Area				
Baseline: Oncology				
Disease Field		0.628** (0.135)	0.632** (0.138)	0.664* (0.146)
RT-Fields		0.931 (0.308)	0.942 (0.303)	1.040 (0.362)
Practice Group		2.133*** (0.532)	2.157*** (0.528)	2.019*** (0.508)
Multiple		0.679*** (0.095)	0.715** (0.101)	
Multiple × Approach				
Baseline: Oncology, Standard				
Multiple, Standard				0.449*** (0.084)
Oncology, Translational				0.219*** (0.080)
Multiple, Translational				0.201*** (0.078)
Diversity × Approach				
Baseline: Low, Standard				
Medium, Standard			0.603** (0.129)	
High, Standard			0.859 (0.197)	
Low, Translational			0.127*** (0.055)	
Medium, Translational			0.210*** (0.083)	
High, Translational			0.207*** (0.078)	
Orientation	1.084 (0.162)	1.313* (0.188)	1.316* (0.183)	1.285* (0.180)
Base: Clinical				
Cumulative	1.092 (0.160)	1.164 (0.152)	1.190 (0.149)	1.150 (0.149)
Age	1.026 (0.044)	1.028 (0.041)	1.038 (0.039)	1.028 (0.040)
Team-Size				
Baseline: Small				
Medium	0.999 (0.151)	1.039 (0.157)	1.035 (0.156)	1.057 (0.158)
Large	2.730*** (0.510)	2.283*** (0.382)	2.314*** (0.381)	2.298*** (0.378)
Years from publication	(Exposure)	(Exposure)	(Exposure)	(Exposure)
Lab Leader (dummies)	YES	YES	YES	YES
InAlpha	0.098 (0.080)	0.020 (0.075)	−0.007 (0.074)	−0.006 (0.076)
Alpha	1.103 (0.088)	1.020 (0.077)	0.993 (0.074)	1.006 (0.076)
Log pseudolikelihood	−1447.11	−1432.07	−1426.67	−1429.24
Wald chi2	130.75 (12)	176.04 (18)	194.30 (20)	193.77 (19)

Significance at 0.10, 0.05 and 0.01 levels is indicated by \*, \*\*, and \*\*\* respectively.

of a penalizing effect is associated also with investigations in RT-fields – undertaken only in translational research – while another model (not presented here) indicates that the payoff from investigations in the Disease-Fields is negative for both approaches, but significantly less rewarding for the standard (–60%) than the translational approach (–40%). Overall these results seem to suggest a better ability of Translational Medicine to broaden the scope of investigation.

Finally, we observe that all the models consistently show a penalty related to the citation rate associated with Translational Medicine. This penalty is attached to the translational approach independent of the cognitive configuration of the focal paper in terms of cognitive complementarities or scope. The lower impact of translational studies may be a consequence of the divergence of its selection criteria from those of standard research, combined with its comparatively smaller scientific constituency. Indeed, a field in its early stages of evolution is not likely to have developed a broad scientific community and so seeks recognition from other related communities.

## 5. Discussion and conclusion

The emergence of Translational Medicine allows us to analyze an aspect of the relationship between science and technology that has received limited interest in Innovation Studies. The history of the life sciences in the second half of the 20th century offers an example of the incorporation of fundamental scientific advances into a set of new research technologies. For this reason, it provides a window onto the reverse effect of how these research technologies affect the production and reception of scientific research. Our study provides evidence of the tight linkage between a new science, such as Translational Medicine, and a set of research technologies.

The research technologies based on advances in molecular biology have enabled the exploration of phenomena that cut across established disciplinary domains. Rather than being homogeneous, the adoption of these research technologies has spurred the formation of distinct epistemic communities with specific characterizations in terms of the object of investigation, methodological approach, and impact on subsequent developments in the field.

Research technologies are an important driver of diversity in the knowledge base of a new science, and enable broadly scoped scientific investigations. Translational Medicine extensively relies on technology-driven cognitive complementarities, differently from standard medical research that exploits these complementarities only marginally. Furthermore, we find that the criteria defining scientific advances and their importance in Translational Medicine are different from those found in “standard” medical research, as only the former relies on cognitive complementarities as a driver of scientific impact. In other words, we find that translational and “standard” medical research are distinct approaches not simply because they apply very different research technologies, but because scientific impact takes quite different cognitive forms in the two approaches. These results provide empirical evidence supporting the conceptualization of Translational Medicine as a “new science” (Bonaccorsi, 2010). However, we do not consider other features of the New Sciences, namely rate of growth and theoretical proliferation. Further studies aimed at characterizing a field as a “new science” should measure these additional dimensions.

We found also that new sciences address issues that are relevant for the development of research technologies, as shown by the high share of translational articles contributing to RT-Fields; by contrast, contributions to knowledge on research technologies is not part of the established sciences agenda, which maintains a strong focus on its main disciplinary field, in our case oncology. An important finding of our work is that broadening the subject matter to issues that span multiple disciplines detracts from the impact of established sciences but does not affect new sciences. This cognitive feature implies that the two approaches represent different regimes of knowledge production. “Standard” research seems to progress via contributions that deepen

knowledge in oncology and closely connected areas, while translational scientists appear more free to investigate a broader space of disciplinary areas. This result seems to confirm that adoption of research technologies opens the opportunity to investigate complex problems that are at the interface between different disciplines.

The high penalty associated with adoption of a translational approach, all other things being equal, is another important finding of our study. From the perspective of Evolutionary Epistemology, this indicates that the outcomes of translational studies do not conform to the criteria currently employed by Medicine to select relevant contributions. As other new sciences, Translational Medicine has emerged “inside” old sciences in the form of a smaller and institutionally more tenuous community. We suggest that the co-existence of distinct models of knowledge production within the same field of medical research may reduce the opportunities for intellectual exchange and limit the space for knowledge combinations. When selection criteria are as dramatically different as we find in this study, the much larger size of the established old science brings about a stronger overall impact and acceptance of its research. In other words, it becomes apparent that Translational Medicine is still far from achieving intellectual maturity.

The different potential causes for the weaker impact of Translational Medicine should be disentangled in further research. Whatever the answers derived, we observe a misalignment between the priorities of science policy and the positions of the most influential scientific opinion leaders, which advocates for increasing diffusion of the translational approach, and the internal rewards offered by the scientific system. So far, policy debate on Translational Research emphasizes the need to broaden the competence portfolios of scientists through appropriate education so that they can master multiple areas of the life sciences. Another issue highlighted by this debate concerns the high complexity of the ultimate goal of medical research, prevention and treatment of disease, so that even an interdisciplinary approach such as Translational Medicine might not be sufficient to tackle such a complex problem. Our study highlights another constraint on the diffusion of the translational approach, i.e. the disincentives offered to scholars by the academic community. This finding provides an additional rationale for policy support for Translational Medicine. Further research on this topic is needed to appreciate the effectiveness of these instruments and to identify the individual characteristics of scientists who decide to adopt the emerging approach. Indeed, deeper knowledge of the resource endowments and motivations of scientists embracing an emerging approach – compared to those pursuing the standard approach – would help our understanding of the patterns of diffusion of new research technologies. The literature on these issues focuses more on the consequences of than the antecedents to the adoption of research technologies.

Comparing the scientific impact of the various cognitive drivers, we see that in both approaches scientists pursue research strategies which do not fully realize the potential scientific impact from their comparative advantage. We showed that *Scope* has a neutral effect on impact in Translational Medicine and a negative effect in standard clinical research; but the two approaches have produced a very similar share of papers (about one-fifth) spanning multiple fields. Moreover, we find that the majority of translational publications presents a high level of *Diversity*, despite the fact that a medium level of *Diversity* is more rewarding and implies lower cognitive costs. In standard studies, the rewards associated with low and high *Diversity* are similar, while a medium level is penalizing. However, medium *Diversity* accounts for more papers than high *Diversity*. Overall, these results suggest that the full potential of scientific contributions associated with their particular comparative advantages may not be being realized by scientists operating in a changing field such as Medicine. There seems to be an absence of “research strategizing” in the sense that scientists in neither approach capitalize efficiently on their comparative advantages.

We showed that there are systematic penalties associated with Translational Medicine compared to the standard approach. So why



do translational and clinical studies at the descriptive level (Table 1) present similar average performance? Our regressions show that orientation towards more basic issues is an important driver of impact, and by definition, the production of the two approaches differs significantly along this dimension. The lack of significant differences among other drivers of impact suggests that an important source of variability in performance lies in the characteristics of Lab Leaders and their teams. In this study we considered some of these organizational features, compatible with the restrictions of a quantitative approach: we included controls for size of teams and for team leader. Further research could investigate these dynamics in more depth by employing of qualitative studies focused, e.g. on the mechanisms deployed by teams to effectively integrate different sources of knowledge.

The discrepancy between the descriptive statistics and the results of the econometric analysis is a strong reminder to be cautious about citations data in research evaluations. These exercises should carefully consider possible confounding factors affecting performance and use appropriate statistical tools.

Finally, we should emphasize the limited generalizability of our results. Our empirical analysis is based on the production of a small sample of Lab Leaders. The selection of cases capitalizes on the possibility to refer Lab Leaders precisely to either one or the other approach. The drawback of this methodology is the limitations it imposes on generalizability to Medicine. Large-scale studies are needed to validate our findings. The elaboration of objective indicators capable of capturing the “translational” nature of a piece of research would seem a necessary initial step in such a research program.

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## Appendix I. Procedures for selecting Laboratory-Leaders

We defined the subfield of breast cancer research searching for journal articles indexed in ISI-WoS with the words “breast cancer” or synonyms in their title or abstract, published in 2003–2007. We generated a list of the most prolific European authors; We then identified those who published at least two-thirds of their production in breast cancer research and could thus be considered “specialized”. We considered only European cases to avoid influence from the notable differences between Europe and the USA regarding the organization and funding of medical research (Owen-Smith et al., 2002). To avoid country-specific effects, we did not allow the same country to be represented in the translational and the standard group more than once. Combining publications data and other sources of documentation - such as institutional and personal websites, and affiliation to medical societies - we identified Lab Leaders, i.e. scientists who establish a stable team of collaborators endowed with technological and financial resources and lend to the group a shared vision and a coherent strategy, unifying the contributions of specialists. We excluded from the definition scientists who had co-authored a substantial share of their production with more prolific scientists, or those responsible of larger organizations, such as entire departments.

We identified Lab Leaders who represented each approach on the basis of the predominant CHI-Level of their production. Translational Lab Leaders are required to publish at least 25% of their work in Levels-3 or 4. Furthermore, the principles and organization of their work must be translational, as per publicly available documents on their research units. “Standard” Lab Leaders were identified among those with fewer than 25% of their articles in CHI-3 and 4 and indicating no engagement in translational objectives or organization of their work.

The set of translational contributions then is a blend of CHI-2 and 3 articles with a marginal presence of *clinical observations* and *basic research*. The control set concentrates 75% of its articles in CHI-2, and the remainder is split evenly between *clinical observations* and *clinical investigations*, with no *basic research*. This comparison suggests a more pronounced attitude of translational Laboratory Leaders to span different CHI-Levels, and higher intensity of analytical-oriented studies.

We identified three translational Lab Leaders, for whom we collected complete publication records from 2003 to 2007. Given the lower productivity of “standard” scientists meeting the selection criteria, we considered five cases in order to gather a comparable set of publications. We checked for homonymy and we included three publications not appearing in ISI-WoS records because of misspelt names.

We obtained 184 translational and 200 “standard” articles - a total of 384. We excluded articles with more than 50 co-authors because they can hardly be considered the result of real collaboration: translational Laboratory Leaders had 4 such articles and the other group 12. We finally obtained a valid dataset of 356 articles.

## Appendix II. Attribution of Subject-Categories to Disciplinary Areas

Disciplinary Areas
Oncology
Disease-Fields
Endocrinology & Metabolism
Gastroenterology & Hepatology
Hematology
Immunology
Obstetrics & Gynecology
Peripheral Vascular Disease
Psychology
Psychology, Multidisciplinary
Public, Environmental & Occupational Health
Respiratory System
RT-Fields
Biochemical Research Methods
Biochemistry & Molecular Biology
Biophysics
Biotechnology & Applied-Microbiology
Cell & Tissue Engineering
Cell Biology
Genetics & Heredity
Medical Laboratory Technology
Microbiology
Reproductive Biology
Practice-Group
Health Care Sciences & Services
Medicine, General & Internal
Medicine, Research & Experimental
Pathology
Pharmacology & Pharmacy
Physiology
Radiology, Nuclear Medicine & Medical Imaging
Rehabilitation
Surgery
Transplantation

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