Commentary

Strategies for Translational Research in the United Kingdom

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In the United Kingdom, many foundations and institutions and the government have made substantial investments in translational research. We examine the structures that surround this support and consider some of the results of this prodigious push toward enhancing translational research pursuits and thus improved clinical medicine.

The past few years have seen a greatly increased investment in funding for translational research, both in terms of infrastructure and a degree of reorientation of grant awards. Here, we describe key aspects of the UK translational research strategy in the context of recent international developments and, where relevant, draw on specific examples from the Biomedical Research Centre at Guy’s and St. Thomas’ Hospitals and King’s College London, one of the five comprehensive translational institutes funded in 2007 by the UK National Institute for Health Research.

STRUCTURE AND INFRASTRUCTURE

United Kingdom. In the United Kingdom, translational research is sponsored by a number of charitable and governmental organizations. Charitable foundations have made a substantial contribution to translational research, and one example of this is the Wellcome Trust Millennial grants for clinical research facilities (1). The main governmental sponsors of research into human health and disease are the Medical Research Council (MRC) and the National Institute of Health Research (NIHR). Geographically, the MRC covers medical research across the United Kingdom, while NIHR covers research specifically in England and Wales and then works with counterparts in the devolved administrations of Scotland and Northern Ireland. The MRC and NIHR are coordinated by the Office for Strategic Coordination of Health Research. This structure recognizes the differences in the organization and specific aims of the two bodies. The MRC is part of the UK research councils and is focused on high-quality research into underlying disease biology; NIHR is embedded in the UK National Health Service (NHS) and supports more patient-focused research within the NHS, specifically to improve patient care (Fig. 1). To this end, NIHR has funded new infrastructure to support translational research, such as the comprehensive and specialist Biomedical Research Centres (BRCs) and the Biomedical Research Units (BRUs). Five comprehensive BRCs were established in 2007 to cover a broad spectrum of major translational research topics; in contrast, the seven specialist BRCs each revolve around one specific area of research (Table 1). Both types of centers have created a tangible focus on translational research in the United Kingdom and an efficient interface through which scientists working on more basic biological mechanisms can interact and contribute to translational medicine. Providing infrastructure for translational research is a key aim of NIHR, and further details on the specialist

Fig. 1. The research and development path, UK style. An overview of a typical health research pipeline (from basic research to clinical delivery) is depicted by showing the kinds of questions asked at each stage of the process. Translational research is not a linear process, and questions flow in both directions along the pipeline; results from both basic and clinical research can raise translational questions. The ultimate goal of the process is to deliver better care to patients. The bodies that fund research at each stage and the organizations to which they report are shown on the right. The BBSRC (Biotechnology and Biological Sciences Research Council) and MRC report to the RCUK (Research Councils UK), which includes all governmental research councils in the United Kingdom for both the sciences and humanities and reports to the UK governmental Department for Business, Innovation and Skills. NIHR and the MRC report to the OSCHR (Office for Strategic Coordination of Health Research). NIHR and NHS providers report to the NHS (National Health Service).
BRCs, BRUs, and other NIHR-commissioned infrastructures can be found here (2).

Each BRC is located within a NHS hospital, which allows access to patient populations and is held in collaboration with a university partner. UK health care is predominantly provided by one national system. Therefore, it has the distinctive potential to provide a strong framework for collaboration between different hospitals and research groups. Further research integration is provided by clinical research networks that allow all health care providers and their patients to participate in relevant clinical trials at no cost to patients. There are several clinical research networks themed around different disease areas. As an example of the impact these networks have had, the network for cancer has doubled the number of cancer patients involved in clinical trials in two years (3).

United States. In the United States, governmental funding for basic and translational biomedical research is channeled through the National Institutes of Health (NIH) (4). On a time scale that is roughly parallel to that of the United Kingdom, NIH has commissioned Clinical and Translational Science Awards (CTSA) to create a specific focus on translational research in a manner similar to the United Kingdom’s comprehensive BRCs (5, 6). The NIH granted $675 million (~£430 million) over 5 years to its first 12 CTSA (7), and a similar amount (£450 million, $710 million) was used to establish the five comprehensive and seven specialist BRCs by NIHR (8). In the United Kingdom, the separation of NIHR and the MRC and their supervision by the Office for Strategic Coordination of Health Research is designed to protect current basic science funding while phasing additional funding toward translational science (9). A reoccurring theme in any analysis of translational research is that all stakeholders need to maintain constant communication at all stages in the scientific research pipeline so as to ensure maximum efficiency. In the United States, NIH must balance both basic sciences and translational research, which is likely to continue to receive prominence, but the funding-level integration of NIH has the potential to allow basic scientists to engage more easily with the translational research agenda (10).

Given the recent establishment of NIHR and the Office of Strategic Health Care Research as institutions, it is difficult at this time point to determine whether the demarcation of this system or the integration of NIH is the better model to encourage translational research. Indeed, it may be that each model is the better for the country in which it is situated. The United States has not, historically, had a universal health care system in which a body such as NIHR could reside, and even now it is difficult to see how an NIHR-like institution could function within the less-integrated system of U.S. health care.

An enhancing environment. Increased funding for translational research need not be a zero-sum game. Instead, the increased emphasis on translational research on both sides of the Atlantic can increase the resources for and prominence of all biomedical research. This growth can benefit the entire research community by attracting more re-
sources for biological research from government and industry and by providing a pathway for both clinical and basic researchers to collaborate and access funding streams that are dependent on this interaction. Furthermore, by investing in cutting-edge analytical hardware embedded in the translational research environment, basic scientists are able to address key biological questions of human pathophysiology in vivo with a substantially enhanced level of resolution.

The European Union (E.U.), of which the United Kingdom is a member, specifically emphasizes translational research as a key area of its health budget for the seventh framework program, the main method by which the E.U. will fund research from 2007 to 2013. The total health budget for framework 7 is €6.1 billion over 7 years (11).

**UK BIOMEDICAL RESEARCH CENTRES**

Within the framework of the United Kingdom’s NIHR, a good portion of the frontline translational research occurs within the BRCs, which provide a coordinating center for patient-oriented research projects (12). Although each center falls under a NHS trust in partnership with a university, translational research tends to be project-based and not confined to one specific academic department. The research centers provide a means of coordinating and producing a coherent research strategy that is patient-focused (Fig. 2). Researchers work with specific diseases and health issues in mind and are in direct contact with resources needed to carry that research forward, creating a more streamlined pipeline from research into the clinic (13). The comprehensive BRC at Guy’s and St. Thomas’ fulfills a range of requirements, from the need to coordinate high-level strategy to the provision of meeting rooms to physically bringing together team members split across multiple sites within a university and one or more hospitals. The centers also provide access to necessary tools specific to the translational research process, such as guidance on ethics, clinical trials, patient recruitment into studies, and research governance processes.

In many cases, the comprehensive BRCs have formed a key platform for further hospital-university integration, and their hosts have gone on to develop as Academic Health Science Centres (AHSCs). AHSCs were established by the UK Department of Health in 2009 to integrate medical practice with research and teaching and thus implement research results more quickly in the hospital setting. Like the BRCs, the AHSCs are formed of NHS hospitals and university partners. However, they are larger than the comprehensive BRCs, incorporating a much wider range of staff within the hospital and university—not just those focused on research—and sometimes including more than one hospital. The AHSCs have a tripartite mission of integrating research, teaching, and clinical care in order to drive synergy between these areas, with the ultimate goal of improving the health of the local and national population. Therefore, although the BRC catalyzes translational research at the heart of an AHSC, the findings of this research can be spread outward and scaled up into large patient populations with an eventual positive impact on public health. The new UK coalition government elected in May 2010 voiced its support for the continuing roles of the BRCs and AHSCs in the recent white paper “Equity and Excellence: Liberating the NHS” (14). (For institutions with BRC and AHSC status, see Table 1.)

At Guy’s and St. Thomas’ Hospitals, the comprehensive BRC facilitates coordination of groups across two hospitals plus other sites that belong to the hospitals’ university partner, King’s College London. The comprehensive BRC is also well placed to collaborate with the mental health specialist BRC at South London and Maudsley NHS Foundation Trust and King’s College Hospital, and these four bodies are part of King’s Health Partners AHSC, which directly covers a population of 2 million people (15).

**CAPACITY BUILDING**

Given the relatively recent focus on translation, it is not surprising that no cadre of specifically trained individuals exists. The extent to which translational research training should differ from the core disciplines of basic science and clinical research still needs to be defined.

Any career route requires that there be facilities for training and career progression. Both the university and NHS systems should feed into training translational researchers, especially in terms of providing early education, such as for undergraduate science and medical degrees. However, much biomedical research has been until now either an academic pursuit that follows a traditional sci-

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**Table 1. BRCs and AHSCs in England and Wales.**

<table>
<thead>
<tr>
<th>Comprehensive BRCs (NHS* trust/academic partner)</th>
<th>AHSCs</th>
<th>Specialist BRCs [NHS trust/academic partner (specialty)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cambridge University Hospitals NHS Foundation Trust/University of Cambridge</td>
<td>• Cambridge University Health partners</td>
<td>• Great Ormond Street Hospital for Children NHS Trust/UCL Institute of Child Health (pediatric/child health)</td>
</tr>
<tr>
<td>• Guy’s and St. Thomas’ NHS Foundation Trust/King’s College London</td>
<td>• Imperial AHSC</td>
<td>• Central Manchester and Manchester Children’s University Hospitals NHS Trust/University of Manchester (genetics and developmental medicine)</td>
</tr>
<tr>
<td>• Imperial College Healthcare NHS Trust/Imperial College London</td>
<td>• King’s Health Partners</td>
<td>• Moorfields Eye Hospital NHS Foundation Trust/UCL Institute of Ophthalmology (ophthalmology)</td>
</tr>
<tr>
<td>• Oxford Radcliffe Hospitals NHS Trust/University of Oxford</td>
<td>• Manchester AHSC</td>
<td>• Newcastle upon Tyne Hospitals NHS Trust/Newcastle University (aging)</td>
</tr>
<tr>
<td>• University College London Hospitals NHS Foundation Trust/University College London</td>
<td>• UCL ‡ Partners</td>
<td>• Royal Liverpool and Broadgreen University Hospitals NHS Trust/University of Liverpool (microbial diseases)</td>
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<td></td>
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<td>• Royal Marsden NHS Foundation Trust/Institute of Cancer Research (cancer)</td>
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<td></td>
<td></td>
<td>• South London and Maudsley NHS Trust/KCL † Institute of Psychiatry (mental health)</td>
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</tbody>
</table>

*NHS, National Health Service; † UCL, University College London; ‡ KCL, King’s College London

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11. £6.1 billion over 7 years.
12. Each center falls under a NHS trust in partnership with a university.
13. Patient-focused.
14. “Equity and Excellence: Liberating the NHS.”
15. Covers a population of 2 million people.
enence career path or a pursuit of clinicians who have not always been properly supported in terms of research training, funding, recognition, and career development (16, 17). One of the key aims of NIHR is to change this situation, producing recognizable and respected organizations that will attract researchers from appropriate disciplines.

Because translational research is highly interdisciplinary, training protocols must be sensitive to the needs of different kinds of researchers. A key advantage of a project- and center-based system over the academic department system is that a researcher can, to an extent, draw on members of his or her own team to fill in gaps in their training in an informal yet practical way. For clinically trained researchers, this may mean learning the theory behind and the practical execution of standard laboratory-based techniques, such as cell culture. In contrast, researchers from the basic sciences may need to expand their medical vocabulary, better understand how a patient is diagnosed with the disease or condition on which they are working, and appreciate the limitations of clinical diagnoses and current therapies. This big-picture approach is often lost in basic-science training, which focuses on a deep understanding of specific biological mechanisms, and is more quickly learned from clinicians—who better know the practicalities and controversies of their disease specialism—than from the published literature. Formal training schemes are becoming more common and tend to be based around Ph.D. schemes and master's degree courses (17).

The comprehensive BRC at Guy's and St. Thomas' has established a training program in translational research that starts at the level of undergraduate medicine and has entry points all the way through to senior clinical and nonclinical researchers (13). These types of comprehensive training programs will be necessary to ensure the sustainability and scalability of the translational research endeavor. Although many training schemes have been established recently, one aspect of the Guy's training program that has been particularly successful is its clinical training fellowships, in which clinicians interested in translational research are funded to work in a research laboratory for 1 year. During this time, clinicians gain practical experimental skills, produce preliminary data, and construct grant applications to help them continue their research after the fellowship has ended. This scheme currently has a success rate of more than 80% in securing extramural funding to continue translational research projects for a further 3 years.

**PUBLIC AND PATIENT ENGAGEMENT**

Patient groups are growing in strength in terms of their ability to influence disease-related research funding and clinical trial design and recruitment. In the United Kingdom, there is an increasing realization among researchers of the need to engage the general public in an open yet straightforward way, and efforts are being made toward this goal [for example, see the National Health Service Choices Web site (18)]. Health research both affects and interests the public. However, in reporting information a balance must be found between conveying the main scientific take-home message and the caveats of that message, and between arousing interest in the results and stressing the length and complexity of the research process. Only by making clear the implications of scientific achievements and the challenges of the translational process can we avoid the hype surrounding a new drug target (that turns to disappointment when the drug itself fails to immediately materialize) or the undermining of key results by perceived controversies.

A health science–aware population will be able to make informed decisions about health and medical issues. In today's society, treatment options work on a model of informed consent, in which a patient makes his or her own decisions about whether he or she would like to be treated on the basis of advice from a medical professional. Obtaining informed consent from patients can only be made easier by a better general engagement between medical scientists and the public.

Furthermore, to be able to perform translational research it is important to engage productively with patient populations. The BRCs and other translational research centers provide necessary support in coordinating and disseminating specific information that is both relevant and sensitive to different patient groups. Similar to all translational research, patient engagement is a multidirectional process, and mechanisms also exist for patients to provide feedback to researchers. At Guy's hospital, patients sit on various review boards, such as a renal project board, which oversees all kidney-related research projects at the hospital and comprises surgeons, physicians, researchers, nurses, and patients. This board has overseen an increase in the number of renal patient–based translational studies from single figures to more than 55 in less than 3 years. Groups that consist of a mixture of researchers and patient advocates are well placed to help drive and focus research and to present a coherent case for the research in the public sphere (19).

**TIES TO INDUSTRY**

In 2009, the UK Office of Life Sciences (OLS) examined ways of better connecting industry with universities and the NHS to encourage industrial investment in UK translational research. In consultation with representatives from the pharmaceutical industry, the OLS published the Life Sciences Blueprint (20, 21). This report details ways of attracting to the United Kingdom the companies that wish to license university-developed research or partner with universities on translational research projects. The blueprint also outlines ways of developing essential resources for industry-based translational research, such as an appropriately skilled work force. One aim proposed by this report was the generation of a Life Sciences Super Cluster, overseen by the Office for Strategic Coordination of Health Research, which will connect industry, academia, and the NHS. The cluster will consist of several Therapeutic Capability Clusters (22), each of which will be formed from a few academic and NHS centers and specialize in one therapeutic area deemed a priority in the United Kingdom, with particular focus on early clinical trials. These clusters form a single point of contact for and are expected to work in close collaboration with companies working on or wanting to invest in the research area that is the focus of the cluster. The first clusters are currently being established in inflammatory respiratory diseases and joint and related inflammatory diseases (22). Another UK cluster in this arena that overlaps with the comprehensive BRCs is the Global Medical Excellence Cluster (23), which constitutes a broad interface between the academic community and the commercial sector.

Collaborations between academic and NHS researchers and industry have many potential benefits, including a widened skill set, shared infrastructure, and income generation. Because translational research is interdisciplinary, the skill base needed for this research arena is wider than can be achieved sufficiently by any one group of people. The
experts needed for laboratory research differ from those needed for running a clinical trial, for example, and partnerships between research institutions and industry can allow the traditional strengths of the two to be pooled for use in one project. At the BRC at Guy’s and St. Thomas’, a partnership with the clinical trials specialist Quintiles allows expertise required for early-phase and first-in-human trials to be shared, providing mutual benefit.

Another potential benefit to industrial collaboration is income generation. The production and protection of intellectual property (IP) in health and biomedical research has not been without its issues (24). Universities must maintain a fine balance between pursuing appropriate IP without stifling collaboration within their own institution and across the academic field. By establishing standardized channels of constant and open communication between all stakeholders—academic researchers, industry, and patients and the NHS as potential consumers—throughout the research process, the OLS and NIHR infrastructure should allow all parties to work together toward the ultimate goal of producing a product that generates revenue because it substantially improves human health.

PROGRESS AND POTENTIAL

In a relatively short time frame, much has been achieved in terms of establishing a cutting-edge UK translational research infrastructure. The impact of this movement is reflected in the number of NIHR clinical studies in the United Kingdom, which has increased from 290 in 2005 to 850 in 2009–2010; this growth in the number of clinical studies has been accompanied by an increase in patient recruitment from ~100,000 to >450,000 over the same time period. The global financial climate will provide a challenging environment in which to deliver on the promise of translation, but the relevant platforms have been put into place. As well as the vital role of improving the health of our patients, translational research has great potential for wealth generation. Further investment in this arena to drive gross domestic product growth is now more critical than ever.

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