Found in Translation: Training the Next Generation of Translational Neuroscientists

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Integrated, multidisciplinary programs for training physicians and scientists in translational science have become essential in efforts to meet the demand for more effective translation of basic science discoveries into new clinical applications.

Neuroscience and its workforce are rapidly evolving and widening in scope. The WHO estimates that neuropsychiatric disorders in aggregate account for almost 20% of disability-adjusted life years, making it the highest source of health care burden nationally (US Burden of Disease Collaborators, 2013). With the aging population, and the increased survivorship due to therapeutic successes in many areas of medicine, there is much demand for rapid translation of basic science discoveries into clinical application for pharmacologic therapies, diagnostics, biologics, and device development. However, there are several challenges we face in order to sustain and grow our pipeline of new scientists and physicians: sustaining them through the early years of training, providing career choices and stability, obtaining research funding, and enabling their discoveries to more effectively advance clinical care. We are at a critical point where we are poised to accelerate translation of knowledge from the bench to the beside and vice versa, yet we lack standardized systems for aligning experimental animal outcomes with those in the human, and replicability is an issue in both domains. Additionally, while the need is growing, the next generation of the translational workforce is facing funding cuts and lengthy training, both of which may serve to redirect them to other career choices. Finally, translational research can involve handoffs, and team science, which has the unintended effect of decreasing opportunities for first or last authorship and often lengthens time to publication, resulting in concerns over delaying the promotion process and career advancement.

Facilitating the Transition from Preclinical Data to Translational Research

There is an urgent need to move to greater harmonization of study design between experimental models and human clinical trials. Ideally, translation of a therapy, biomarker, or device is accelerated if there is good alignment between the experimental model and a human clinical outcome. Advancements in proteomic, genomic, and metabolomic assays now permit parallel studies in animal and human biospecimens. The last two decades of research on cellular and molecular signaling involved in disease pathogenesis are revealing new targets for modification in disease models. In addition, clinical imaging techniques are now available for small and large animals, and use similar protocols to those in human. Despite the convergence of tools and methodology, both the training for the basic science and the clinical studies require many years of expertise and often afford little opportunity for cross-training. There remains a relative isolation of the training processes that does not encourage appreciation of items like experimental design methodology, pharmacokinetics/pharmacodynamics, and statistical approaches that could enhance translation. As the clinical neurosciences become more quantitative and are now routinely including assays that in the past were limited only to the experimentalists, there is much to share from bed to bench side. Another relative weakness is the lack of organized information from the rapidly evolving arena of clinical discovery back to the bench side researchers. One concern is that ongoing preclinical work may be based on "out-of-date" information about the clinical condition, and every effort must be made to keep the information flow current.

Other events have underscored the importance of training scientists in rigorous study design as a basis for accelerating translational research. Over the past few years concerns over failures in the reproducibility of preclinical studies that form the basis for drug discovery and development, particularly those conducted in animal models, have led to a call for greater transparency and validation of how data are collected in these studies (Landis et al., 2012). This topic is addressed in more detail in a Perspective in this issue (Steward and Balice-Gordon, 2014). Pharmaceutical and biotech companies have become increasingly hesitant to base strategies for drug discovery on findings published in the scientific literature. Because of inadequacies in reporting that fail to include randomization, blinding, sample size, and details on data analysis, studies in manuscripts and grant applications yield insufficient data to advance work toward clinical applications and trials. There are multiple elements that have converged to create this problem: limited journal space for data and methods, poor data handling and statistical analysis, and little incentive for reporting negative data. However, training has a long-term role in the prescription for improving the process. Training that emphasizes rigorous experimental design, transparency, appropriate statistical analyses, as well as attentive mentorship has the potential to improve many aspects of data handling and study design in biomedical research. Professional societies have a role to play by conveying the importance of these issues to their members, maintaining standards for data reporting in their journals, and providing educational opportunities that highlight these issues.

Training Scientists for Translational Research

The challenges faced by newly minted PhDs and postdoctoral fellows have led many to rethink the conventional academic path as the only measure of success. Even in as dynamic a field as neuroscience, with its remarkable advances and the momentum inspired by the new Brain Initiative, only a subset of students who earn a doctorate will obtain faculty positions that enable them to secure sufficient, sustained grant funding to support an independent research laboratory. The consequences of reductions in support have been dramatic: the duration of postdoctoral training has escalated, trainees seek careers outside of science, and those who become independent investigators do so much later, often waiting until their early 40s to obtain their first R01 grant. In addition, the decline in the number of funded applications, the increased competition and focus on grant writing rather than experiments, have led to concerns about the sustainability of a system predicated on continued growth (Alberts et al., 2014). In this difficult environment, many young investigators have begun to explore diverse options and think more broadly about their career goals.

To better align the pipeline to future workforce needs and help students identify a sustainable niche, a number of graduate programs, including several in neuroscience, have already begun to offer different tracks and specialized training plans that prepare their students not only for research careers in academia, but also for careers in teaching, in biotech and pharma, in clinical trials, and in science policy. The NIH Common Fund's Broadening Experience in Scientific Training (BEST) award was developed in response to a growing need for enhanced training for graduate students and postdoctoral fellows to prepare them for careers in the biomedical research workforce outside of conventional academic research. While continuing to produce trainees with a core knowledge of their discipline, as well as critical thinking and problem solving skills, such programs provide additional exposure and hands on experience relevant to one or more of these career paths. Translational science also lends itself well to this kind of "cross-training" experience, offering a means to gain fluency in the principles of clinical medicine and specialized expertise in linking basic science observations to the complexities of human disease. Given an unmet need for investigators rigorously trained to move preclinical studies towards developing new treatments, translational science provides another career option for any student or fellow who is passionate about moving scientific knowledge from bench to bedside. Although basic research—including work on model organisms, complex biological systems, and emerging technologies—remains the major driving force for discovery, translational research has the potential to transform scientific knowledge into treatments for diseases of the brain and other organs.

A recent addition to the translational training mix has been the development of comprehensive programs to engage and train bench scientists specifically for careers in translational research. For example, in 2005 the Howard Hughes Medical Institute (HHMI) created the "Med-Into-Grad" initiative with the overarching goal of creating innovative programs to expose graduate students to clinical medicine in a variety of ways and to promote their development into skilled translational researchers. Initiated at 13 institutions in 2005, these HHMI-sponsored programs train basic science and engineering students in translational science by increasing their exposure to clinical medicine, creating curricula that integrate basic science and clinical medicine, providing opportunities for interdisciplinary team science, and facilitating clinical comentorship. Initial evaluations appear promising, with students having greater success and being more confident of their approach to clinical problems (Knowlton et al., 2013).

Opportunities for postgraduate training in translational science exist as well, through training initiatives and grant award mechanisms coordinated by the newly established National Center for Advancing Translational Sciences (NCATS). In 2006, the first NIH Clinical Trials Research Awards were launched and since then they have been established at many major institutions. These centers offer training and core specifically for the late preclinical and early phase 1 and 2 trials. In addition, many CTSA centers offer a wide variety of training experiences, bioinformatics, and clinical trial support. With opportunities for MDs, PhDs, and other health professionals from postdoc to faculty, as well as graduate and medical students, these flexible programs aim to prepare researchers for careers that span clinical and translational sciences with an emphasis on interdisciplinary team science (Begg et al., 2014). Professional societies are also playing a greater role in providing educational programs that are beginning to provide such lifelong learning and education to established investigators: maintaining updated knowledge will be key for sustaining successful translational programs.

In the current landscape, young scientists also must be prepared to work across traditional academic boundaries that traverse biological, translational, clinical, computational, statistical, and even engineering and materials sciences to advance complex problems. Communication across disciplinary boundaries and the ability to contribute to research teams and collaborations is an essential element in most kinds of biomedical research. Neuroscience has always attracted scientists from new fields at all levels, whether it be for very basic or more applied studies. One implication of this multidisciplinary approach to clinically relevant problems is the need to engage and reshape researchers trained in other fields—physics, engineering, informatics, and materials science, to name a few—for work on innovative translational projects. Inclusion of these newer arrivals to the field in the kinds of programs outlined above could provide an effective means to convey the language and knowledge base needed to frame questions in translational neuroscience.

The Lengthy Process of Becoming a Physician/Scientist

Clinical training through medical school, residency, and clinical subspecialty