Translational Neuroscience:
Applications in Psychiatry, Neurology, and Neurodevelopmental Disorders
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Applications in Psychiatry, Neurology, and Neurodevelopmental Disorders

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Frontmatter
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Translational medicine has emerged as a dominant theme within the context of the biomedical sciences. It has been somewhat difficult to define translational medicine as a formal discipline because, at the present time, there are no commonly accepted techniques or procedures that specifically delineate the methodological approaches or the conceptual framework within which the discipline is to evolve. In its most elemental form, translational medicine represents an effort to bridge the bidirectional gap between basic preclinical research and clinical studies in order to expedite the development of safe and effective therapeutics – the frequently articulated “bench to bedside” perspective. In a broader sense, translational medicine incorporates areas such as biomarker development, pharmacogenomics, clinical pharmacology, and clinical trial methodology to name just a few disciplines that have either embraced, or offer potential applications that can be applied to, translational research. Although the term translational medicine is relatively recent, the effort to bridge the divide between basic and clinical research is not new, having a clear precedent in the Congressional authorization to establish the National Institutes of Health Clinical Center in 1944. A substantial impetus for the recent emphasis to form a translational science initiative was based on the current paucity of new drugs, despite a considerable explosion of new technologies, insights into the molecular biology of new targets and mechanisms, and the discovery of new genetic pathways involved in various diseases. This lack of new drugs is all the more striking when one considers that research and development expenditures within the pharmaceutical industry have increased substantially over the past several years without a concomitant increase in the approval of new chemical entities and with many compounds failing in the later stages of development. No single factor is responsible for this outcome nor does a single solution or prescription address the many issues that are involved in the lengthy, exceedingly difficult process of drug discovery and development.

Multiple initiatives within the Federal Government that were launched by the creation of the “NIH Roadmap” in 2003, as well as those within academic research centers and the pharmaceutical industry, have emphasized the concept of translational medicine in an effort to address these many issues. These efforts have spawned the creation of approximately 60 Clinical and Translational Science Centers and the formation of the National Center for Advancing Translational Sciences. These efforts have prompted a nearly constant reexamination of drug discovery and development processes. It is too early to assess the impact of these and other initiatives because the drug discovery and development process is exceptionally complex, takes several years, and has numerous regulatory steps that are immutable in terms of timing and duration (e.g., toxicology studies). The transformational potential of these many efforts remains to be determined but, without question, the many concepts surrounding translational medicine have generated considerable activity and an appropriate as well as continuing evaluation of how to more effectively translate fundamental discoveries in basic science into clinical application. In these efforts to establish and apply translational research, it will be crucial not to neglect the need for continued support of basic research. Those activities, being the wellspring of new directions, provide essential insight into pathophysiological mechanisms and are therefore fundamental in translating basic research findings into new therapeutic benefits.

The dearth of novel therapeutics that has so frequently been raised as a critical issue is particularly true in the neurosciences where many of the current drugs used to treat neuropsychiatric and neurological disorders are derivatives of those discovered initially in the 1950s. It has been stated often that animal models of these disorders are poorly predictive of clinical
efficacy, that psychiatric disorders in particular have overlapping phenotypes and show considerable comorbidity, making diagnosis and treatment difficult, and that there are no reliable or distinct biomarkers available. Furthermore, our understanding of the pathophysiology of both psychiatric and neurological disorders remains limited at the present time, thereby thwarting the development of more effective therapeutics. Although all of these factors are more or less true, it is also evident that basic and clinical neuroscience has made considerable progress in recent years in identifying new biological targets, molecular pathways, and potential points of therapeutic intervention that offer promising avenues and hope for patients suffering from these disorders, many of which are at this point intractable. Recently, it has also been recognized that some disorders have not been fully characterized from a phenotypic perspective. For example, treatments for schizophrenia need to address the currently neglected cognitive impairments and negative symptoms in addition to the positive symptoms, which are targeted by existing antipsychotics. As such, an effort to capture these exciting advances and couple them to developments emerging in translational and experimental medicine in a comprehensive text is timely and essential to facilitate progress in neuroscience and in the delivery of new medications to patients.

Translational Neuroscience: Applications in Psychiatry, Neurology, and Neurodevelopmental Disorders was conceived to provide a comprehensive disorder-focused perspective of this evolving discipline for individuals in academia, government, and industry. The text is divided into three major sections, focused separately on (i) psychiatric disorders such as anxiety, depression, and schizophrenia; (ii) neurological disorders such as Alzheimer’s disease, pain, and Parkinson’s disease; and (iii) neurodevelopmental disorders such as autism and fragile X syndrome. The authors of each chapter are experts in their field and represent a blend of individuals from academia and the pharmaceutical industry. It is our hope that the chapters that follow not only summarize the current status of research and clinical science in the respective therapeutic areas but also open new perspectives and spur translational initiatives in each of these critical areas of unmet medical need that will help to advance the scientific framework and approaches to translational neuroscience.

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