OBAMA-BIDEN TRANSITION PROJECT

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UCP United Cerebral Palsy™
Life without limits for people with disabilities™

Altering the Course of Life and Improving Quality of Life: The Translational Research Program To Revolutionize the Care of Cerebral Palsy

Bringing science from the bench to the bedside

Supporting clinical research for innovative therapies and technologies that greatly improve outcomes and impact the quality of life for individuals with disabilities is of paramount importance to any health-related organization. With the ever-growing number of new scientific findings, organizations are looking for ways to speed up therapeutic development and make these new therapies available to those in need. This paper's objective is to introduce you to a research program model that would accelerate the movement of promising advancements out of the laboratory and into clinical trials producing powerful new therapies that could potentially revolutionize the care of cerebral palsy.

Translating Basic Science into Practical Applications - A Glance at Research Findings and Advancements

Despite several decades of research, known causes of cerebral palsy account for only a small proportion of cases. The identification of these causes led to the formulation of effective preventions and therapies. One of the best examples of this was the development of the rubella vaccine to prevent German measles, a risk factor for the development of cerebral palsy. Kernicterus was also identified as a treatable cause of cerebral palsy. As a result, phototherapy was developed to prevent it. In another well-known example, pregnant women who test Rh negative are immunized after giving birth to prevent maternal-fetal blood type incompatibility – another risk factor for the development

of cerebral palsy. Despite these early scientific successes, the rate of cerebral palsy and the extent of the disability increased during the 1960's through the 1980's (the only time period such data is available). However, progress continues to be made in identifying other risk factors for cerebral palsy. These risk factors include perinatal asphyxia, congenital abnormalities, stroke, intracranial hemorrhage, premature birth, and infection.

Another area of vast research is motor dysfunction. A prominent component of motor dysfunction and a significant cause of disability for individuals with cerebral palsy is spasticity. Traditional medical therapy for the relief of spasticity has included both oral and intrathecal administration (i.e., direct infusion into the spinal canal) of antispasmotics (baclofen being the most commonly prescribed drug for this therapy). Recently, a new class of antispasmotics has become available for the treatment of spasticity. Botulinum toxin A has broad application for individuals with cerebral palsy. Early studies indicate it is much safer and more efficacious than the traditionally prescribed antispasmotics. Other therapies include innovative surgical procedures targeted at relieving spasticity - selective dorsal rhizotomy (SDR) and stereotactic encephalotomy. SDR is an effective surgical procedure that selectively disrupts the sensory nerves involved in the reflex arc, which contributes to spasticity. Stereotactic encephalotomy is an invasive though effective procedure that selectively cuts neural tracts at the base of the brain in order to alleviate spasticity. Other more traditional therapies, such as physical and speech therapy, are still employed and are important components in the treatment of cerebral palsy.

Research has led to a revision of the definition and classification of cerebral palsy and has resulted in greater precision in determining the most effective treatment modalities. This revision was prompted by changes in delivery of care to children with disabilities, increased availability of high-quality brain imaging, and increased understanding of potential risk factors for cerebral palsy.

Diagnostic methods have also improved as a result of research. Breakthroughs in clinical and laboratory techniques have led to improved methods for gathering

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reliable evidence of developmental brain damage and better evaluation of the neurologic and muscular impairments that result from it. Such advancements include improved methods in medical imaging used to evaluate structural changes as well as changes in brain physiology in utero and in the postnatal period; more effective methods of screening for jaundice and metabolic disturbances such as thyroid function; and improved methods for measuring the functional performance of the infant, child, and adult with motor dysfunction.

Despite these significant advancements, more therapies must be investigated in order to continue to improve the quality of life of individuals with cerebral palsy.

Basic Research Outpaces Clinical Research

Obstacles on the Highway to Clinical Research

Translational research *applies ideas, insights, and discoveries generated through basic scientific inquiry to the treatment or prevention of human disease – as defined by the National Institute of Neurological Disorders and Stroke*

Translational research applies ideas, insights, and discoveries generated through basic scientific inquiry to the treatment or prevention of human disease. Improvement of health and quality of life is contingent upon the translation of basic scientific discoveries into practical applications. Such discoveries start with basic scientific research (research done by scientists at the cellular and molecular level). The results of basic scientific research are then translated into effective therapies that are subsequently tested at the clinical trial level.

Translational research is a powerful process that drives basic scientific and clinical research

The lab-to-clinic approach to translational research is fundamental to scientific investigation. Basic scientists provide new information that is translated into treatments that clinical researchers test in patients. During testing, the clinical researcher makes observations about the impact the tested treatment has on the disease. These observations can lead to new questions begging basic scientific research, or to licensing and marketing for consumer use. Thus, translational research has proven to be a powerful process that drives basic scientific and clinical research.

Translational research has not kept pace with the increasing number of basic scientific discoveries

Today, there is a wealth of basic scientific research waiting to be translated into powerful therapies and technologies.

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Despite the increasing volume of basic scientific discoveries, the process of translating them into practical therapies has not kept pace.

A weak research infrastructure impedes the lab-to-clinic process and contributes to inefficiency and wasteful spending

Obstacles between basic and clinical research discourage professional interest in the translational and clinical fields

According to the National Institutes of Health (NIH), growing obstacles between clinical and basic research, along with ever increasing complexities involved in conducting clinical research, are making it more difficult to translate basic research from the lab to the clinic. NIH suggests that a weak research infrastructure is one such obstacle that contributes to inefficiency and wasteful spending. There is a lack of entities that serve to concentrate basic, translational, and clinical researchers in order to develop professional interactions that foster the exchange of information, ideas, and knowledge. Without a forum for the free exchange of ideas and information, the scope of research is narrowed and sometimes duplicated. Such inefficiencies are costly, exhausting funds and time that could be better spent addressing research questions. Challenges like these also discourage professional interest in the translational and clinical fields of research and further impede the clinical research enterprise at a time when it should be flourishing. Most importantly, as a result of these obstacles, potentially life-changing therapies are not getting to those who need them.

A strong research infrastructure would eliminate inefficiency and wasteful spending and speed-up the lab-to-clinic process

In summary, translational research is an essential component of scientific investigation. Increasingly, however, obstacles between basic and clinical scientific research have slowed the lab-to-clinic process and, as a result, fewer therapies are reaching those in need. The ideal solution to this slow down would increase efficiency and eliminate wasteful spending by establishing a network of researchers that work together by sharing ideas, knowledge, and information in order to translate basic scientific discoveries into new therapies as quickly as possible.

A New Focus

Translational Research Programs – A Look at What Others Have Done

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Clinical research is essential to the biomedical research enterprise. Before a therapy can be approved for general use, it is carefully studied in the laboratory to understand how it works, its effectiveness, and its potential risks. Only after rigorous testing does a therapy go to clinical trial where its safety and benefit is proven through a series of tests in people. Individuals with disabilities cannot benefit from basic scientific research unless the results of that research are translated into practical applications that can be tested on a large population. However, despite the increasing number of basic scientific advancements, translational and clinical research has not kept pace.

Other health-related organizations have created translational research programs in an effort to accelerate the lab-to-clinic process

In an effort to accelerate the clinical research process, organizations such as the Muscular Dystrophy Association (MDA), Christopher Reeves Foundation (CRF), and NIH have created or conceptualized translational research program models aimed at overcoming funding issues and weak infrastructure. The most comprehensive of these three models is one conceptualized at NIH. While NIH does not have an actual translational research program in place like MDA and CRF, its Institutional Clinical and Translational Science Awards (CTSA) initiative (at the NIH Roadmap for Medical Research website) provides a plan to enhance translational and clinical research. By increasing efficiency through the concentration of expertise; incubation and dissemination of knowledge and information; and a synergistic approach among basic, translational, and clinical researchers, the initiative strives to accelerate the application of new knowledge to clinical practice.

On a smaller scale, the Christopher Reeves Foundation (CRF) has launched the NeuroRecovery Network grant program (funded by joint agreement between CRF and the Centers for Disease Control and Prevention) in order to provide support for the translation of basic science and applied research into intensive activity-based rehabilitation treatments. This program also provides for the establishment of specialized centers that offer standardized care based on current scientific and clinical evidence. The Network's long term goals include: maximizing the availability and quality of rehabilitative care for patients with spinal cord injuries and other neurological disorders; developing a comprehensive database to track the success

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of activity-based therapeutic interventions; identifying the optimal locomotor training regimens for specific patient populations; and maintaining an administrative network that can supply logistical, technical, and personnel-based support for rehabilitation programs. An advisory board predominantly comprised of physicians, clinicians, and scientists leads the program.

Another organization well known for its support of research, the Muscular Dystrophy Association (MDA), has also established a translational research program. The MDA's Translational Research Program is designed simply to move new drug therapies into clinical trial as rapidly and efficiently as possible. According to the MDA, this program was developed in response to the increasing number of promising basic research discoveries and the lack of translational research needed to advance the basic research discoveries to clinical trials. In an effort to jumpstart the translational research process, MDA's Translational Research Program directs funds to drug development projects in four main categories: direct drug development, infrastructure, regulatory compliance, and clinical research. An advisory board made up of scientists, clinicians, and businessmen guides the program.

MDA's and CRF's programs and NIH's concept feature similar components that suggests a program standard for reducing inefficiency and wasteful spending by:

A program standard for building a strong research infrastructure and eliminating inefficiency and wasteful spending

- Assembling a well-trained team of basic, translational and clinical researchers (preferably multi- and inter-disciplinary)
- Creating a "think-tank" for innovative research tools and information technologies
- Synergizing basic, translational, and clinical researchers to accelerate the application of new knowledge and techniques to clinical practice

Based on the NIH concept, and the MDA and CRF example, a translational research program that embodies these components is expected to speed up the process of

translating basic scientific research into practical applications for individuals who need them.

Advantages of Implementing a Translational Research Program

The goal of any health-related research supporting organization is to get the science to the people in the form of quality of life changing therapies. In addition to accelerating the lab-to-clinic process, the translational research program would provide other advantages. It would:

Advantages of implementing a translational research program

- **Generate opportunities for new and increased sponsorship** – A successful comprehensive research program would attract the attention of corporations looking for sponsorship opportunities that bring name recognition.

- **Increase potential for new partnerships** – A successful comprehensive research program would attract the attention of pharmaceutical companies, rehabilitation centers, physical therapy groups, and manufacturers of prosthetic devices, braces, orthodics, etc. looking for partnership opportunities that bring name recognition and new business.

- **Provide for a significant financial benefit to society and return on investment** – According to a recent article published in *The Lancet*, the overall incremental net benefit of a 10 year program of clinical trials conducted at the National Institute of Neurological Sciences and Stroke, was a projected gain of $15.5 billion. The 10-year return on investment was 4600%. (S Claiborne Johnston, JD Rootenberg, S Katrak *et al*., Effect of a US National Institutes of Health programme of clinical trials on public health and costs, *The Lancet* 367 (2006), pp. 1319-1327.)

The Translational Research Program – Fast Tracking the Search for Life Changing Therapies

The Translational Research Program is a comprehensive approach to advancing basic scientific research to clinical

The ideal translational research program

trial so that powerful therapies are made available to those in need as soon as possible. The Transitional Research Program:

- Provides an integrative academic home for a cadre of well-trained basic, translational, and clinical researchers dedicated to translating basic scientific discoveries into practical therapeutic applications

- Nurtures an environment for conceiving and conceptualizing ideas for innovative research tools and information technologies

- Synergizes basic, translational, and clinical researchers in order to accelerate the translation of new knowledge and techniques to clinical practice as efficiently and safely as possible

- Draws in basic, translational, and clinical researchers, community clinicians, clinical practices, networks, professional societies, and industry to facilitate the development of new professional interactions, programs, and research projects

By incorporating these components into a single research program model, the Translational Research Program has the infrastructure necessary to safely and efficiently develop cutting-edge therapies and technologies that impact the lives of individuals with cerebral palsy and other disabilities.

Summary

Translational research has proven to be a potent process for catalyzing clinical research. The improvement of human health is contingent upon translating basic scientific research into practical applications. However, translational and clinical research has not kept pace with the increasing number of basic scientific discoveries. A weak research infrastructure is the likely reason behind the growing barriers between basic and clinical research that have slowed the translational and clinical process. Thus, the solution to the slow down would be a research program model that would strengthen the research infrastructure in order to decrease

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inefficiency and accelerate the translational research process.

The United Cerebral Palsy Translational Research Program model features the infrastructure necessary to speed-up the translation of basic scientific discoveries into new therapies that would benefit individuals with cerebral palsy and other disabilities. The UCP Translational Research Program model ensures cutting-edge status by creating a hub where researchers and community clinicians can share ideas, knowledge, and information through intellectual dialogue, as well as conceptualize new ideas for research. By synergizing basic, translational, and clinical researchers, the UCP Translational Research Program model eliminates inefficiency and wasteful spending, and accelerates the translational research process so that powerful new therapies get to those who need them, which ultimately is the most important mission to any medical research supporting organization.