Neurodevelopmental Disorders Symposium

The Neurodevelopmental Disorders (NDD) Symposium was held on October 26, 2015 in collaboration with MIT and MGH at the Joseph B. Martin Conference Center at Harvard Medical School. The theme was “Approaches to studying Neurodevelopmental Disorders”. The oral program included talks from 5 Boston Area research leaders and 3 executive leaders from the neuroscience pharmaceutical industry.

The day was attended by 422 registrants and featured a networking lunchtime poster session with poster presentations from over 40 presenters representing ongoing neurodevelopmental disorders research across the Boston and Cambridge area. Poster themes included cognitive domains, epilepsy, genetic disorders and model development. This conference was sponsored by the Anne and Paul Marcus Family foundation. We are grateful to the Marcus Family for sponsoring this outstanding scientific program.

Coming Soon: Planning for the next NDD Symposium November 21, 2016!

Clinical Trial for Down Syndrome Launched

The interdisciplinary Down Syndrome Program and the Translational Neuroscience Center at Boston Children's Hospital are participating in a nationwide multi-site clinical drug trial sponsored by Hoffmann-La Roche Ltd. The Principal Investigator is Nicole Baumer, MD, MEd (Co-Director, Down Syndrome Program; Neurology/Developmental Medicine). The project is a randomized, double-blind, placebo-controlled trial exploring the pharmacokinetics, pharmacodynamic effects, efficacy, safety and tolerability of RO5186582 in children with Down syndrome, age 6-11 years. As the GABA-ergic system is critically important in cognition, it has been hypothesized that excessive inhibition of the GABA-ergic system may result in the cognitive difficulties seen in individuals with Down syndrome. Developed by Roche, RO5186582 is a GABAA α5 receptor subtype inverse agonist which has
been shown to improve cognition in studies using various animal models. The phase 2 clinical trial will assess PK and PD effects, safety measures through a variety of methods including physical exam, EEG and ECG, as well as the cognitive/global functioning and adaptive behavior of study participants using validated cognitive/adaptive testing and rating scales.

The Roche sponsored study is groundbreaking, as it represents the first opportunity at Boston Children’s Hospital for children with Down syndrome to participate in clinical trials specifically designed to investigate therapeutic targets to improve cognition and behavior. Recognizing that clinical trial opportunities within this community have been scarce, Dr. Nicole Baumer and Dr. David Stein, Co-Directors of the Boston Children’s Hospital Down Syndrome Program, hosted a parent forum this past year to educate families about the clinical research process and current state of research involving individuals with Down syndrome. Many families, as well as members of the Massachusetts Down Syndrome Congress, attended and were overwhelmingly positive about the prospect of increased research within their community and supportive of the program’s research plans moving forward. This Roche sponsored study represents the first of what we hope will be many clinical trials facilitated by the TNC within the Boston Children’s Hospital Down Syndrome Program.

Preclinical Roadmap for drug discovery available

Are you a preclinical scientist considering translation of your basic research discoveries into therapeutic strategies for brain disorders? Do you know where to go to get help with developing assays, chemical probes, or industrial partnerships to develop your ideas? Do you know how to dose your compounds in preclinical animal models or measure drug levels?

The TNC has assembled a preclinical road map to help investigators find help with these questions and more. Download the road map on the TNC web site and find resources to help address your specific drug discovery needs. The content is a modified summary of materials presented in the TNC Summer Workshop Series on Drug Discovery for Neuroscientists. This interactive pdf provides background information, reading lists, web links to online resources and local contacts for specific resources within the Boston Children’s Hospital and surrounding community. We will continue to update the Roadmap with additional resources as they become available. We love feedback. Let us know what you like about it, dislike about it or think we might add to it.

Contact: robin.kleiman@childrens.harvard.edu
Reciprocal Translation Units (RTUs) to focus on Genetic Epilepsies

New treatments for neurodegenerative, neurodevelopmental and neuropsychiatric disorders require target validation in predictive preclinical models using translatable outcome measures. To complement academic screening facilities and industrial outreach initiatives, disease-focused Reciprocal Translational Units made of experts that iteratively evaluate therapeutic approaches across preclinical models and patients are needed. The TNC is sponsoring the creation of disease focused Reciprocal Translation Units (RTUs) to address key translational challenges for brain disorders that affect children. These RTUs will bring together preclinical scientists studying models of brain disorders with clinical teams treating these patients to address key gaps in translation. The successful launch of the TNC sponsored Rett Syndrome RTU is being followed by the Inaugural meeting of the TNC sponsored Epilepsy RTU to be held in Spring at BCH. The goal of this half day meeting is to bring together stakeholders from different disciplines (clinical, preclinical, industrial) to identify the largest challenges and opportunities in developing new anti-epileptic drugs for patients. The format of the half day event will be an overview of the landscape, followed by breakout sessions to discuss key topics: 1) Which epilepsy disorders represent tractable patient populations for small proof of concept studies to provide early proof of efficacy for novel AEDs? 2) What are the most robustly translatable paired preclinical models for specific clinical patient populations? 3) How can clinical trial design be improved for new anti-epileptic medications? A debrief will recap the discussions across the breakout sessions and identify next steps. Epilepsy investigators and industry scientists with an interest in participation should contact the TNC: tnc@childrens.harvard.edu. Participation will be limited to facilitate in-depth discussion.

Measuring Drug levels in preclinical models

Preclinical studies using pharmacological agents are critically dependent upon measurements of target organ drug exposure to support mechanistic understanding of results and translation of results into therapeutic dosing treatments for patients. The consequences of ignoring collection of this data have been highlighted recently in a Perspective titled “Data gaps limit the translational potential of preclinical research” published in Science Translational Medicine by TNC preclinical Research Director Dr. Robin Kleiman and her collaborator Dr. Michael Ehlers, Head of Pfizer’s Biotherapeutics, Neuroscience and Pain Research Units. Read about this important topic in the BCH Vector Blog post. Consult the preclinical drug discovery roadmap or the pharmacometrics core for more information and helpful resources.
BCH Neuroscience Clinical Research Cluster of Excellence

The **TNC** has been selected to direct a new research initiative at BCH- the newly created **Neuroscience Clinical Research Cluster of Excellence**. This cluster represents the first in an effort at BCH to further scientific discovery by organizing clinical researchers with similar research interests into a cluster facilitated by a program with established experience in that designated field. The TNC is honored to be selected as a first program to pilot this initiative. Participating departments/divisions within this new Neuroscience Cluster include those which are already founding members of the TNC, **Division of Developmental Medicine, Division of Genetics and Genomics, Department of Neurology, Department of Neurosurgery and the Department of Psychiatry**, as well as the **Emergency Department**. Over the past 2 years, the TNC has developed an integrated framework and supporting personnel to **accelerate the development of early phase studies and clinical trials in neuroscience**. Through this Clinical Research Cluster of Excellence initiative, the TNC will be able to provide a variety of services to those researchers within the cluster through its Clinical Research and Regulatory Affairs Service and Human Neurobehavioral Core Service. Services provided to support translational neuroscience research will include protocol/consent form development, IRB/regulatory assistance, research staff training, neurobehavioral assessment/consultation and study implementation guidance. The TNC staff will also work with other research support programs within BCH to accelerate discoveries on the neuroscience arena and looks forward to implementing this exciting initiative.

Investigations of Neuroplasticity in Autism Spectrum Disorders

The TNC is working with Dr. Alex Rotenberg to investigate brain plasticity in children with Autism Spectrum Disorder (ASD). Research suggests that during development the brains of individuals with ASD change in response to their experiences differently than the brains of typically developing individuals. This study aims to understand whether and how this difference contributes to ASD symptoms.

Dr. Rotenberg’s team will measure brain plasticity with transcranial magnetic stimulation (TMS), a method to noninvasively activate specific brain areas with strong magnetic fields. TMS has been used for years in neurology and psychiatry. The TNC Human Neurobehavioral Core Service is conducting ADOS-2 and ADI-R assessments for the study. The results of this study could help to establish TMS as a valid and reliable biomarker, a sort of brain stress test, which will be useful to monitor treatment responses in future clinical trials of ASD therapies. **The study involves four visits to Boston Children’s Hospital. Two screening visits that last 2-3 hours, and two TMS visits that last 3-4 hours. The study team is looking for children ages 6-16 with a diagnosis of Autism Spectrum Disorder to participate. Please contact the study coordinator Gabrielle Block for more information about participation (Gabrielle.Block@childrens.harvard.edu).**