

## **Thomas Bourgeron, Ph.D.**

M.I.N.D. Institute Distinguished Lecturer Series – May 13, 2009

### ***Biographical Information***

Thomas Bourgeron is a geneticist and director of the Human Genetics and Cognitive Functions unit in the Department of Neuroscience at the Institute Pasteur in Paris. Dr. Bourgeron's primary research interests involve the genetic origin and evolution of human cognitive functions. In 2003, his laboratory identified mutations affecting the Neuroligins (NLGN3 and NLGN4) in individuals with autism and Asperger syndrome (Jamain et al. Nature Genetics 2003). This finding was the first evidence indicating that a synaptic pathway was associated with Autism Spectrum Disorders (ASD). Subsequently his research group identified several mutations in several other genes associated with ASD that impact the development of neurons and their ability to form synapses. Research in his laboratory is currently focused on the genetic and functional analysis of susceptibility genes for ASD. Dr. Bourgeron is the recipient of several prestigious awards and honors, including the 2005 Young Investigator Award from the European Neuroscience Institute, the French Academy of Sciences' award for Biological Discoveries of 2007, and election in 2008 to membership in the European Molecular Biology Organization.

### ***Presentation Abstracts***

#### ***Synaptic and clock genes in autism spectrum disorders (4 pm)***

Autism spectrum disorders (ASD) affect at least one in every 200 individuals and are characterized by impairments in communication skills and social interaction, as well as restricted, repetitive and stereotyped patterns of behavior. Our genetic studies point to one synaptic pathway, including cell adhesion molecules (neuroligins NLGN3 and NLGN4 and neurexins NRXN1) and scaffolding proteins (SHANK3) associated with the disorder. This pathway is crucial for synapse formation/maintenance, as well as maintenance of the correct balance between GABAergic and glutamatergic synaptic currents. Interestingly, mice with mutations in Nlgn3 or Nlgn4 present with reduced social interaction and ultrasonic vocalizations. Besides this synaptic pathway, we recently reported genetic mutations altering melatonin synthesis in ASD. Melatonin plays a key role in the regulation of circadian rhythms, such as sleep-wake cycles, and was shown to modulate GABAergic currents, as well as axon and memory formation in different animal models such as fish, birds, and mammals. Based on these results, we propose that, in some cases, ASD could be the consequence of an alteration in the homeostasis of the synaptic currents in specific regions of the brain. Indeed, abnormal synaptic proteins could lead to an imbalance of excitatory/inhibitory currents. This imbalance could be revealed or amplified by an alteration of the circadian rhythms. Consistent with this hypothesis, a better characterization of the interplay between synaptic and clock genes may shed light on several features that are atypical in ASD such as sleep and memory formation.

#### ***Toward a better understanding of the genetic susceptibility to autism spectrum disorders (6 pm)***

Recent results from genetic studies have highlighted the crucial role of several synaptic proteins in the susceptibility to autism spectrum disorders. Dr. Bourgeron will present research that parallels this finding by showing that an abnormal setting of the biological clock may increase the risk of sleep problems in patients with ASD. Our ongoing projects are focused on the interplay between synaptic and clock genes in the susceptibility to ASD by using high-throughput genotyping and investigating specific traits such as sleep and memory.