Title: Neurogenetic pathways implicated in speech and language disorders

Lecturer: Dr. Simon E. Fisher, Max Planck Institute for Psycholinguistics in Nijmegen, the Netherlands

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People who carry rare heterozygous mutations disrupting the FOXP2 gene have problems mastering the complex sequences of mouth movements needed for speech, along with deficits in many aspects of expressive and receptive language.

The gene encodes a highly conserved transcription factor that helps regulate development/function of neuronal subpopulations in a wide range of vertebrates, although evidence suggests that its roles may have been modified during human evolution.

I will describe how FOXP2 can provide a unique window into key neurogenetic pathways via an array of complementary approaches. For example, using functional genomic screening of human neuronal-like cells grown in the laboratory, we identified CNTNAP2 (a member of the neurexin superfamily) as a downstream target directly regulated by FOXP2.

Intriguingly, CNTNAP2 is itself associated with common language impairments, and has also been implicated in language delays of autistic children. High-throughput screening has enabled us to isolate additional FOXP2 targets, including genetic networks involved in neurite outgrowth and synaptic plasticity.

Moving to animal models of FOXP2 dysfunction, we have shown that point mutations implicated in human speech deficits yield impaired motor-skill learning in mutant mice. Electrophysiological recording suggests that this may be mediated by altered plasticity of Foxp2-expressing circuitry.

This work demonstrates how we can begin to bridge gaps between genes, brains and speech and language.