Targeting TAO2 and its downstream pathway as critical effectors of Autism spectrum disorders in 16p11.2 microdeletion patients (TAO2PATHY)

Project Coordinator: Dr. Froylan Calderon de Anda, Center for Molecular Neurobiology, ZMNH, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
Project Partners:
Dr. Peter Soba, Center for Molecular Neurobiology, ZMNH, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
PhD Joris de Wit, Department of Neuroscience, VIB Center for Brain & Disease Research/KU Leuven, Leuven, Belgium
Prof. Karun Singh, Stem Cell and Cancer Research Institute, McMaster University, Hamilton, Canada
Prof. Stephen Scherer, Center for Applied Genomics, Hospital for Sick Children, Toronto, Canada

Genomic copy number variations generated through de novo micro-deletion or -duplication are contributing significantly to mental disorders. The 16p11.2 region, which encompasses 31 genes, is a site for common microdeletion/duplication accounting for up to 1% of individuals diagnosed with Autism spectrum disorders (ASDs). Although several genes within the 16p11.2 region have been proposed to be critical for ASDs, so far none of them recapitulates all physiological and anatomical abnormalities associated with 16p11.2 deletion.
We have recently identified the existence of de novo and inherited mutations in the 16p11.2 gene TAO2, from a large cohort of ASD patients. Moreover, we have established a TAO2 KO mouse model which recapitulates anatomical, physiological and behavioral abnormalities of 16p11.2 patients.
We hypothesize that TAO2 is a bona fide risk gene for mental disorders and causally involved in ASDs linked to 16p11.2 microdeletion. In the current proposal, we will unveil the TAO2-dependent molecular network using genetic and proteomic approaches. We will generate a genetic and molecular network of TAO2 and combine it with functional analyses to gain comprehensive insight into ASD-relevant functions of TAO2 and its downstream effectors. We will elucidate pharmacologically targetable TAO2 effectors to assess novel treatment strategies for 16p11.2-linked ASD.