Symptomatic *de novo* balanced chromosomal translocation breakpoints mapping for identification of novel loci associated with developmental disabilities

Developmental disabilities (DD) are a group of phenotypically and etiologically heterogeneous conditions associated with functional impairment in mental, physical, learning, language, or behavior areas. DD patients often require lifelong individual and family support or treatment which has a profound impact on families and society. Thus, DDs has become a considerable public health, social and economic challenge.

Genetic origin of DDs is estimated at 40-50% of all cases. Many different genomic changes have been revealed in DD patients. However, for majority of these variants disease-associations are provisional, and are referred as “identified” in DDs. Thus, still many of DD cases remain undiagnosed.

Small number of DD patients (6%) are a carriers of balanced chromosomal translocations (BCTs), which are chromosomal structure rearrangements. In a translocation, two chromosomes break and a segment from one chromosome is transferred to another chromosome. Translocation is balanced when despite transfer, the amount of genetic material is unchanged. Translocation can be inherited from one parent or occur *de novo*. BCTs are usually associated with normal phenotype; however, in some cases BCTs may produce clinical manifestations. Thus, at the breakpoint sites of symptomatic BCT functionally important gene(s) and/or regulatory elements are usually located. Therefore, detailed determination of disease-associated BCT breakpoints may offer a unique opportunity to elucidate the genetic cause of clinical condition in a given patient.

Carriers of symptomatic BCTs represent a natural experimental design for gene disruption and/or deregulation with the breakpoint position directly pointing to the candidate gene(s) and/or regulatory elements critical for observed clinical phenotype manifestation. This approach may be particularly powerful in finding causes of diseases with extreme phenotype and genetic background heterogeneity such as DDs. Thus, we expect that the proposed study will identify novel *loci* associated with developmental disabilities which will improve diagnostic possibilities and, hopefully, at least in some cases provide clues for treatment.