

Abstract

The presented dissertation summarizes the results of research focused on the study of cryptic rearrangements of human chromosomes. Specifically, it focuses on three core areas of research.

The first area is the research of cryptic rearrangements identified as causal causes of mental retardation in patients with previously unknown aetiology. The most common are the so-called microdeletion syndromes. The large variability of the phenotype and often overlapping symptoms of microdeletion syndromes require a whole-genome approach. Within the research, 64 probands were investigated and in 10 (16%) cryptic rearrangements were found and further analyzed.

The second area is the research of cryptic rearrangements associated with the pseudoautosomal region 1 (specifically with the *SHOX* gene region), which may be both natural components of population variability and the cause of the disease. Within the research, 98 patients with Léri-Weill dyschondrosteosis or idiopathic short stature were examined, with a causal mutation found in 68.8%, and 7.8% probands respectively. At the same time, the minor deletion (so-called L05101 deletion) was evaluated as a population polymorphism without an apparent phenotypic impact. Duplications with high pathogenic potential were identified by mean of comparative analysis of duplications detected in a set of 250 healthy individuals and patients. The results were supported by meta-analysis of published duplications in the observed area.

The third area is the research of rearrangements of chromosomal region 8q24 and *TRPS1* gene mutations associated with the rare trichorhinophalangeal syndrome. The probable cause of the disease was found in 7 patients out of 9. The chosen methodology also allowed analysis of extensive 5' and 3' untranslated regions of the *TRPS1* gene and detected a number of polymorphisms.

The dissertation highlights the importance of the research of cryptic rearrangements of human chromosomes in order to better understand the structural variability of the human genome and the origin of pathologies both with simple and complex genetic background.

Keywords

cryptic rearrangements of human chromosomes; mental retardation; *SHOX* gene; *SHOX* area duplications; trichorhinophalangeal syndrome; *TRPS1* gene; human molecular cytogenetics