REFERENCES


Author: Iosif Lurie, M.D., Ph.D.

CONTACT US

Chromosome Disorder Outreach
P.O. Box 724
Boca Raton, FL 33429-0724

Family Helpline 561.395.4252
info@chromodisorder.org
www.chromodisorder.org

ABOUT US

Chromosome Disorder Outreach provides support and information to anyone diagnosed with a rare chromosome change, rearrangement or disorder. CDO actively promotes research and a positive community understanding of all chromosome disorders.

CDO is a 501c3 organization founded in 1992.
In 1969 Langer and Giedion independently described patients who above the usual phenotype of TRPS-I revealed multiple exostoses – benign bone tumors. These exostoses may appear in different bones producing pain and cosmetic problems. Moreover, these patients usually reveal delays in psychomotor development. This condition (the association of TRPS-I traits, exostoses and intellectual disability) was coined Langer-Giedion syndrome (or tricho-rhinophalangeal syndrome type II).

In 1984 it was found that patients with Langer-Giedion syndrome have small deletions in the long arm of chromosome 8 (8q24). It was shown that a critical segment of 8q24 necessary for the occurrence of LGS includes at least three genes: TRPS1, EXT1 and RAD21. TRPS1 is a gene responsible (when mutated) for tricho-rhinophalangeal syndrome type 1. Deletion of the EXT1 gene is the cause of the exostoses. The RAD21 gene is considered to be involved in intellectual development. From the genetic point of view, Langer-Giedion syndrome is a classic consecutive deletion syndrome – a condition, where each main symptom is caused by deletion of one specific gene. The persons who have deletions of EXT1 but not TPRS1 show exostoses, but do not have dysmorphic features, typical for Langer-Giedion syndrome, or intellectual disability. Of course, most patients have deletions involving some additional genes (more proximal or more distal to the critical segment). This explains why many patients have some characteristics (microcephaly, missing or additional teeth, aplastic skin of the scalp, preauricular tags, polydactyly, partial syndactyly, absent tibia, heart defects [mostly defects of the atrial septum], annular pancreas, hydronephrosis, imperforate hymen) which are in addition to the typical clinical manifestations of TRPS-II.

Patients with Langer-Giedion syndrome usually do not have life-threatening birth defects, and life expectancy is basically normal.

Molecular cytogenetics is essential for the diagnosis of Langer-Giedion syndrome because in many patients deletions are relatively small and cannot be recognized upon “standard” cytogenetic examination.