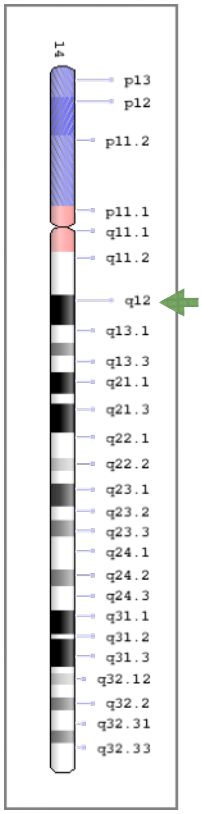
# DELETION 14Q12

## Deletion 14q12 (FOXG1-Syndrome)




The wide implementation of molecular cytogenetics which started ~15 years ago drastically changed our perception of what is known as a "chromosomal disorder". Routine cytogenetics can recognize only relatively large deletions or duplications, and most syndromes reported in the "pre-molecular" era involve abnormalities affecting at least 10 Mb of genetic material. Such large segments usually contain several disease-causing genes. The introduction of molecular methods showed that basically each chromosome carries several morbid genes, and the malfunction of any of these genes may cause a specific genetic (chromosomal) disorder. Chromosome 14 is no exception.

The segment 14q12 (an area of the long arm located close to the centromere) contains the FOXG1 gene. This tiny gene (it has only one exon) encodes a developmental transcription factor with repressive activity important for the development of the telencephalon (brain)[1]. If this gene does not work it causes a wide spectrum of neurodevelopmental problems. Patients with FOXG1 syndrome reveal microcephaly (sometimes congenital, but sometimes postnatal), poor eye contact, absent language, irritability, sleep disturbances, frequent gastro-esophageal reflux, seizures starting in infancy, and early-onset movement problems. The movement disorder may include generalized chorea, dystonia, facial dyskinesias and myoclonic jerks[2]. These manifestations are similar to the so-called Rett syndrome and before the implementation of molecular techniques, such patients were considered to have a congenital variant of Rett syndrome[3] (in classic Rett syndrome, caused by a mutation of the MECP2 gene, patients start their development as normal, but show a loss of acquired skills after several months). An MRI examination

of patients with FOXG1 syndrome shows agenesis or hypoplasia of the corpus callosum in almost all patients. Other defects include delayed myelination and a simplified gyral pattern. These manifestations are basically the same for patients with mutations of the FOXG1 gene and for patients with deletions of this gene[4]. Currently there are at least 60 publications detailing patients who have FOXG1 syndrome caused by 14q12 deletion. The segment 14q12 does not contains many genes. The frequent involvement of the neighboring NOVA1 gene does not produce any additional abnormalities. Several patients with deletions in close proximity to FOXG1 and not directly affecting the gene had the same manifestations as typical FOXG1 deletion patients. Most likely, deletions in these cases affect areas containing elements controlling activity of the FOXG1 gene.

There are no defects outside the nervous system in patients with 14q12 deletions. Of course, if deletions are relatively large and involve more distal segments of 14q (14q13 or even 14q21) the patients may show defects in other systems or other manifestations unrelated to FOXG1 syndrome.

All known 14q12 deletions causing FOXG1 syndrome are sporadic. However, the possibility of an unrecognized low-level mosaicism in one parent cannot be excluded.

## REFERENCES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