STUDY on RING CHROMOSOME 14 SYNDROME

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Duration of research: 3 years
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Chromosome 14 Ring Syndrome is a condition with multiple abnormalities of phenotype and psychomotor retardation, caused by partial loss of genetic material on chromosome 14. Clinical manifestations vary considerably between patients, even in view of mitotic instability of the ring, with the possible states of mosaicism (46, ring (14)/45, -14), which may vary in different tissues. The most common signs and symptoms include, along with psychomotor retardation and distinctive facial appearance, epilepsy and retinitis pigmentosa. However, a precise definition of this condition is lacking, both at the genetic and phenotypal levels. It should also be noted that chromosome 14 is subject to "imprinting" in the human species, and thus some of its regions have distinct functions depending on parental origin.

We planned a genotype-phenotype correlation study in a group of patients with ring chromosome 14. The study is divided into the following phases:

1) karyotype analysis on 100 peripheral blood cells, to be repeated after two years (determination of a state of mosaicism, and its possible evolution over time).
   In case of mosaicism found in blood, possible analysis of the karyotype of 100 skin cells, to be performed only once (to check the tissue distribution of this anomaly)
2) identification of the parental origin of the rearranged chromosome 14 (assessment of the possible effects of deregulation of imprinting)
3) the definition, using molecular cytogenetic techniques, of the deleted regions in individual patients

The technical requirements are:

1) conventional chromosomal examination to an average resolution of 550 bands
2) fluorescent in situ hybridization (FISH) with specific BACs for the distal half of the long arm of chromosome 14, at a mutual distance of 500-800 kb
3) segregation analysis of polymorphic microsatellites amplified by PCR
4) establishment of lymphoblastoid cell lines from each family (patient and both parents)
5) clinical evaluation of patients and correlation with the underlying genetic defect