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## **BASAL GENETIC DEFECT IN CHROMOSOME RING 14 SYNDROME AND IN PARTIAL 14q DELETIONS.**

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The "chromosome ring 14" syndrome is a rare pathology characterized mainly by psychomotor development delay and seizures. Other common features include microcephaly, hypotonia, retinal pigmentation abnormalities and facial dysmorfisms. Most of these features are also found in patients with a linear terminal deletion of chromosome 14, except for retinal abnormalities and seizures. To the aim to determine the genotype-phenotype correlations, we have executed one cytogenetics and cytogenetic-molecular study (FISH with multiple probes and microsatellites segregation analysis) in a total of 19 families with different chromosome 14 rearrangements. Of these: 11 patients with ring (14) (10 cases de novo and 1 of paternal origin); 5 patients with interstitial deletions affecting 14q11q11.2, 14q11q12, 14q11.2q12, 14q24.3q32.12 and 14q31.3q32.2 regions, respectively; 1 terminal deletion affecting the 14q32.31qter region; 1 patient with an apparently balanced translocation t(10;14)(q25.3;q12); 1 patient with 14q31.3qter trisomy and 18q22.1qter monosomy. In this last case, the rearrangement segregates from one paternal balanced translocation t(14;18). In particular we have observed that in patients with ring 14: 1) the deletion size is variable in the single patients, from 0.65 Mb to 3.8 Mb; 2) in any case a concomitant cell line with complete chromosome 14 monosomy is present (approximately 20% of the cells); 3) the parents had a normal karyotype, except in one circumstance, in which a ring (14) was present in low mosaicism (3%) in the father. The comparative analysis of cases with ring (14) and cases with interstitial deletions of different regions in 14q has suggested that the phenotypic features of patients with ring 14 are probably a consequence of the formation of the ring itself. In particular, in order to explain the prevalence of seizures and retinal abnormalities in ring 14 syndrome, we have been formulated the following hypotheses: 1) somatic mosaicism, due to mitotic instability of the ring, that may vary in degree between different tissues; 2) telomere position effect.