ANALYSIS OF RING14 CHROMOSOME IN HUMAN NEURONAL TISSUES

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Abstract:

Individuals with a Ring Chromosome 14 have a rare genetic disorder characterized by intractable seizures. Ring chromosomes have been observed for every human chromosome and although ring associated phenotypes may vary depending on the affected chromosome, patients with ring chromosomes exhibit some commonality, leading to the hypothesis that the ring itself, irrespective of the specific sequences involved, causes abnormalities. Several ring chromosomes are associated with seizures, with chromosome 14 and 20 having the highest correlation. While the mechanism(s) underlying chromosomal ring formation are not completely understood, it is clear that the rings result from intra chromosomal fusions, which may be accompanied by additional aberrations such as deletions or duplications. The timing of the fusion event determines how many cells are affected, and ring formation can occur in either the parental germ line (with non-mosaic rings then appearing in every cell) or somatic cells (resulting in mosaic rings). Ring chromosome 14 can occur with deletions or duplications on the ring chromosome, or in some cases, there is no evidence for alterations of
genomic material besides the ring. Nevertheless, in all cases, the rings are associated with seizures.
Our goal is to determine the molecular etiology of the seizures associated with the ring chromosome 14 syndrome. We will test the hypothesis that gene expression is altered on ring chromosomes without accompanying genomic alterations and hopefully identify altered expression profiles that are the cause of the seizures. We will utilize cell lines from mosaic patients, who have some cells with the ring, and other cells with two normal chromosomes 14. We will also compare the profiles generated to those from patients with deletions or duplications.