CENTROMERES IN TRISOMY 21

The extra chromosome 21 in Down syndrome is a result of nondisjunction during a meiotic or a post zygotic mitotic cell division, maternal meiotic MI errors being the most common.

Analysis of the structure of the centromeres involved in nondisjunction was thus far not possible due to limitations of the sequencing technology.

Mastrorosa et al. (1, BioRchiv) have now used long read sequencing to analyze a parent-child trio, where the child has trisomy 21. They found a notable size difference in the two maternally derived centromeres of chromosome 21 (H1, H2). But, more interestingly, they found a significant reduction of the CENP-A epigenetic signal on the larger one (H1), suggesting a lower competence of this centromere. A comparison of the three centromeres of the proband with a population sample of 35 fully sequenced chromosome 21 centromeres showed that H2 is the smallest centromere sequenced to date. It also showed that all three haplotypes (H1-H2-H3) share a common origin of approximately 15 thousand years ago. The results suggest that size asymmetry and epigenetic differences in centromeres of 21 may contribute to the risk of non-disjunction.

1. https://www.biorxiv.org/content/10.1101/2024.02.25.581464v1