CHROMOSOME 21 CENTROMERE SIZE AND DOWN SYNDROME

Small chromosome 21 centromeres had been proposed as a risk factor for non-disjunction in mothers of children with Down syndrome — a hypothesis consistent with mouse data showing that larger centromeres, with stronger kinetochores, are preferentially retained in the egg during female meiosis. A new paper in Am J Hum Genet (1) puts this hypothesis to rest. Comparing completely assembled chromosome 21 centromeres from eight trisomy 21 families with those of over 280 population controls, the authors found no enrichment of small centromeres in trisomy 21 cases ($p = 0.72$).

However, they did find a subset of mothers among the trisomy 21 families in whom the size of the centromere in the two chromosomes 21 differed by more than tenfold, an extreme asymmetry not observed in any control individual. This imbalance may impair homologous pairing during maternal meiosis I and predispose to non-disjunction in a minority of families.

1. https://www.sciencedirect.com/science/article/pii/S0002929726001977