CHROMOSOME POLYMORPHIC VARIANTS: NO EVIDENCE OF HARM

In the last two decades at least 38 publications have claimed that chromosome polymorphic variants (CPs) are harmful. Another series of 16 publications found no evidence of harm. A recent paper[1] has critically analysed all 54 articles.

Papers concerning all variants in both series have the same major drawback: lack of a clear definition of a variant. Anyhow all papers in the second series have suitable controls. Papers claiming harm, however, have several other drawbacks: absent or inadequate controls; classification of chromosome abnormalities as CPs, incorrect identification of CPs; absence or poor quality of chromosome images. In fact, only one of the 33 articles with controls had no apparent problems with CP identification

The only unequivocally identifiable variant in these studies is inv(9)(p12q13). Five papers in the first series claim that it is associated with a wide range of phenotypic abnormalities. Six studies in the second series show that it is not associated with adverse effect on phenotype, fertility, pregnancy loss or risk of aneuploidy. In addition, the frequency of inv(9)(p12q13), which was recorded in 26/38 papers in the first and 9/16 papers in the second series, was not different from that in the general population.

In short, critical analysis of the 54 papers has provided no evidence that the CPs are harmful.

Sequencing of pericentromeric heterochromatin is in its early stages; fully understanding its structure and function will take some time. Information from hundreds of thousands of genomes will be needed before any possible association between heterochromatin and disease can be studied.

The author concludes that while we need to keep an open mind about any new insights that may emerge, there is at present no convincing evidence to contradict the information on chromosomal polymorphic variants as published in the International System for Human Cytogenomic Nomenclature (ISCN, 2024).

PdF attached

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