LETTER

Does aneuploidy destabilize karyotypes automatically?

In their recent paper, Valind et al. test the theory that "aneuploidy automatically" destabilizes the karyotype (1). According to this theory, aneuploidy, an abnormal balance of chromosomes, destabilizes the karyotype automatically by unbalancing the cooperations of thousands of genes, especially mitosis genes: The more aneuploid the cell the more unstable is the karyotype (2–5).

To test this theory, Valind et al. (1) compare chromosomal instabilities of normal diploid cells, cells from congenital near-diploid aneuploidies and from rare-balanced triploids, and cells from highly aneuploid, clonal cancers. Chromosomal instability is measured as the percentage of cells with abnormal chromosome copy numbers, defined as the aneusomy index (AI).

Valind et al.'s (1) results show that the chromosomal instability indices of normal human cells are between 0.09 and 0.18 AI, those of congenital near-diploid aneuplodies—like Down, Patau, Edward, and other syndromes—range from 0.2 to 0.7 AI, and those of near-diploid to highly aneuploid, near-triploid colon cancers range from 1.2 to 4.7 AI. Accordingly, the authors conclude that congenital "aneuploidy was . . . insufficient to generate . . . cancer-like chromosomal instability" (1). It would seem, therefore, that the new data of Valind et al. support the concept that chromosomal instability is directly proportional to the degree of aneuploidy.

As an argument against the theory that aneuploidy destabilizes the karyotype automatically or "per se," Valind et al. (1) cite the relatively low chromosomal instability of 0.66–1.8 AI of two congenital, chromosomally balanced triploidies, compared with the very high chromosomal instability of 4.8 AI of the chromosomally highly unbalanced near-triploid colon carcinoma SW480.

However, this argument fails to consider that the congenital triploidies are threefold normal haploid karyotypes, rather than the highly aneuploid and highly unbalanced near-triploid karyotypes of the colon carcinoma SW480. In other words, the balance of chromosomes in congenital triploids is the same as that in normal cells, and thus very different from that of the "near-triploid" carcinoma.

The theory that aneuploidy destabilizes the karyotype in proportion to the degree of aneuploidy would thus predict a low near-normal AI for the congenital triploidies and a high AI for the near-triploid carcinoma. The fact that the two triploid cases of Valind et al. (1) developed sufficiently for cytogenetic analysis, while others described previously were even born alive (6) confirms this prediction. Nevertheless, a threefold polyploidy is still likely to unbalance gene teams optimized for diploidy, as the higher-than-normal instability of the two triploids suggests.

I conclude, therefore, that Valind et al. (1) confirm and extend the theory that aneuploidy automatically destabilizes the karyotype in proportion to the degree of aneuploidy, namely with new, very accurate determinations of common congenital aneuploidies and of very exceptional congenital, chromosomally balanced triploids.

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