CENTROMERE FISSION AND WHOLE-ARM ANEUPLOIDIES IN CANCER

Whole-arm aneuploidies, resulting from the loss or gain of entire chromosome arms, are among the most frequent chromosomal alterations in human cancers. While these have often been attributed to mitotic missegregation, Zheng et al.[1] show that centromere breakage, a structural form of chromosomal instability, plays a dominant role in driving such alterations. Across 17 tumor types, whole-arm losses occur more frequently than gains, and their distribution patterns strongly suggest structural origins. The authors demonstrate that, mechanistically, the centromeres become prone to breakage during S phase due to replication stress, in part linked to histone overexpression. These breaks lead to the loss of entire chromosome arms and are strongly associated with poor patient outcomes. Importantly, the prevalence of centromere break-induced arm aneuploidy highlights a mechanism distinct from classical mitotic errors.

Beyond cancer biology, this phenomenon recalls similar processes in evolutionary cytogenetics, where centromeric fissions have contributed to karyotype diversification in various species, including reptiles. Such parallels underscore the broader biological impact of centromere instability as a driver of both somatic genome remodeling and long-term evolutionary change.

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