

ARE DE NOVO TERMINAL DELETIONS THE RESCUE OF UNFAVORABLE ZYGOTIC IMBALANCES?

A recent review article ([Eur J Hum Genet, by Zuffardi et al.](#)¹) examines the evidence which suggests that many *de novo* unbalanced structural rearrangements are not representative of the genomic constitution of the zygote but are rather the result of modifications of genomic imbalances that are incompatible with embryonic development. It has long been known that a cell with trisomy can undergo a rescue process, which can result in a cell with 46 chromosomes with segmental or complete uniparental disomy. More recently, it has been demonstrated that both unbalanced *de novo* translocations and small supernumerary chromosomes may result from modifications of an entire supernumerary chromosome. The article, in addition to reviewing this evidence, focuses on distal *de novo* deletions that could result from the breakdown of an isodicentric chromosome present in a zygote, which, despite having 46 chromosomes, has in fact an almost complete functional trisomy. The authors underline how the rescue events of the deletion can, through somatic recombination with the normal homolog, create errors of interpretation if adequate methodologies are not used to highlight segmental disomies. Furthermore, the dicentrics break and the resulting products, which lack telomeres, undergo repeated breakage-fusion-bridge cycles. This can lead to the production of a variety of rearrangements such as unbalanced translocations and ring chromosomes, which can then be present in the embryo but more frequently in the placental cells.

1. <https://www.sciencedirect.com/science/article/pii/S1769721222001136?via%3Dihub>