

Chromosome segregation errors and aneuploidy

Chromosome segregation errors cause aneuploidy, a state of numerical alterations in chromosomes that contributes to tumor initiation and progression. Improper attachments between chromosomes and microtubules are the most common mechanism causing chromosome mis-segregation [1]. However, frequency and identity of error mechanisms have not been studied extensively. Here, we quantitatively assessed errors in chromosome segregation in 2D cultures, both in healthy (RPE1) and cancer cell lines (U2OS and HeLa) and found that cancer cells can enter anaphase with persistent mono-oriented chromosomes. We found this rate to be 3-4% in U2OS and HeLa cells. Prior to anaphase, the frequency of mono-oriented chromosomes was roughly 2x higher in U2OS than in HeLa cells. In U2OS cells, we found a 70 minute-delay in anaphase entry during which most of the mono-oriented chromosomes were resolved. Interestingly, we found multiple mono-oriented chromosomes in 2% of U2OS cells. Our results demonstrate that mono-oriented chromosomes can lead to aneuploidy, presumably due to spindle assembly checkpoint override, and indicate that multiple errors per cell are due to defects in the mitotic machinery.

[1] Compton DA. *Curr Opin Cell Biol*, 2011.

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