

Why chromosomal translocations are cell type-specific?

Most cancer-related chromosomal translocations appear to be cell type-specific. It is currently unknown why different chromosomal translocations occur in different cells. This can be either due to the occurrence of particular translocations in specific cell types or adaptive survival advantage conferred by translocations only in specific cells. We experimentally addressed this question by double-strand break (DSB) induction at *MYC*, *IGH*, *AML*, *ETO* loci in the same cell to generate chromosomal translocations in different cell lineages. Our results show that any translocation can potentially arise in any cell type. We have analyzed different factors that could affect the frequency of the translocations and only the spatial proximity between gene loci after the DSB induction correlated with the resulting translocation frequency, supporting the “breakage-first” model. Furthermore, upon long term culture of cells with the generated chromosomal translocations, only oncogenic *MYC*-*IGH* and *AML*-*ETO* translocations persisted over a 60-day period. Overall, the results suggest that chromosomal translocation can be generated after DSB induction in any type of cell, but as to whether the cell with the translocation would persist in a cell population depends on the cell type-specific selective survival advantage that the chromosomal translocation confers to the cell.

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