“Variant requirements for DNA repair proteins in cancer cell lines that use alternative lengthening of telomeres”

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ABSTRACT

The human genome relies on DNA repair proteins and the telomere to maintain genome stability and integrity. Genome instability can result in disease and is recognized as an enabling characteristic of cancer. Another characteristic of cancer is limitless replicative capacity. Cancer cells require telomere maintenance to enable this uncontrolled growth. Most often telomerase is activated, although a subset of human cancers are telomerase-negative and depend on recombination-based mechanisms known as ALT (Alternative Lengthening of Telomeres). ALT depends invariably on homologous recombination to extend telomeres and DNA repair proteins. This study surveyed the requirement for requisite homologous recombination proteins yet to be studied in ALT cell lines. Effects on ALT were evaluated by measuring C-circle abundance, a marker of ALT. The requirement for homologous recombination proteins varied between the ALT cell lines compared. Several proteins essential for homologous recombination were dispensable for C-circle production while proteins grouped into excision DNA repair processes stimulated C-circle production in some ALT cell lines. A mismatch repair protein also stimulated recombination at telomeres using intertelomeric exchange. In sum, our study suggests that ALT proceeds by multiple mechanisms that differ between human tumor cell lines and that some of these depend on DNA repair proteins not associated with homologous recombination pathways. Further studies of all DNA repair pathways in ALT will likely lead to a better understanding of ALT mechanisms which could lead to the development of ALT therapeutics.
RECENT PUBLICATIONS


AWARDS AND HONORS

OSU Center for Microbial Interface Biology NIH T32 Training Grant Fellowship Fall 2011

FUTURE PLANS

Alaina is currently looking for a position in clinical research in Northeast Ohio.