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The effect of chemotherapeutic agents on telomere maintenance in Breast cancer

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Telomeres are made up of G-rich nucleotide repeats of the sequence TTAGGG that protect chromosome ends in mammalian cells. A six-protein complex called Shelterin packages telomeric DNA and helps to hide the chromosome ends from being recognized as sites of DNA damage during replication. It is well known that cancer is implicated with short telomeres and the telomerase enzyme is activated in 90% of cancers including breast cancer, but the length of telomeres is short suggesting that telomerase is responsible for telomere maintenance. Short telomere in breast cancer cells confers telomere dysfunction and this can be related to Shelterin proteins and their level of expression in breast cancer cells. Our studies have shown that Shelterin genes are down-regulated in breast cancer cell lines; therefore, to understand a possible mechanism behind the loss of "Shelterin" expression, these genes may possibly be under the control of methylation in some epithelial breast cancer cells. Treatment of the 21NT breast cancer cell line with the demethylating agent 5-aza-CdR (5-Aza-2'-deoxycytidine) and TSA (Trichostatin A) resulted in up-regulation of the expression of shelterin genes. Based on these findings, the telomere length of 21NT at different time points of treatment was measured by FLOW-FISH, Q-FISH, Southern blot, and Q-PCR. Our results represent increase telomere length of 21NT cell line which was treated by 5-aza-CdR after 72 hours and 3 weeks. Therefore, increases in some of Shelterin gene expression can stabilize telomere length elongation.

Biography

Azadeh Motevalli successfully completed my M.Sc. degree in Molecular Medicine and cancer research at Brunel University in 2008. Subsequently, he started my Ph.D. degree at Brunel University working with Professor Rob New bold and Dr. Terry Roberts. He currently in the process of submitting my thesis and publishing my experimental results.

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