Pif1 Gene Integration to Inhibit Telomerase Activation in Cancer

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Increased telomerase activity and sustained telomeres are hallmarks of non-small cell lung cancer (NSCLC) and encourage cancer growth by inhibiting cellular apoptosis. This study analyzes Pif1, a 5'-to-3' DNA helicase, as a potential chemosensitizing agent. Pif1 is suggested to be involved in several functions including telomere maintenance and the facilitation of cell-cycle progression. However, current research depicting Pif1's telomere maintenance processes is inconsistent and its anti-cancer potential has not been studied in relation to chemosensitivity. Cisplatin, the chemotherapeutic used primarily against NSCLC, binds to guanine structures, found abundantly in telomeres and causes DNA damage, that if not repaired, may result in the induction of apoptosis. In this study, a Pif1 integration vector was transfected into a NSCLC cell line (A549) and qPCR analysis indicated an 88 fold increase in Pif1 gene expression. Results demonstrated a decrease in telomerase activity in Pif1 induced cells suggesting that Pif1 inactivates telomerase at elongated telomeres. Furthermore, cisplatin treatment of Pif1 induced cells decreased cell viability to a significantly greater extent than in control cells suggesting that Pif1 may override DNA damage repair mechanisms. Results suggest that Pif1-cisplatin combinatorial therapy caused an induction of apoptosis through the p53 apoptotic pathway and increased the expression of apoptotic caspases. Interestingly, telomere length analysis also suggests that Pif1 induced cells maintained elongated telomeres possibly allowing for increased targets for cisplatin. Current research works to develop a variant transport peptide to force endothelial cells to produce cancer targeting Pif1 integration peptides to increase chemosensitivity in NSCLC