Human Telomerase Reverse Transcriptase and Cancer

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The reactivation of human telomerase reverse transcriptase (hTERT) is a critical event towards tumorigenesis in human cancers. We have previously reported that ectopic expression of the C-terminal fragment of the human telomerase reverse transcriptase (hTERTC27) inhibits the growth and reduces the tumorigenicity of human cervical cancer Hela cells. Here we further demonstrated the therapeutic effect and molecular mechanisms of hTERTC27-mediated cancer gene therapy in vivo in established human glioblastoma U87 tumor. We showed that intra-tumoral injection of rAAV-hTERTC27 is highly effective in treating the subcutaneously transplanted glioblastoma tumors in vivo. Histological analysis showed that hTERTC27 caused profound apoptosis and necrosis in the TERT positive U87 tumors. To study the molecular mechanism of rAAV-hTERTC27-mediated anti-tumor effects, we analyzed the global gene expression profile of the rAAV-hTERTC27-injected tumor tissues as compared to that of the control AAV-EGFP-injected tumor tissues using cDNA microarray and proteomic approaches. Our results suggest that hTERTC27 exerts its effect by complex mechanisms which involve pathways in apoptosis, cell cycle, and more importantly marked host immune responses. Furthermore, the potential role of human PinX1, a newly identified gene whose product is a potent inhibitor of telomerase, in the nuclear translocation and TERT-mediated tumorigenicity was investigated.