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**#1834 Simultaneous siRNA mediated downregulation of hTERT and treatment with interferon-gamma in human glioblastoma SNB-19 and LN-18 cells causes cell cycle arrest and inhibits invasion, angiogenesis, and tumor growth in nude mice.** Joseph George, James S. Norris, Naren L. Banik, Swapan K. Ray. Medical University of South Carolina, Charleston, SC.

Telomerase is highly upregulated in majority of the cancers including glioblastoma to provide immortality. Human telomerase reverse transcriptase (hTERT) is the catalytic component that regulates the telomerase activity. Interferon-γ orchestrates several cellular activities including cell cycle and growth through transcriptional regulation. In the present investigation we downregulated hTERT using cognate siRNA in two highly invasive human glioblastoma cell lines SNB-19 and LN-18 and simultaneously treated them with interferon-γ for 48 h. Matrigel invasion, spheroid migration, and cell proliferation studies demonstrated inhibition of cell invasion, migration, and proliferation in both glioblastoma cell lines after treatment with hTERT siRNA and interferon-γ. In vitro (co-culture with endothelial cells) and in vivo angiogenesis (in immunocompromised mice) assays demonstrated inhibition of capillary-like structure and neovascularization, respectively, after treatment with both agents. Furthermore, the combination treatment showed remarkable reduction in tumor growth in the subcutaneous and intracerebrum of nude mice. Western blot analysis demonstrated significant decreases of PCNA, MMP-9, VEGF, c-Myc, CDK2, CDK4, and cyclin D1 and marked increases of p21Waf1 and p27Kip1 after treatment with both agents. Semiquantitative and real-time reverse transcription-polymerase chain reaction (RT-PCR) studies showed downregulation of PCNA, c-Myc and VEGF and increased expression of p21Waf1 and p27Kip1. Taken together, the results of the present study indicate that the combination treatment of hTERT siRNA and interferon-γ in glioblastoma cells effectively prevents cell invasion, angiogenesis, and tumor growth through downregulation of molecules involved in angiogenesis and cell cycle. This unique combination of hTERT siRNA and interferon-γ offers a potential therapeutic approach for treatment of glioblastomas. This work was supported by the R01 CA-91460 grant from the NCI.

**Citation Format**

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