Category: Experimental and Molecular Therapeutics 2

Session Title: Biochemical Modulators

#578 Combination of 4-HPR and EGCG induces apoptosis and inhibits angiogenesis and tumorigenesis of neuroblastoma SH-SY5Y and SK-N-DZ cells.

Joseph George[1], Naren L. Banik[2], Swapan K. Ray[1]. [1]University of South Carolina School of Medicine, Columbia, SC; [2]Medical University of South Carolina, Charleston, SC .

Neuroblastomas are extracranial, malignant solid tumors in childhood with a dismal prognosis. N-(4-Hydroxyphenyl) retinamide (4-HPR) is a synthetic retinoid that induces apoptosis in tumor cells. (-)-Epigallocatechin-3-gallate (EGCG) is a potent antioxidant abundant in green tea with anticancer properties. In the present investigation, we have studied the combined effect of 4-HPR and EGCG to induce apoptosis and to inhibit angiogenesis and tumor progression of human neuroblastoma malignant SH-SY5Y and SK-N-DZ cells in vivo. The cells were treated with 1 μM 4-HPR, 10 μM EGCG, or combination of both and subjected to MTT assay and TUNEL staining. Western blotting was performed for molecules involved in both receptor and mitochondria mediated apoptotic pathways. Angiogenesis and subcutaneous tumor growth studies were performed in immunocompromised mice. Treatment with combination of 4-HPR and EGCG resulted in more than 70% apoptosis and 80% inhibition in cell proliferation in both cell lines. Apoptosis was associated with induction of both receptor and mitochondria mediated pathways. Our in vivo angiogenesis studies demonstrated significant inhibition of neovascularization after treatment with either agent alone and complete inhibition after treatment with combination of both agents. Studies also demonstrated marked suppression of subcutaneous tumorigenesis and solid tumor formation after treatment with combination of 4-HPR and EGCG. In conclusion, our studies demonstrated that treatment with combination of 4-HPR and EGCG effectively induced apoptosis and inhibited cell proliferation, angiogenesis, and growth of neuroblastomas in vivo. Therefore, the combination of 4-HPR and EGCG could be used as a potential therapeutic regimen for effectively controlling the growth of human malignant neuroblastomas. This investigation was supported in part by the R01 grants (NS-57811 and CA-91460) from the National Institutes of Health (Bethesda, MD).

Citation Format

George J, Banik N, Ray S. Combination of 4-HPR and EGCG induces apoptosis and inhibits angiogenesis and tumorigenesis of neuroblastoma SH-SY5Y and SK-N-DZ cells [abstract]. In: Proceedings of the 101st Annual Meeting of the American Association for Cancer Research; 2010 Apr 17-21; Washington, DC. Philadelphia (PA): AACR; 2010. Abstract nr 578.