Paul J Davis, J Cell Sci Ther 2016, 7:1 (Suppl)
http://dx.doi.org/10.4172/2157-7013.C1.034

OMICS International
conferenceseries.com
6th World Congress on
Cell & Stem Cell Research
February 29-March 02, 2016 Philadelphia, USA

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Anti-angiogenic and pro-apoptotic activity of nano-diamino-tetrac (Nanotetrac) initiated at a cell surface target on integrin αvβ3

Integrin αvβ3 is concentrated and activated on the surface of tumor cells and dividing endothelial cells where it is critical to cell-cell and cell-extracellular matrix protein interactions and to function of cell surface vascular growth factor receptors. Exploration of the functions of a receptor for thyroid hormone and hormone analogues on the integrin has linked hormone analogues to regulation of expression of genes relevant to angiogenesis to differential regulation of apoptosis (pro and anti apoptosis) and to repair of double-strand DNA breaks. Tetraiodothyro-acetic acid (tetrac) is a naturally occurring deaminated analogue of L-thyroxine (T4) that, when covalently bound to a nanoparticle that precludes its cellular uptake acts exclusively at αvβ3 via a variety of signal transducing kinases and other mechanisms as an anti-cancer/anti-angiogenesis agent. We report here the action of systemic nanoparticulate tetrac (Nano-diamino-tetrac, NDAT or Nanotetrac) on human glioblastoma (U87MG) xenograft size and histology. Ten days' daily subcutaneous treatment of tumor-bearing nude mice with NDAT (1 mg tetrac-equivalent/kg/day) resulted in a 38% decrease in tumor volume in situ and 47% decrease in tumor weight at sacrifice ($p<0.01$ vs. control). Blinded histopathologic review of tumors from control and treated animals has revealed essentially complete loss of vascularity without hemorrhage and consequent 5-fold increase in necrotic cells in drug exposed tumors. There was 4.5-fold increase in apoptotic cells in treated tumors. Changes were significant at $p<0.01$. NDAT is a novel nanopharmaceutical that acts exclusively on cancer and endothelial cell surfaces to induce apoptosis and systematic devascularization with necrosis.

Biography

Paul J Davis has obtained his MD degree at Harvard Medical School and his Clinical and Research Training at Albert Einstein College of Medicine; NIH. He is a Professor of Medicine at Albany Medical College (Albany, NY USA) and a Former Chair of the Department of Medicine at Albany. He has Co-authored 250 refereed papers and he and his colleagues described the cell surface receptor for thyroid hormone. He and co-workers at the Albany College of Pharmacy have generated nanopharmaceuticals of thyroid hormone and hormone analogues that modulate angiogenesis and tumor cell proliferation and viability.

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