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# Stem Cell Research 2017 : Nano-diamino-tetrac (NDAT; Nanotetrac) acts at its target on integrin Ã‚Â±vÃ‚Â²3 in human glioblastoma xenografts to induce necrosis via. anti-angiogenesis and apoptosis_ Paul J Davis_ Albany College of Pharmacy and Health Sciences, USA

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Clinical evidence in a limited number of patients supports the concept that glioblastoma multiforme (GBM) is a thyroid hormone-dependent cancer. In vitro evidence indicates that L-thyroxine (T4), the principal secretory product of the thyroid gland, at physiological concentrations stimulates proliferation of glioma /GBM cancer cells via a poly-functional cell surface receptor for T4 on the extracellular domain of cancer cell plasma membrane integrin αvβ3. This action of T4 is blocked by nanoparticulate tetraiodothyroacetic acid (Nanotetrac, Nano-diamino-tetrac, NDAT). Tetrac in this NDAT formulation is covalently bound via a diaminopropane linker to a poly(lactic-co-glycolic acid) (PLGA) nanoparticle. We have examined histopathologically the induction by NDAT of devascularization, of necrosis and apoptosis in U87MG human GBM cell xenografts in nude mice. Treatment regimen was 1 mg tetrac equivalent/kg body weight s.c. as NDAT daily X10 d, begun 2 d following tumor cell implantation when tumor volume estimates were 350 mm3. Xenografted control animals received void nanoparticulate PLGA. Xenograft weight in treated animals at sacrifice was reduced by 50% ($P<0.01$). Tumor area measured in histologic sections was reduced by 80% in treated animals compared to controls ($P<0.001$). Blinded analysis of changes in histologic slides from xenografts revealed essentially complete loss of tumor blood vessels with NDAT ($P<0.001$ vs. control xenografts). This finding was associated with no evidence of hemorrhage. Eighty percent of the cell population in grafts was either necrotic or apoptotic ($P<0.001$ vs. control) and cell density was reduced by 60% vs. control tumors ($P <0.001$ vs. control). Mitotic figures/field examined was reduced by 80%. In summary, NDAT, acting at the thyroid hormone- tetrac receptor on the extracellular domain of integrin α vβ3, devascularized human GBM xenografts with resultant widespread necrosis. In the tumor cell population that was not necrotic, drug-induced apoptosis was documented. The thyroid hormone receptor on αvβ3 in U87MG cells is a single endocrine target with multiple downstream functions that are exploited by anticancer and antiangiogenic actions of NDAT ($P<0.001$ vs. control). Nano-diamino-tetrac (NDAT; Nano-tetrac) is an anticancer/anti-angiogenic agent targeted to the thyroid hormone-tetrac receptor on the extracellular domain of integrin α vβ3. He has good experience in the field of Cancer cell and stem cells and cell Biology . He is former Chair at the Department of Medicine, Albany Medical College. He is also an Endocrine Researcher. He described about thyroid hormone-tetrac receptor on integrin α vβ3.

NDAT inhibits PD-L1 inducible expression and protein accumulation by inhibition of activated ERK1/2 and PI3K. Knockdown PD-L1 has also inhibited the proliferation of oral cancer cells which suggests that the inhibitory effect of NDAT on the expression PD-L1 is perhaps one of the critical mechanisms for the NDAT-induced anti-proliferation effect in oral cancer cells. The graft shrinkage per day 10 in treated animals was at least 50% in weight/volume and 80% in the area on histological slides, compared to controls.

Its nano-particulate analogue, nano-diamino-tetrac (NDAT; Nanotetrac) is an anti-cancer/anti-angiogenic agent. In this study, the inhibitory mechanism by which NDAT inhibited the abundance of PD-L1 RNAM and the content of PD-L1 proteins in oral cancer cells was studied

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