## conferenceseries.com

8th World Congress and Expo on

## Cell & Stem Cell Research

March 20-22, 2017 Orlando, USA

## PD-L1 and PD-1 gene expression are both stimulated by thyroid hormone in cancer cells

Paul J Davis

Albany College of Pharmacy and Health Sciences, USA

The programmed death-1 (PD-1)/PD-ligand 1 (PD-L1) immune checkpoint modulates activated T cell-cancer cell interactions. The PD-L1 protein generated by tumor cells engages T lymphocyte PD-1 to suppress T cell engagement of tumor cells—protecting tumor cells from immune destruction-and may also induce T cell apoptosis. Overexpression of PD-L1 is seen in various human cancer cells and correlates with decreased patient survival. PD-1 antibodies (Opdivo\*; Keytruda\*) are effective anticancer agents in subsets of solid tumor and hematologic malignancy patients. Because these antibodies are effective in subsets of patients and also induce important adverse events (AE) in normal tissues that elaborate PD-L1, it is desirable to seek non-immunologic strategies for attacking the PD-1/PD-L1 checkpoint. We have shown that thyroid hormone (L-thyroxine, T4) at physiological concentrations acts non-genomically to stimulate cancer cell proliferation, to block apoptosis and to stimulate tumor-related angiogenesis. We report here that T4 stimulates PD-L1 gene expression by a mechanism that is initiated at the cell surface receptor for T4 on the extracellular domain of plasma membrane integrin avß3. T4 was studied in cultured human colon cancer HT-29 and HCT116 cells and triplenegative breast cancer MDA-MB-231 cells, at concentrations ranging from 10[-8] to 10[-6] M, where 10[-7] M yields physiological concentrations of free T4 in the culture system. T4 significantly increased PD-L1 mRNA abundance by 2-to-6-fold in HT-29 cells, by 2-fold in HCT116 cells and by 1.6-fold in breast cancer cells. An inhibitor of T4 actions at the integrin, tetraiodothyroacetic acid (tetrac), in a nanoparticulate formulation (Nano-diamino-tetrac, NDAT) intended to increase tetrac residence time at the integrin, blocked the actions of T4 on PD-L1 gene expression and significantly reduced basal PD-L1 expression. Basal expression is defined here as that which occurs in the absence of added T4. T4 also significantly increased PD-1 mRNA abundance in these tumor cell lines and NDAT blocked the T4 effect and significantly reduced basal levels of PD-1 mRNA. PD-1 is viewed primarily as T cell product, but has been reported to be expressed by a variety of solid tumor cells and we speculate in such cells, which may be anti-apoptotic. In summary, the components of the PD-1/PD-L1 check point are subject to non-immunologic modulation by T4 and by NDAT. The actions of NDAT in these in vitro studies have possible therapeutic implications

## Biography

Paul J Davis is a Professor of Medicine at Albany Medical College, and Chief Scientific Officer at NanoPharmaceuticals LLC, Rensselaer, NY. He is former Chair at the Department of Medicine, Albany Medical College. As an Endocrine Researcher, he has co-authored 250 scientific publications and has co-edited two text books on Angiogenesis (Springer, 2013; Elsevier, 2016). He and Dr. Shaker Mousa described the thyroid hormone-tetrac receptor on integrin αvβ3.).

pdavis.ordwayst@gmail.com

Notes: