

# 5<sup>th</sup> World Congress on Cell & Stem Cell Research

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## Anti-apoptotic actions of thyroid hormone in cancer cells may limit effectiveness of chemotherapy

Thyroid hormone as L-thyroxine (T<sub>4</sub>) is anti-apoptotic at physiological concentrations in a number of cancer cell lines. Among the mechanisms of anti-apoptosis activated by T<sub>4</sub> is interference with Ser-15 phosphorylation (activation) of p53 and with TNF $\alpha$ /Fas-induced apoptosis, as well as decreased cellular abundance of caspases and of BAX. Such actions of T<sub>4</sub> may oppose pharmaceutical anti-apoptotic strategies. The anti-apoptotic effects of thyroid hormone largely are initiated at a cell surface thyroid hormone receptor on integrin  $\alpha\beta$ 3. The integrin is amply expressed and activated in cancer cells, but not in nonmalignant, non-dividing cells. Nanoparticulate tetraiodothyroacetic acid (Nanotetrac) opposes actions of thyroid hormone initiated at  $\alpha\beta$ 3. We have studied the effects of Nanotetrac (10<sup>-7</sup> M) in vitro on expression of a panel of apoptosis-relevant cancer cell genes in human breast cancer MDA-MB-231 and human medullary thyroid carcinoma (mTC, CRL-1803) cell lines. CASP2, MCL2L14, DFFA, BAD and Bcl-Xs are pro-apoptotic genes whose expression was stimulated by Nanotetrac; XIAP and MCL1 are anti-apoptotic genes and their transcription in tumor cells was down regulated by Nanotetrac. Nanotetrac blocked the anti-apoptotic action of thyroid hormone in a stilbene-induced model of apoptosis in glioma cells. Thus, thyroid hormone (T<sub>4</sub>) is an endogenous anti-apoptotic factor that may oppose chemotherapy-induced apoptosis in  $\alpha\beta$ 3-expressing cancer cells. These actions of T<sub>4</sub> have been blocked in vitro by Nanotetrac and rationalize medical induction of euthyroidhypothyroxinemia.

### Biography

Davis is a graduate of Harvard Medical School and had his postgraduate medical training at Albert Einstein College of Medicine and the NIH. His academic positions have included Chair, Department of Medicine, Albany Medical College. He has served as President, American Thyroid Association, as a member of the Board of Directors of the American Board of Internal Medicine and he is Co-Head, Faculty of 1000 – Endocrinology. He serves on multiple Editorial Boards of His scientific interests include molecular mechanisms of actions of nonpeptide hormones, particularly, thyroid hormone. He and his colleagues described the cell surface receptor for thyroid hormone on integrin  $\alpha\beta$ 3 that underlies the pro-angiogenic activity of the hormone and the proliferative action of the hormone on cancer cells. He has co-authored more than 200 original research articles and 30 text book chapters and he has edited three medical text books.

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