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Possible clinical significance of reverse T3 (rT_3) and L-thyroxine (T_4) levels in cancer-related nonthyroidal illness syndrome (NTIS)

The nonthyroidal illness syndrome (NTIS) is a clinical constellation of changes in circulating thyroid hormone levels that occur in euthyroid patients with acute or chronic systemic diseases. The changes that occur include reduction in serum T_3, increase in serum rT_3 and variable changes in circulating T_4 levels. rT_3 and T_4 both have been viewed as metabolically inactive and as a result, no consensus yet exists on therapeutic intervention in the setting of NTIS. However, published observations from a number of laboratories and our own have described physiological actions of T_4 and of rT_3 that appear to be particularly relevant to cancer cells and endothelial cells. We analyze specifically here, the apparent significance of changes in circulating T_4 and T_3 and suggest that, in the setting of NTIS in cancer patients, therapeutic management of T_4 and rT_3should be considered. rT_3 can convert soluble to fibrous actin (F-actin), a critical contribution to mitosis, cell migration and invasiveness. rT_3 also has metabolic activity in certain brain cells and induces platelet aggregation that may contribute to increased coagulation observed in cancer patients. In the case of T_4, cancer-relevant actions include tumor cell proliferation and cancer-related angiogenesis. These effects are initiated at a cancer or endothelial cell plasma membrane receptor on integrin $\alpha v\beta_3$ that is generously expressed by tumor cells and blood vessel cells. T_4 also increases F-actin content of cells. The possible utility thus emerges of therapeutic intervention in NTIS in cancer patients in terms of T_4 reduction and of T_3 support. This prospective study is proposed of pharmacological reduction of normal or elevated T_4 in cancer-associated NTIS and of reduction of circulating rT_3 levels.

Biography

Paul J Davis is Professor and former Chair at the Department of Medicine in Albany Medical College. Currently, he is the Executive Vice President and Chief Scientific Officer at Nano Pharmaceuticals LLC, Rensselaer, NY, SA.

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