Thyroid hormone calorigenesis and mitochondrial redox signaling: Upregulation of gene expression

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Thyroid hormone (TH, T3) is required for the normal function of most tissues, with major effects on O2 consumption and metabolic rate. These are due to transcriptional activation of respiratory genes through the interaction of T3-liganded TH receptors with TH response elements or the activation of intermediate factors, with the consequent higher rates of mitochondrial oxidative phosphorylation and reactive O2 species (ROS) generation and antioxidant depletion. The genomic effects of TH are accompanied by redox upregulation of the liver expression of cytokines (tumor necrosis factor-alpha [TNF-alpha]), enzymes (manganese Superoxide dismutase), and antiapoptotic proteins (Bcl-2), via a cascade initiated by TNF-alpha produced by Kupffer cells and involving inhibitor of kappa-B phosphorylation and nuclear factor-kappa-B activation. Thus, TH calorigenesis triggers non-genomic effects leading to an expression pattern that may represent an adaptive mechanism to re-establish redox homeostasis