

# Kupffer cell-dependent signaling in thyroid hormone calorigenesis: Possible applications for liver preconditioning

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Thyroid hormone (L-3,3',5-triiodothyronine, T3) is important for the normal function of most tissues, with major actions on O<sub>2</sub> consumption and metabolic rate. In the liver, these are due to (i) transcriptional activation of respiratory genes leading to increased reactive O<sub>2</sub> species generation in mitochondria and other subcellular sites; and (ii) enhancement in the respiratory burst activity in Kupffer cells (KC), with consequent antioxidant depletion. Under these conditions, the redox upregulation of KC-dependent expression of cytokines (tumor necrosis factor- $\alpha$ , interleukin (IL)-1, IL-6) is achieved, thus triggering the expression of enzymes (inducible nitric oxide synthase, manganese superoxide dismutase), anti-apoptotic proteins (Bcl-2), acute phase proteins (haptoglobin,  $\alpha$ -fibrinogen), and hepatocyte proliferation. The above responses (i) represent adaptive mechanisms to re-establish redox homeostasis and promote cell survival; (ii) occur via nuclear factor- $\kappa$ B, signal transducer and