Thyroid Hormone-Induced Expression of the Hepatic Scaffold Proteins Sestrin2, beta-Klotho, and FRS2 in Relation to FGF21-AMPK Signaling

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Resumen
Thyroid hormone (3,3’, 5-triiodothyronine, T-3) accelerates energy metabolism in the liver through mechanisms involving upregulation of AMP-activated protein kinase (AMPK). This study aims to assess the influence of T-3 on the expression of the scaffold proteins beta-Klotho, fibroblast growth factor receptor substrate 2 alpha (FRS2 alpha), and Sestrin2 in relation to FGF21-AMPK signaling. Male Sprague-Dawley rats were given 0.1 mg T-3/kg or hormone vehicle (controls) and studies were done 24 h after treatment. These include measurements of the mRNA expression (qPCR) of hepatic beta-Klotho, FGF21, FGF21 receptor-1 (FGFR1), extracellular-signal-regulated kinase 1/2 (ERK1/2), FRS2 alpha, ribosomal S6 kinase-1 (RSK1), liver kinase B1 (LKB1), AMPK, and Sestrin2. Also, protein levels of FGF21, FGFR1 (ELISA), and ERK1/2 (Western blot) were measured. T-3 elicited a calorigenic response with higher hepatic mRNA expression of beta-Klotho, FRS2 alpha, and FGF21, increased serum FGF21, without changes in liver FGFR1 mRNA and its plasma levels. In addition, T-3 enhanced ERK1/2 phosphorylation and the mRNA expression of ERK1/2, RSK1, LKB1, AMPK, and Sestrin2. T-3 administration enhances liver FGF21-AMPK signaling involving upregulation of the scaffold proteins beta-Klotho, FRS2 alpha, and Sestrin2. beta-Klotho and FRS2 induction favours the operation of the FGF21-FGFR1-beta-Klotho complex as evidenced by the enhancement in ERK1/2 phosphorylation, whereas that of Sestrin2 recruits LKB1 to achieved AMPK activation, thus supporting a higher energy expenditure condition that may be desirable in some metabolic disorders

Palabras clave
Palabras clave de autor: thyroid hormone; liver; beta-Klotho; Sestrin2; FGF21-AMPK signaling
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