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Potential involvement of mammalian and avian uncoupling proteins in the thermogenic effect of thyroid hormones

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Abstract

Thyroid hormones (THs) have long been known to be involved in the control of thermoregulation in birds and mammals. In particular, they are reported to play a role in the regulation of heat production. The underlying mechanisms could be the stimulation of the nuclear and mitochondrial transcription of several genes involved in energy metabolism and/or a direct action on the activity of components of the mitochondrial respiratory chain. Attention has recently been focussed on a subfamily of mitochondrial anion carriers called uncoupling proteins (UCPs). These proteins are suspected to be involved in a partial dissipation of the mitochondrial proton electrochemical gradient that would uncouple phosphorylations from oxidations and hence produce heat. However, the involvement of uncoupling mechanisms in thermogenesis and particularly in the thermogenic effect of TH is still unclear. The thermogenic role of UCP1, specifically expressed in brown adipose tissue, and its regulation by TH in

Abbreviations: ADP, adenosine diphosphate; AMP, adenosine monophosphate; ANT, adenine nucleotide translocator; ATP, adenosine triphosphate; avUCP, avian uncoupling protein; BAT, brown adipose tissue; BMCP1, brain mitochondrial carrier protein 1; COX, cytochrome oxidase; DNA, deoxyribonucleic acid; HP, heat production; mRNA, messenger ribonucleic acid; FA, fatty acid; MTE I, mitochondrial thioesterase I; RCR, respiratory control ratio; ROS, reactive oxygen species; T_2, diiodothyronine; T_3, triiodothyronine; T_4, thyroxine; TH, thyroid hormone; TRE, T_3 response element; UCP, uncoupling protein

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rodents is quite well recognised, but the involvement in heat production of its mammalian homologues UCP2, ubiquitously expressed, and UCP3, muscle and adipose tissue-specific, as well as the role of the muscular avian UCP (avUCP), are to be further investigated. The expression of the UCP2 and UCP3 genes was shown to be enhanced by TH in muscle of several rodent species, and to be increased in situations where thermogenesis is stimulated, whereas results are more contrasted in pig. There is now increasing evidence that the physiological role of the mammalian UCP3 and UCP2 is rather related to lipid oxidation and/or prevention of reactive oxygen species accumulation than to heat production by uncoupling. The expression of avUCP was also recently demonstrated to be strongly regulated by thyroid status in chicken, and overexpressed in experimental conditions favouring high triiodothyronine concentrations and thermogenesis. However, its real uncoupling activity and contribution to thermogenesis remain to be established.

Keywords: Thyroid hormones; Uncoupling proteins; UCP; Thermogenesis

Thyroid hormones (THs), especially triiodothyronine (T_3), are considered to be major regulators of energy metabolism and mitochondrial functioning in both mammalian and avian species [1,2]. Although the calorigenic role of THs has been known for a long time, the pathways mediating thyroid thermogenesis are still debated. During the last decades, an increasing number of publications have highlighted both short- and long-term increases in mitochondrial O_2 consumption after a TH treatment (Fig. 1).

1. Thyroid hormones and thermogenesis

It is now well established that the effect of THs on thermogenesis occurs within the first hour post-treatment, especially with changes in calcium signalling and stimulation of catecholamine-induced lipolysis [3,4]. More recently, THs were also shown to affect directly the functioning of some protein and enzymes, including protein kinase C, cAMP-dependent

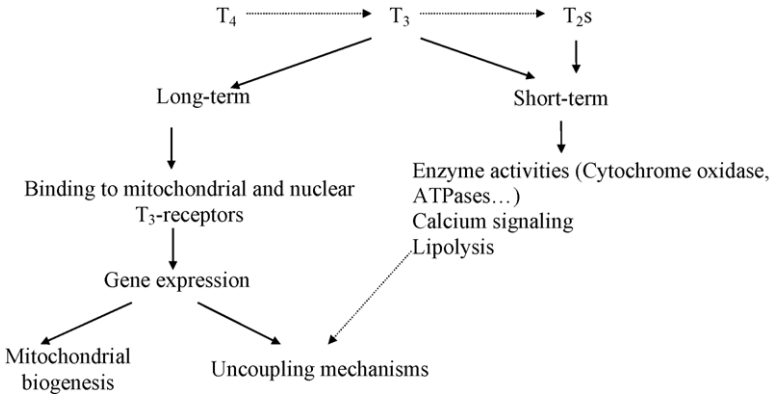

Fig. 1. Short-and long-term mechanisms involved in thyroid thermogenesis.