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## Thyrotropin-Releasing Hormone Selectively Stimulates Human Hair Follicle Pigmentation.

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## Abstract

In amphibians, thyrotropin-releasing hormone (TRH) stimulates skin melanophores by inducing secretion of  $\alpha$ -melanocyte-stimulating hormone in the pituitary gland. However, it is unknown whether this tripeptide neurohormone exerts any direct effects on pigment cells, namely, on human melanocytes, under physiological conditions. Therefore, we have investigated whether TRH stimulates pigment production in organ-cultured human hair follicles (HFs), the epithelium of which expresses both TRH and its receptor, and/or in full-thickness human skin in situ. TRH stimulated melanin synthesis, tyrosinase transcription and activity, melanosome formation, melanocyte dendricity, gp100 immunoreactivity, and microphthalmia-associated transcription factor expression in human HFs in a pituitary gland-independent manner. TRH also stimulated proliferation, gp100 expression, tyrosinase activity, and dendricity of isolated human HF melanocytes. However, intraepidermal melanogenesis was unaffected. As TRH upregulated the intrafollicular production of "pituitary" neurohormones (proopiomelanocortin transcription and ACTH immunoreactivity) and as agouti-signaling protein counteracted TRH-induced HF pigmentation, these pigmentary TRH effects may be mediated in part by locally generated melanocortins and/or by MC-1 signaling. Our study introduces TRH as a novel, potent, selective, and evolutionarily highly conserved neuroendocrine factor controlling human pigmentation in situ. This physiologically relevant and melanocyte sub-population-specific neuroendocrine control of human pigmentation deserves clinical exploration, e.g., for preventing or reversing hair graying. Journal of Investigative Dermatology advance online publication, 29 September 2011; doi:10.1038/jid.2011.221.

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