

## EXPRESSION OF THE UNCOUPLING PROTEIN (UCP) FROM RAT BROWN ADIPOSE TISSUE BY TRANSPLATABLE HUMAN EPIDERMAL CELLS

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The brown adipose tissue (BAT) is the major site of facultative non shivering thermogenesis in small mammals and is the only known tissue which has as main function the heat production. The high capacity of BAT to increase heat production rests on its capacity to respond to sympathetic stimulation with marked increments in respiration that are uncoupled from ATP synthesis. The abundant BAT mitochondria contain a unique uncoupling protein (UCP) that dissipates the proton gradient created by the respiratory chain, bypassing the less abundant ATP synthetase. This markedly accelerates mitochondrial respiration without the corresponding synthesis of ATP. Using different technical approaches, i.e. western blotting, PCR, northern blotting, it was found that this gene is only expressed in the brown adipocytes, what makes it a marker for the BAT.

The purpose of the present work was to obtain transduced primary human keratinocytes able to express rat UCP. For this purpose a retroviral vector has been constructed introducing rat UCP cDNA, under transcriptional control of the strong " long terminal repeat" (LTR) promoter, into the well known LXS vector, already successfully used in human cells transduction. Work is in progress in order to obtain UCP into human keratinocyte mitochondria and to graft an epithelial sheet, prepared with the transduced cells, on mice (nude, scid or ob/ob mutant), to observe a possible phenotypic alteration. This gene therapy approach represents a valuable model that may aid studies of the pathogenesis and treatment of human obesity and insulin resistance.

Financial support: RHAЕ-CNPq (Brasilia), FAPESP (São Paulo)