TRANSPORT OF UROCORTIN AND LEPTIN IN CEREBRAL MICROVESSELS AND THE IMPLICATIONS IN OBESITY

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The endogenous peptides/polypeptides produced in peripheral tissue may affect the functions of the central nervous system (CNS) by crossing the blood-brain barrier (BBB). Both urocortin and leptin reduce feeding behavior, thus decreasing diet-induced obesity. We show that the blood-to-brain permeation of urocortin is facilitated by leptin in mice, and that urocortin binding and endocytosis in cultured endothelial cells are increased in the presence of leptin. Fluorescent trafficking studies further illustrate the interactions of the two ligands and their receptors as well as the role of signaling transduction in the trafficking process. We also determined the cytoplasmic domains partitioning clathrin- or caveolae-mediated endocytosis and intracellular degradation by lysosomes and proteasomes. Results from the cellular studies will help further understanding of the regulation of obesity in animals and humans.

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