

ICCN Poster Presentations

Obesity

Genetic linkage of uncoupling proteins (UCP2 and UCP3) with body weight regulation

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Body weight depends on the balance between energy intake and energy expenditure. The discovery of the novel UCPs (UCP2/UCP3) in 1997 led to an explosive reinvestigation of thermogenesis, fuel utilization and possibility that these new gene products might be genetically linked to certain metabolic disorders. Also, UCPs might be targets for therapeutic interventions for obesity, Type II diabetes, pathophysiological cachexia conditions (e.g. AIDS, cancer) and above all their utility in the search for drugs to combat obesity. The UCP2 (a gene transcribed in various tissues) is located on chromosome 7 of the mouse and chromosome 11 of humans, near to region linked to diabetes and obesity (QTL linkage to hyperinsulinemia and high plasma Leptin levels). UCP3 (a gene transcribed predominantly in skeletal muscles of rodent and human) is very close to UCP2 gene location. These two genes have an organization similar to that of UCP1 gene. The exon 8 ins/del polymorphism of UCP2 appears to be associated with childhood-onset obesity. The UCP2 / UCP3 genetic locus may play a role in childhood body weight. All physiological situations involving notable changes in energy balance (fasting, over eating, infections, most hormones and neuromediators such as catecholamins and Leptin) alter the expression of the UCP2 and UCP3 genes thus pointing the role UCPs in energy expenditure. Some studies showed that level of UCP2 and UCP3 increased during starvation without changing heat production and suggested that these genes are involved in diet - induced thermogenesis. The expression of UCP2 by using fat - rich diet was specifically elevated in white adipose tissues in strains of mice that are relatively resistant to the diet - induced obesity and diabetes, but not in obesity - prone mice. Phenotypes of mice with targeted disruption of the UCP3 gene were at the very least, disappointing from the perspective of metabolic control of body weight and glucose homeostasis. It has been shown that the changes in UCP2 and UCP3 gene and protein expression are involved in the regulation of substrate utilization in post traumatic insulin resistance and systemic EGF administration of rats. Expression of UCP2 and UCP3 seems to be related to lipid metabolism. However the molecular mechanisms regulating these genes are currently under investigation and after 2 to 3 years of research the role of UCPs in metabolism, oxidation of lipids and other substrates and the control of body weight is still relatively unclear.