Obesity results from an imbalance between caloric intake and energy expenditure, which is partly genetically determined.

Objectives: We have investigated, using a PCR-RFLP assay, the effects on weight gain of two genetic variants of the uncoupling protein and the β3-adrenoceptor, two major expressed proteins of the brown adipose tissue (BAT) involved in thermo-genesis.

Subjects: 238 morbidly obese and 91 non-obese Caucasians subjects.

Results: A high prevalence (27%) in French Caucasians of the A→G change variation located in the 5' flanking domain of the UCP gene was observed with no significant difference between morbidly obese patients and non-obsese subjects, suggesting that UCP gene is not a major gene for obesity. However, in the population of morbidly obese subjects, the presence of the A→G allelic variant of the UCP gene showed to be an associated factor of high weight gain during adult life (odd-ratio: 1.4, $P = 0.02$). Such an association was previously described for the Trp64Arg mutation of the β3-AR gene. Furthermore, an additive effect of these two gene variants on weight gain was observed (odd-ratio: 4.95, trend test: $P = 0.05$). The attributable risks for UCP gene and β3-AR gene variants were respectively 25% and 9%.

Conclusion: These data support the hypothesis of a possible link between energy balance, BAT and weight gain in obsese human subjects.

Hyperglycemia, but not hyperinsulinemia, inhibits liver glucose-6 phosphatase activity in rat. L Guignot, G Mithieux *(Inserm U 449, faculté de médecine René-Laënnec, 69372 Lyon cedex 08, France).*

It has recently been reported that liver glucose-6 phosphatase (Glc6Pase) activity is inhibited by 3 h-refeeding in rats. To study the respective roles of hyperglycemia and hyperinsulinemia in this inhibition, we have performed hyperinsulinic euglycemic and hyperglycemic clamps in rats. Five hours after food removal, anesthetized rats were perfuse for 3 h with saline (S), or with insulin at 480 pmol/h (I), or with glucose at 2.4 mmol/h (G1) and 3.9 mmol/h (G2). In group I, the perfusion of 1.29 ± 0.01 mmol/h glucose (mean ± SEM, $n = 5$) has been required to maintain glycemia at the basal level. Hepatic glucose production (HGP) was assessed by [3-^{3}H]glucose dilution and Glc6Pase assayed in homogenates from liver lobes freeze-clamped in situ. The results were:

Group	n	*Final glycemia mmol/L*	*Final insulinemia pmol/L*	*HGP µmol/kg/min*	*Glc6Pase U/g wet liver*
S	5	8.6 ± 0.5	185 ± 17	77 ± 9	8.1 ± 0.1
I	5	7.7 ± 1.4	461 ± 45*	21 ± 12*	7.7 ± 0.6
G1	4	12.6 ± 0.1*	567 ± 47*	27 ± 2*	6.1 ± 0.6°
G2	4	17.3 ± 0.9*	876 ± 68*	0.3 ± 6*	6.0 ± 0.4*

The data are expressed as mean ± SEM
°, *: different from S value, $P < 0.05$, $P < 0.01$, respectively.

GlcPase was not inhibited under euglycemic hyperinsulinic conditions (group I), and was significantly inhibited under hyperglycemic conditions (G1 and G2). Our data strongly suggest that hyperglycemia, but not hyperinsulinemia, could account for the inhibition of liver Glc6Pase activity during the postprandial period. This phenomenon might play an important role in the suppression of HGP in this situation.

The expression of ob gene is not acutely regulated by insulin and fasting in human abdominal subcutaneous adipose tissue. H Vidal [1], D Aubœuf [1], P de Vos [3], B Staels [3], JP Riou [1,2], J Auwerx [3], M Laville [1,2] *([1] Inserm U 449, faculté de médecine René-Laënnec, 69373 Lyon cedex 08; [2] Centre de recherche en nutrition humaine de Lyon, Hôpital Edouard-Herriot, 69472 Lyon cedex; [3] Inserm U 325, Institut Pasteur, rue Professeur Calmette, 59019 Lille, France).*

In rodents, the expression of leptin, the product of ob gene, is increased by insulin and decreased by fasting [Saladin et al (1995), *Nature* 377, 527-529; Trayhurn et al (1995), *FEBS Lett* 368, 488-490; Frederich et al (1995), *J Clin Invest* 96, 1658-1663]. In the present work, we investigated the regulation of ob gene expression in human abdominal subcutaneous adipose tissue using a reverse transcription-competitive PCR method to quantify the mRNA level of leptin. Leptin mRNA level was highly correlated ($r = 0.9$) with the body mass index of 26 subjects (12 lean, seven non insulin-dependent diabetic and seven obese patients). The effect of fasting on ob gene expression was investigated in ten subjects maintained on a hypocaloric diet (250 Kcal/day) for 5 days. While their metabolic parameters significantly changed (decrease in insulinemia, glycemia and resting metabolic rate and increase in plasma ketone bodies), the caloric restriction did not modify significantly the leptin mRNA level in the adipose tissue. To verify whether insulin acutely regulates ob gene expression, six lean subjects underwent a 3 h euglycemic hyperinsulinemic (846 ± 138 pmol/L) clamp. Leptin and Glut 4 mRNA levels were quantified in adipose tissue biopsies taken before and at the end of the clamp. Insulin infusion produced a significant 3-fold increase in Glut 4 mRNA while leptin mRNA was not affected. It is concluded that ob gene expression is not acutely regulated by insulin or by metabolic factors related to fasting in human abdominal subcutaneous adipose tissue. Our data question therefore the role of leptin as a tightly controlled satiety factor in human but rather suggest that leptin signals the size of the adipose tissue deposit.

Glucose inhibits expression of the cytosolic aspartate aminotransferase gene in 3T3-F442A adipocytes: involvement of the promoter-regulatory region. E Plee-Gautier [1], M Aggerbeck [2], R Barouki [2], C Forest [1] *([1] Centre de recherche sur l'endocrinologie moléculaire et le développement, CNRS, 9, rue Jules-Hetzel, 92190 Meudon; [2] Inserm U 99, Hôpital Henri-Mondor, 51, av Maréchal de Lattre-de-Tassigny, 94010 Créteil, France).*

Aspartate aminotransferase (AspAT) is an ubiquitous enzyme involved in the malate-aspartate shuttle, urogenesis, gluconeogenesis and amino-acid metabolism. Two isoforms of the enzyme have been described: a cytosolic one (cAspAT) and a mitochondrial one (mAspAT). Although cAspAT is expressed at similar levels in all tissues, it is specifically regulated by glucocorticoids and glucagon in liver [Pavé-Preux et al (1988), *J Biol Chem* 263, 17459-17466] in which the enzyme is involved in gluconeogenesis. Regulation of cAspAT gene expression has been extensively studied in Fao hepatoma cells. In such cells, the rate of cAspAT gene transcription is increased by