International Journal of Obesity (2007) 31, 392–393
 0307-0565/07 $30.00
www.nature.com/ijo

LETTER TO THE EDITOR

The link between obesity and allergy: a role of ACP1 genetic polymorphism?

International Journal of Obesity (2007) **31,** 392–393.
doi:10.1038/sj.ijo.0803396; published online 13 June 2006

In a recent commentary[1] on the relationship between asthma and obesity, Weiss has stressed that 'among the most interesting area of research in this field, is the possible inter-relationship between genes known to be important in asthma that may also be important in obesity'. Pleiotropic genes could have an important role in both complex traits. This interesting concept prompted us to compare the association between ACP1 genetic polymorphism and obesity previously described by us[2] with more recent data showing a relationship between ACP1 and allergy.

ACP1 is a polymorphic gene located on chromosome 2 showing three common codominant alleles: ACP1*A, ACP1*B and ACP1*C. These three alleles are associated with different enzymatic activity. At present, the term ACP1 is used to indicate the gene, whereas the protein product is called LMPTP (Low Molecular Weight Protein Tyrosine Phosphatase). Two functions have been suggested for LMPTP: flavin mononucleotide phosphatase and protein tyrosine phosphatase. By catalyzing the conversion of flavin mononucleotide to riboflavin, LMPTP may have a role in regulating the cellular concentration of flavin adenine dinucleotide, flavo enzyme activity and energy metabolism. As protein tyrosine phosphatase, the enzyme may have an important role in modulation of glycolytic rate through the control of insulin receptor activities and of band 3 protein phosphorylation (see Bottini *et al.*[3] for review).

More recently,[4] it has been shown that LMPTP dephosphorylates a negative regulatory phosphorylation site in the ZAP70 tyrosine kinase in T cells, leading to increased activation of this kinase and enhanced signalling through the T-cell antigen receptor.

Table 1 shows a summary of our observations in the relationship between the ACP1*A allele and degree of obesity. Subjects carrying the *A allele show more severe deviation of body mass index. The study includes 173 female and 55 male subjects. No significant difference has been observed between sexes.

Table 2 shows the relationship between the presence of *A allele and prick test positivity separately in male and female subjects. In female subjects, there is a highly significant positive association between prick test positivity and presence of *A allele. In male subjects, the pattern is reversed but the association between prick test and *A allele does not reach the level of statistical significance.

Our data suggest that the presence of *A allele in female subjects is associated positively with both prick test positivity and severe obesity. More data are necessary to define the situation in male subjects.

Table 1 The relationship between the presence of *A allele and degree of obesity (see Paggi *et al.*[2] for details)

Obesity	*Proportion of phenotypes carrying the *A allele (A, BA and CA phenotypes)*	*Total no.*
Moderate, BMI $\leqslant$ 35	36.8%	163
Severe, BMI $>$ 35	61.5%	65
χ^2 test of independence = 8.60, d.f. = 1, P = 0.008, OR = 2.45 (95% CI 1.32–4.56)		

Abbreviation; BMI, body mass index.

Table 2 The relationship between the presence of *A allele and allergy (prick test positivity)

	Proportion of subjects prick positive (%)	*Total no.*	
Male subjects			
Carrying the *A allele (A, BA and CA phenotypes)	20.4	49	
Not carrying the *A allele	38.2	34	
Female subjects			
Carrying the *A allele (A, BA and CA phenotypes)	47.5	101	
Not carrying the *A allele	19.7	71	
Three-way contingency table analysis by a log-linear model (x = prick; y = ACP1; z = gender)	G	*df*	P
x, y, z interaction	12.96	1	$<$0.001
Independence of prick test from ACP1 Males: P = NS, OR = 0.41 (95% CI 0.14–1.22) Females: $P<0.001$, OR = 3.69 (95% CI 1.73–7.94)			

The data refer in part to randomly selected subjects from the general population and in part to subjects admitted to the hospital for surgical problems. No difference in the pattern of association with ACP1 was observed between the two samples.

Table 3 A scheme depicting the function of ACP1

Function as protein tyrosine phosphatase	Possible effects of low enzymatic activity
● Dephosphorylation of the negative regulatory Tyr 292 of ZAP-70	● Favours Th2 orientation[5]
● Dephosphorylation of the insulin receptor	● Increases the effects of insulin on adipocytes
● Dephosphorylation of adipocyte lipid binding protein	● Favours lipid deposition in adipocyte
Function as flavin mononucleotide phosphatase	
● Dephosphorylation of FMN	● Increases FMN concentration, flavoenzyme activity and metabolic output

Abbreviation; FMN, flavin mononucleotide.

The function of LMPTP and the possible effects of low enzymatic activity are described in Table 3. Clearly, LMPTP could have a pleiotropic influence on many systems and metabolic pathways with possible effects on immune reaction, glycide metabolism, fat disposal and metabolic output.

Our observations suggest that ACP1 could be a pleiotropic gene contributing to the epidemiological link between asthma and obesity.

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