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A novel missense mutation T101N in the melanocortin-4 receptor gene associated with obesity

S. Buchbinder[1], U. Bärtsch[1], M. Müller[2], M. Zorn[1], P.P. Nawroth[1] and T. Schilling[1]

[1]Department of Internal Medicine 1 and Clinical Chemistry, University of Heidelberg, Heidelberg, Germany
[2]Department of Internal Medicine 4, University of Heidelberg, Heidelberg, Germany

Corresponding author: T. Schilling
E-mail: Tobias_Schilling@med.uni-heidelberg.de

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ABSTRACT. Mutations in the melanocortin-4 receptor (MC4R) are associated with severe obesity, independent of their effect on cortisol or thyroid-stimulating hormone levels. We examined a morbidly obese male (BMI = 62 kg/m^2) with a binge-eating disorder and eight family members for mutations in the MC4R gene and potential differences in leptin levels. Fifty healthy individuals served as controls. Sequence analysis revealed a novel heterozygous missense mutation (c.302 C>A, p.T101N) located in the second transmembrane domain of the receptor, which was not detected in controls. The Fisher exact test revealed an association between the T101N mutation and history of obesity ($P < 0.05$) in the family. The Kruskal-Wallis test showed an association between the mutation and the leptin/BMI ratio ($P < 0.05$), while there was no association between the T101N mutation and diabetes or arterial hypertension in the family. Although the available family was small, we could show a significant association between the heterozygous T101N mutation and obesity.

Key words: MC4R gene; BMI; Leptin; Obesity

