

Association of Ghrelin Polymorphisms with Metabolic Syndrome in Han Nationality Chinese¹

LING-LING XU[#], HONG-DING XIANG^{#,2}, CHANG-CHUN QIU⁺, AND QUN XU⁺

[#]Department of Endocrinology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing 100730, China; ⁺National Laboratory of Medical Molecular Biology, School of Basic Medicine, Peking Union Medical College, Institute of Basic Medical Science, Chinese Academy of Medical Science, Beijing 100005, China

Objective To investigate the association of ghrelin gene polymorphisms with metabolic syndrome in Han Nationality Chinese. **Methods** A total of 240 patients with metabolic syndrome and 427 adults aged above forty years were recruited. Genotypes were determined by polymerase chain reaction and restriction fragment length polymorphism analysis. **Results** The allelic frequency of the Leu72Met polymorphism was 17.3% in the patient group and 11.9% in the control group ($\chi^2=7.36$, $P=0.007$). Metabolic syndrome was more prevalent among carriers of the Met72 variant (43.8 vs 33.1%, age- and sex-adjusted odds ratio=1.57, $P=0.01$). No Arg51Gln variants were found in our study subjects. **Conclusion** Rather than being associated with its individual components, Leu72Met polymorphism is associated with metabolic syndrome in the Han Nationality Chinese. Arg51Gln polymorphism is rare in the Han Nationality Chinese.

Key words: Ghrelin; Polymorphism; Metabolic syndrome; the Han Nationality

REFERENCES

1. Kojima M, Hosoda H, Date Y, *et al.* (1999). Ghrelin is a growth —hormone—releasing acylated peptide from stomach. *Nature* **402**, 656-660.
2. Broglio F, Arvat E, Benso A, *et al.* (2002). Ghrelin, a natural GH secretagogue produced by the stomach, induces hyperglycemia and reduces insulin secretion in humans. *J Clin Endocrinol Metab* **86**, 5083-5086.
3. Wren A M, Small C J, Ward H L, *et al.* (2000). The novel hypothalamic peptide ghrelin stimulates food intake and growth hormone secretion. *Endocrinology* **141**, 4325-4328.
4. Nakazato M, Murakami N, Date Y, *et al.* (2001). A role for ghrelin in the central regulation of feeding. *Nature* **409**, 194-198.
5. Muccioli G, Tshop M, Papotti M, *et al.* (2002). Neuroendocrine and peripheral activities of ghrelin: implications in metabolism and obesity. *Eur J Pharmacol* **440**, 235-254.
6. Mclaughlin T, Abbasi F, Lamendola C, *et al.* (2004). Plasma ghrelin concentrations are decreased in insulin-resistant obese adults relative to equally obese insulin-sensitive controls. *J Clin Endocrinol Metab* **89**, 1630-1635.
7. Katsuki A, Urakawa H, Gabazza E C, *et al.* (2004). Circulating levels of active ghrelin is associated with abdominal adiposity, hyperinsulinemia and insulin resistance in patients with type 2 diabetes mellitus. *Eur J Endocrinol* **151**, 573-577.
8. Dezaki K, Hosoda H, Kakei M, *et al.* (2004). Endogenous ghrelin in pancreatic islets restricts insulin release by attenuating Ca^{2+} signaling in β -cells. *Diabetes* **53**, 3142-3151.
9. Wierup N, Yang S, McEvelly R J, *et al.* (2004). Ghrelin is expressed in a novel endocrine cell type in developing rat islets and inhibits insulin secretion from INS-1(832/13) cells. *J Histochem Cytochem* **52**, 301-310.
10. Langenberg C, Bergstrom J, Laughlin G A, *et al.* (2005). Ghrelin and the Metabolic syndrome in older Adults. *J Clin Endocrinol Metab* **90**, 6448-6453.
11. Wajanrajch M P, Ten I S, Gertner J M, *et al.* (2000). Genomic organization of human ghrelin gene. *J Endocr Genet* **1**, 231-233.
12. Poykko S, Ukkola O, Kauma H, *et al.* (2003). Ghrelin Arg51Gln mutation is a risk factor for type 2 diabetes and hypertension in a random sample of middle-aged subjects. *Diabetologia* **46**, 455-458.
13. Poykko S M, Kellokoski E, Horkko S, *et al.* (2003). Low plasma ghrelin is associated with insulin resistance, hypertension, and the prevalence of type 2 diabetes. *Diabetes* **52**, 2546-2553.
14. Ukkola O, Ravussin E, Jacobson P, *et al.* (2002). Role of ghrelin polymorphisms in obesity based on three different studies. *Obes Res* **10**, 782-791.
15. Bing C, Ambye L, Fenger M, *et al.* (2005). Large-scale studies of the Leu72Met polymorphism of the ghrelin gene in relation to the metabolic syndrome and associated quantitative traits. *Diabet Med* **22**, 1157-1160.
16. International Diabetes Federation (2005). The IDF consensus worldwide definition of the metabolic syndrome. Available from http://www.idf.org/webdata/docs/Metabolic_syndrome_definition.

¹This study was supported by the Capital Development Fund Project (Grant No. 2002-1017).

²Correspondence should be addressed to Hong-Ding XIANG. Tel: 86-10-65295084. E-mail: Xiang_hd@sohu.com

Biographical note of the first author: Ling-Ling XU, female, born in 1972, attending physician, M. D., majoring in endocrinology.

- Pdf. Accessed 2 September.
17. Kim S Y, Jo D S, Hwang P H, *et al.* (2006). Preproghrelin Leu72Met polymorphism is not associated with type 2 diabetes mellitus. *Metabolism Clin & Exp* **55**, 366-370.
 18. Dunstan D W, Zimmet P Z, Welborn T A, *et al.* (2002). The rising prevalence of diabetes and impaired glucose tolerance. The Australian Diabetes, Obesity and Lifestyle Study. *Diabetes Care* **25**, 829-834.
 19. Ford E S, Giles W H, Dietz W H (2002). Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA* **287**, 356-359.
 20. Gu D F, Reynolds K, Yang W J, *et al.* (2005). The prevalence of metabolic syndrome in the general adult population aged 35-74 years in China. *Chin J Diabetes* **13**, 181-186.
 21. Ott V, Fasshauer M, Dalski A, *et al.* (2002). Direct peripheral effects of ghrelin include suppression of adiponectin expression. *Horm Metab Res* **34**, 640-645.
 22. Dixit V D, Schaffer E M, Pyle R S, *et al.* (2004). Ghrelin inhibits leptin- and activation-induced proinflammatory cytokine expression by human monocytes and T cells. *J Clin Invest* **114**, 57-66.
 23. Misquitta C M, Iyer V R, Werdyuk E S, *et al.* (2001). The role of 3'-untranslated region (3'-UTR) mediated mRNA stability in cardiovascular pathophysiology. *Mol Cell Biochem* **224**, 53-67.
 24. Tanaka M, Hayashida Y, Nakao N, *et al.* (2001). Testis-specific and developmentally induced expression of a ghrelin gene-derived transcript that encodes a novel polypeptide in the mouse. *Biochim Biophys Acta* **1522**, 62-65.
 25. Steinle N I, Pollin T I, O'Connell J R, *et al.* (2005). Variants in the ghrelin gene are associated with metabolic syndrome in the Old Order Amish. *J Clin Endocrinol Metab* **90**, 6672-6677.

(Received February 20, 2007 Accepted December 3, 2007)