RESEARCH NOTE

Strong association of the SNP rs17822931 with wet earwax and bromhidrosis in a Chinese family

DANDAN SHANG[1]*, XUE ZHANG[2], MIAO SUN[2], YANG WEI[2] and YARAN WEN[3]

[1]*Department of Biochemistry and Molecular Biology, Hebei Key Laboratory of Medical Biotechnology, Hebei Medical University, Shijiazhuang, Hebei Province 050017, People's Republic of China*
[2]*McKusick-Zhang Center for Genetic Medicine and State Key Laboratory of Medical Molecular Biology, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100005, People's Republic of China*
[3]*Department of Human Genetics, Emory University School of Medicine, Atlanta, GA 30322, USA*

[Shang D., Zhang X., Sun M., Wei Y. and Wen Y. 2013 Strong association of the SNP rs17822931 with wet earwax and bromhidrosis in a Chinese family. *J. Genet*. **92**, 289–291]

Introduction

Wet earwax is a dominant Mendelian trait associated with the GA/GG genotype of SNP rs17822931 in the *ABCC11* gene. It is also often associated with the axillary odour (bromhidrosis). To investigate their possible relationship we genotyped rs17822931 in a Chinese family affected with axillary odour. Direct sequencing and RFLP analysis of *ABCC11* reveal that all the available eight family members with wet earwax and bromhidrosis harbour the same genotype (AG) in rs17822931 without any pathogenic mutations in *ABCC11* exons. We confirmed the relationship between allele A, wet earwax and axillary odour in a Chinese family for the first time.

Earwax (cerumen, a secretory product of ceruminous glands) is a dimorphic Mendelian trait of wet and dry types (Matsunaga 1992). An association study in 33 different populations around the world proved that the wet earwax phenotype is dominant over the dry one. The SNP rs17822931 in the *ABCC11* gene determines the earwax type; the AA genotype corresponds to dry earwax and GA or GG to the wet type. This is the first example of a DNA polymorphism determining an easily detectable phenotype (Yoshiura *et al.* 2006).

Bromhidrosis is a clinical disorder characterized by excessive or abnormal foul axillary odour due to the interaction of apocrine glands with microorganisms (Hurley 1992). Presence of axillary odours is a common phenomenon in postpubertal individuals among black and white populations, but in Asian populations the condition interferes with the lives of affected individuals and people around (Leyden *et al.* 1981).

Wet earwax is often associated with axillary odour as the two characters sometimes appear in combination in populations. Both conditions have a common origin of involvement of secretory glands, which suggest that wet earwax may be genetically related to axillary odour (Bang *et al.* 1996; Shugyo *et al.* 1988).

Here we report findings from a Chinese family where all members have wet earwax phenotype in addition to bromhidrosis. We performed genetic analysis of the *ABCC11* gene in this family in an effort to explore the relationship of the two phenotypes.

Materials and methods

Family

The family consists of 17 members of four generations including nine affected individuals with both wet earwax and bromhidrosis (figure 1a). Bromhidrosis, which varies in severity among different family members, was the main reason for genetic counselling. None of the eight unaffected members has wet earwax or bromhidrosis.

Methods

We performed PCR amplification with a 378-bp product including rs17822931 and directly sequenced the products in family member III-5. RFLP analysis was performed with the same PCR products of all the 14 available samples. The existence of allele A generates a 311-bp product following *Bse*MII digestion. Mutation screening of 30 exons in the *ABCC11* gene (GenBank accession no. NM_032583) was also performed by PCR amplification and subsequent direct sequencing using DNA samples of III-5 using

*For correspondence. E-mail: lily.dandan@163.com.

Keywords. rs17822931; *ABCC11*; wet earwax; bromhidrosis.

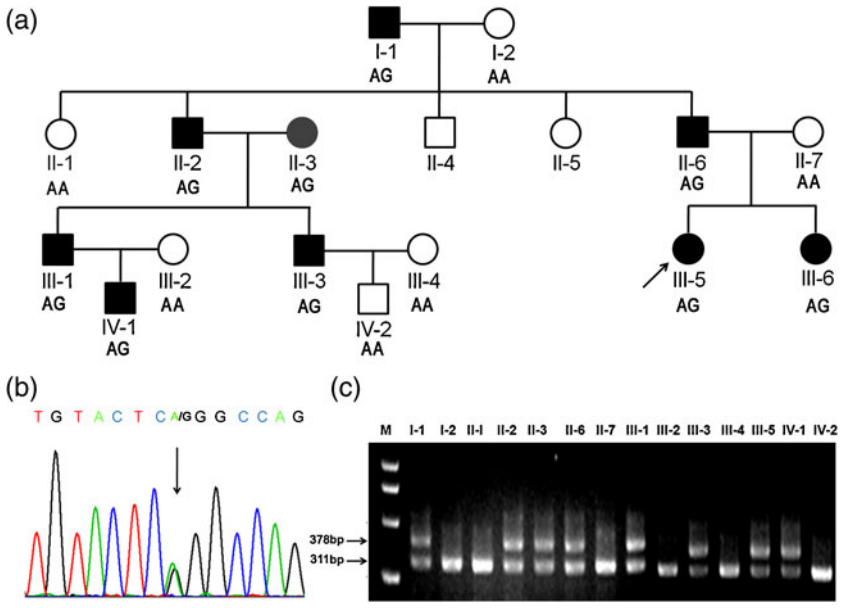

Figure 1. (a) Pedigree of the family with wet earwax and bromhidrosis. Blood samples of family members II-4 and II-5 are not available. Genotype of rs17822931 for each member available are also noted. (b) Sequencing chromatogram of SNP rs17822931 in III-5. Arrow indicates genotype AG of rs17822931 in III-5. (c) RFLP analysis of exon 5 in *ABCC11* in the family members. AG and AA genotypes of rs17822931 give two bands and one band respectively in 1.5% agarose gel electrophoresis.

standard conditions. Information on the primers is available on request.

Results

The genotype of rs17822931 in the proband was confirmed to be AG by direct sequencing (figure 1b). RFLP analysis revealed that all of the available eight family members with both wet earwax and bromhidrosis harbour the same genotype (AG) in rs17822931 (figure 1c). The other, unaffected members have genotype AA.

Screening of 30 exons in the *ABCC11* gene in III-5 did not reveal any pathogenic mutations except for a synonymous mutation of c.964A>G (Gly300) in exon 7 which was reported before (Yoshiura *et al.* 2006).

Discussion and conclusion

This is the first report of a Chinese family with both wet earwax and bromhidrosis. Genotyping of rs17822931 confirmed the relationship between allele A and wet earwax as a dominant phenotype which is consistent with the result of a previous population association study (Yoshiura *et al.* 2006). The correlation between bromhidrosis and wet earwax has been noticed in populations and their coexistence in the members of this family further proved this, but the genetic relationship of these two phenotypes remained unclear. In this study all the members in the family with wet earwax were also affected with bromhidrosis and harbour the genotype AG in rs17822931. This raised the possibility that bromhidrosis as a phenotype or pathogenic condition may be the second condition associated with the genotype of rs17822931.

The ceruminous gland secreting wet earwax is an apocrine gland, as are axillary and breast glands (Petrakis *et al.* 1990). Mammary gland colostrum secretion, which is another apocrine-gland-related secretion, has also been shown to be associated with human earwax type (Miura *et al.* 2007). Histological study of axillary skin has found that axillary odour is also related to the excessive secretion of large-sized apocrine glands (Bang *et al.* 1996). Combined with our findings in this family, there is a possibility that wet earwax and bromhidrosis are strongly correlated or determined by the same genetic factor.

Large-scale population association studies may be necessary to confirm bromhidrosis as the second genetic trait determined by SNP rs17822931. This is worthy of serious attention, especially in Asian countries, such as Japan and China where it is considered to be a pathogenic condition owing to its rarity and usually requires medical attention. As in this Chinese case axillary odour is an unpleasant and distressing problem for affected persons as evidenced by the fact that some of them seek prenatal diagnosis to prevent transmission to the next generation.

Acknowledgements

We thank all family members for their cooperation in this study. This work was supported by the National Natural Science

Foundation of China to Dandan Shang (grant number 81100242), the Natural Science Foundation of Hebei province to Dandan Shang (grant number H2012206161) and the Scientific Research Plan Projects for Higher Schools in Hebei Province to Dandan Shang (grant number 2010147).

References

Bang Y. H., Kim J. H., Paik S. W., Park S. H., Jackson I. T. and Lebeda R. 1996 Histopathology of apocrine bromhidrosis. *Plast. Reconstr. Surg.* **98**, 288–292.

Hurley H. J. 1992 Diseases of the apocrine sweat glands. In *Dermatology* (ed. S. L. Moschella and H. J. Hurley) 3rd edition, pp. 1459–1513. Saunders, Philadelphia, USA.

Leyden J. J., McGinley K. J., Holzle E., Labows J. N. and Kligman A. M. 1981 The microbiology of the human axilla and its relationship to axillary odor. *J. Invest. Dermatol.* **77**, 413–416.

Matsunaga E. 1992 The dimorphism in human normal cerumen. *Ann. Hum. Genet.* **25**, 273–286.

Miura K., Yoshiura K., Miura S., Shimada T., Yamasaki K., Yoshida A. *et al.* 2007 A strong association between human earwax-type and apocrine colostrum secretion from the mammary gland. *Hum. Genet.* **121**, 631–633.

Petrakis N. L., King E. B., Lee M. and Miike R. 1990 Cerumen phenotype and proliferative epithelium in breast Xuids of US-born versus immigrant Asian women: a possible genetic-environmental interaction. *Breast Cancer Res. Treat.* **16**, 279–285.

Shugyo Y., Sudo N., Kanai K., Yamashita T., Kumazawa T. and Kanamura S. 1988 Morphological differences between secretory cells of wet and dry types of human ceruminous glands. *Am. J. Anat.* **181**, 377–384.

Yoshiura K., Kinoshita A., Ishida T., Ninokata A., Ishikawa T., Kaname T. *et al.* 2006 A SNP in the ABCC11 gene is the determinant of human earwax type. *Nat. Genet.* **38**, 324–330.

Received 5 November 2012; in revised form 20 January 2013; accepted 22 January 2013
Published on the Web: 20 May 2013