#117800
APOCRINE GLAND SECRETION, VARIATION IN

Alternative titles; symbols

EAR WAX, WET/DRY; EWWD
WET WAX; WW
CERUMEN, VARIATION IN
AXILLARY ODOR, VARIATION IN
COLOSTRUM SECRETION, VARIATION IN

Phenotype-Gene Relationships

Location	Phenotype	Phenotype MIM number	Phenotype mapping key	Gene/Locus	Gene/Locus MIM number
16q12.1	[Earwax, wet/dry]	117800	3	ABCC11	607040
16q12.1	[Colostrum secretion, variation in]	117800	3	ABCC11	607040
16q12.1	[Axillary odor, variation in]	117800	3	ABCC11	607040

Clinical Synopsis

TEXT

A number sign (#) is used with this entry because of evidence that a single-nucleotide polymorphism (SNP) in the ABCC11 gene (607040) is responsible for variation in apocrine gland secretion, which manifests as wet or dry ear wax type, presence or absence of axillary odor, and variation in colostrum secretion.

Clinical Features

In Japanese, Matsunaga (1962) described a dimorphism of ear wax, the 2 types being wet and dry. This variation has been studied extensively in Japan since at least 1934. Less attention has been given to this variation elsewhere, probably because Caucasians and blacks have only the wet type of cerumen. In 80 to 85% of Japanese, the cerumen is gray, dry, and brittle. It is referred to as 'rice-bran ear wax' in Japanese. In the other Japanese, the cerumen is brown, sticky, and wet. This is referred to as 'honey ear wax,' 'oily ear wax' or 'cat ear wax.' In all except about 0.5% of Japanese, classification is simple. Family studies indicate monofactorial inheritance, with the rarer phenotype, wet wax, being dominant. Wet cerumen is often associated with axillary odor, which, because of its rarity in Japan, is considered in the lay mind a pathologic state requiring medical attention.

Petrakis et al. (1967) found a high frequency of dry cerumen in pure-blooded American Indians. No qualitative differences in the chemical composition of the dry and wet types of cerumen were identified by Kataura and Kataura (1967).

Petrakis (1971) noted a positive correlation between wet ear wax and breast cancer in several countries and suggested an association. In a study of Chinese women in Hong Kong, Ing et al. (1973) could not confirm the association.

Ibraimov (1991) presented data on the high frequency of dry cerumen in Mongoloid populations and low frequency among Europoids. Intermediate frequencies were found among peoples of subequatorial Africa.

Tomita et al. (2002) noted that the difference in nature of wet and dry cerumen is attributed to secretory products of ceruminous glands. Histologic studies have shown abundant lipid droplets and pigment granules in the cytoplasm of secretory cells in individuals with wet cerumen, whereas these cytoplasmic components are scarce in individuals with dry cerumen (Matsunaga, 1962). The ceruminous gland is an apocrine gland, as are axillary and breast glands. In individuals with dry cerumen, the axillary apocrine gland is usually much less developed than in those with wet cerumen, and therefore the dry type is associated with less axillary odor.

The wet cerumen phenotype is completely dominant to the dry type. Yoshiura et al. (2006) stated that the dry ear wax type is seen frequently (80 to 95%) among East Asians, but uncommonly (0 to 3%) in populations of European and African origins. Intermediate frequencies (30 to 50%) of the dry type are seen in populations of southern Asia, the Pacific Islands, central Asia, and Asia Minor, as well as among the native North American and Inuit of Asian ancestry. These figures show geographic gradient distributions.

Among 225 Japanese women, Miura et al. (2007) reported an association between ear wax type and apocrine colostrum secretion from the mammary gland on the first postpartum day. The absence of colostrum secretion was more common among women with dry ear wax (105 of 155, 67.7%) compared to women with wet ear wax (28 of 70, 40%). The authors noted that both colostrum and cerumen have a common origin in the secretory glands and suggested that the ABCC11 gene product may play a role in colostrum secretion independent of endocrine control.

Mapping

In a Japanese family with paroxysmal kinesigenic choreoathetosis (128200) caused by mutation in a gene situated in the centromeric region of chromosome 16, Tomita et al. (2002) found 7 individuals who had the neurologic disorder and wet ear wax. Because the 2 characteristics were possibly cosegregating in the family, Tomita et al. (2002) undertook a study in 8 Japanese families segregating the dimorphism. They chose 11 microsatellite markers from the region 16p11.2-q12.1 where the neurologic disorder had been mapped. They calculated lod scores based on the assumption that wet ear wax is inherited in an autosomal dominant manner with complete penetrance, and that allele frequencies of W and w in the general Japanese population are 0.085 and 0.915, respectively. Two-point linkage analysis gave a maximum lod score of 11.15 at the locus D16S3044. Haplotype analysis assigned the ear wax locus to 16p11.2-q12.1.

Molecular Genetics

With the aim of further mapping of the ear wax locus, Yoshiura et al. (2006) performed genotyping in a case-control study of 64 Japanese individuals with dry ear wax and 54 with the wet type using 134 CA repeat markers. Two SNPs that showed an association with ear wax type localized to a 2.5-Mb pericentromeric region of 16q. All 64 individuals with dry ear wax were homozygotes for 1 allele each, consistent with an autosomal recessive trait and supporting the presence of the ear wax locus in this region. An association study of the 118 samples using 37 SNPs within a 5-gene interval showed that a nonsynonymous SNP (538G-A, G180R; 607040.0001) in exon 4 of the ABCC11 gene was 1 of 3 SNPs showing the lowest P values. Genotyping of a new series of 126 Japanese individuals whose ear wax types had been identified otologically showed 87 of 88 individuals with dry ear wax were AA homozygotes, and that all 38 individuals with the wet type were either GA heterozygotes or GG homozygotes at each of the 3 SNP loci with the lowest P values. Among the 3, only G180R was nonsynonymous; 1 of the others did not create any splicing sites or affect splicing factor binding motifs or known promoter sequences, and the third was located within the Alu-repetitive sequence. One exceptional individual showed discordance between phenotype (dry ear wax) and genotype; sequencing showed that he had a 27-bp deletion in ABCC11 exon 29 (607040.0002). This deletion was also found in a few individuals of Asian ancestry. By a functional assay, Yoshiura et al. (2006) determined that cells with allele A showed a lower excretory activity for cGMP than those with allele G. The allele A frequency showed a north-south and east-west downward geographic gradient; worldwide, it was highest in Chinese and Koreans, and a common dry-type haplotype was retained among various ethnic populations. These results suggested that the allele A arose in northeast Asia and thereafter spread through

the world. The 538G-A SNP was the first example of DNA polymorphism determining a visible genetic trait.

Martin et al. (2010) performed chemical analysis of axillary sweat samples from 25 individuals with different ABCC11 538G-A genotypes, including 18 Asian participants (11 AA homozygotes, 5 AG heterozygotes, and 2 GG homozygotes) and 7 Caucasian participants (2 AG heterozygotes and 5 GG homozygotes). Levels of 3 glutamine conjugates that are precursors for key body odorants were below detection limits in all participants with the AA genotype but were present in all AG and GG individuals, indicating that ABCC11 is essential for secretion of amino-acid conjugates of relevant axillary odors.

Population Genetics

The aboriginal Ainu population of the Japanese island of Hokkaido has an exceptionally high frequency of the dominant wet ear wax phenotype compared to those of neighboring Asian populations (see Yoshiura et al., 2006). Sato et al. (2009) genotyped specimens from various Okhotsk and Jomon/Epi-Jomon archaeologic sites on Hokkaido for rs17822931. Analysis of 31 specimens of the Okhotsk people and 19 specimens of the Jomon/Epi-Jomon people showed that the frequency of the wet-type allele was higher among the Jomon/Epi-Jomon compared to other northeastern Asian populations, including even modern Ainu. In contrast, the Okhotsk had relatively higher frequencies of the dry-type allele compared to Ainu and Jomon/Epi-Jomon. The findings suggested that gene flow occurred from northeastern Asia to descendants of the Jomon/Epi-Jomon through the Okhotsk, resulting in the establishment of the Ainu.

See Also:

Bera et al. (1971); Kataura and Kataura (1967); Martin and Jackson (1969); Petrakis (1977)

REFERENCES

1. Bera, T. K., Lee, S., Salvatore, G., Lee, B., Pastan, I. MRP8, 1. Hyslop, N. E., Jr. : Ear wax and host defense. (Editorial) New Eng. J. Med. 284: 1099-1100, 1971. [PubMed: 5553201, related citations] [Full Text: Atypon]

2. Ibraimov, A. I. Brief communication: cerumen phenotypes in certain populations of Eurasia and Africa. Am. J. Phys. Anthrop. 84: 209-211, 1991. [PubMed: 2021195, related citations]

3. Ing, R., Petrakis, N. L., Ho, H. C. Evidence against association between wet cerumen and breast cancer. Lancet 301: 41 only, 1973. Note: Originally Volume I. [PubMed: 4118561, related citations]

4. Kataura, A., Kataura, K. The comparison of lipids between dry and wet types of cerumen. Tohoku J. Exp. Med. 91: 227-237, 1967. [PubMed: 6055547, related citations]

5. Kataura, A., Kataura, K. The comparison of free and bound amino acids between dry and wet types of cerumen. Tohoku J. Exp. Med. 91: 215-225, 1967. [PubMed: 6055546, related citations]

6. Martin, A., Saathoff, M., Kuhn, F., Max, H., Terstegen, L., Natsch, A. A functional ABCC11 allele is essential in the biochemical formation of human axillary odor. J. Invest. Derm. 130: 529-540, 2010. [PubMed: 19710689, related citations] [Full Text: Nature Publishing Group]

7. Martin, L. M., Jackson, J. F. Cerumen types in Choctaw Indians. Science 163: 677-678, 1969. [PubMed: 5762929, related citations] [Full Text: HighWire Press]

8. Matsunaga, E. The dimorphism in human normal cerumen. Ann. Hum. Genet. 25: 273-286, 1962. [PubMed: 14471313, related citations]

9. Miura, K., Yoshiura, K., Miura, S., Shimada, T., Yamasaki, K., Yoshida, A., Nakayama, D., Shibata, Y., Niikawa, N., Masuzaki, H. A strong association between human earwax-type and apocrine colostrum secretion from the mammary gland. Hum. Genet. 121: 631-633, 2007. [PubMed: 17394018, related citations] [Full Text: Springer]

10. Petrakis, N. L. Cerumen genetics and human breast cancer. Science 173: 347-349, 1971. [PubMed: 5559907, related citations] [Full Text: HighWire Press]

11. Petrakis, N. L. Genetic cerumen type, breast secretory activity, and breast cancer epidemiology.In: Mulvihill, J. J.; Miller, R. W.; Fraumeni, J. F., Jr. : Genetics of Human Cancer. New York: Raven Press (pub.) 1977. Pp. 297-300.

12. Petrakis, N. L., Molohan, K. T., Tepper, D. J. Cerumen in American Indians: genetic implications of sticky and dry types. Science 158: 1192-1193, 1967. [PubMed: 6075316, related citations] [Full Text: HighWire Press]

13. Sato, T., Amano, T., Ono, H., Ishida, H., Kodera, H., Matsumura, H., Yoneda, M., Masuda, R. Allele frequencies of the ABCC11 gene for earwax phenotypes among ancient populations of Hokkaido, Japan. J. Hum. Genet. 54: 409-413, 2009. [PubMed: 19557017, related citations]

14. Tomita, H., Yamada, K., Ghadami, M., Ogura, T., Yanai, Y., Nakatomi, K., Sadamatsu, M., Masui, A., Kato, N., Niikawa, N. Mapping of the wet/dry ear wax locus to the pericentromeric region of chromosome 16. Lancet 359: 2000-2002, 2002. [PubMed: 12076558, related citations] [Full Text: Elsevier Science]

15. Yoshiura, K., Kinoshita, A., Ishida, T., Ninokata, A., Ishikawa, T., Kaname, T., Bannai, M., Tokunaga, K., Sonoda, S., Komaki, R., Ihara, M., Saenko, V. A., and 27 others. A SNP in the ABCC11 gene is the determinant of human earwax type. Nature Genet. 38: 324-330, 2006. [PubMed: 16444273, related citations] [Full Text: Nature Publishing Group]

▸ Contributors: Marla J. F. O'Neill - updated : 11/22/2010

Creation Date: Victor A. McKusick : 6/4/1986

▸ Edit History: wwang : 11/23/2010