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THE EFFECT OF ETHNICITY ON HUMAN AXILLARY ODORANT PRODUCTION

Katharine A. Prokop-Prigge[1,*], **Kathryn Greene**[1], **Lauren Varallo**[1], **Charles J. Wysocki**[1,2], and **George Preti**[1,3]

[1]Monell Chemical Senses Center, 3500 Market Street, Philadelphia, PA, 19104, USA

[2]School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA, 19104, USA

[3]Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, 19104, USA

Abstract

Previous findings from our laboratory highlighted marked ethnic differences in volatile organic compounds (VOCs) from cerumen among individuals of Caucasian, East Asian, and African-American descent, based, in part, on genetic differences in a gene that codes for a transport protein, which is a member of the ATP-binding cassette transporter, sub-family C, member 11 (*ABCC11*). In the current work, we hypothesized that axillary odorants produced by East Asians would differ markedly from those obtained from individuals of European or African descent based on the pattern of ethnic diversity that exists in *ABCC11*. Using gas chromatography/mass spectrometry (GC/MS) we examined differences in axillary odorant VOCs among 30 individuals of African-American, Caucasian, and East Asian descent with respect to their *ABCC11* genotype. While no qualitative differences in the type of axillary odorants were observed across ethnic groups, we found that characteristic axillary odorants varied quantitatively with respect to ethnic origin. We propose that *ABCC11* is not solely responsible for predicting the relative amounts of volatiles found in axillary secretions and that other biochemical pathways must be involved.

Keywords

Axillary odor; ethnicity/race; volatile organic compounds; genetics; analytical chemistry

INTRODUCTION

The axillae of humans contain a large number of apocrine, eccrine, and sebaceous glands. Volatile organic compounds (VOCs) emanating from this area give rise to the canonical axillary odor (commonly referred to as “body odor”). Although this odor is mainly perceived by modern society as unpleasant, several studies indicate that axillary odorants contain chemical signals that affect the menstrual cycle (Preti et al. 2003) or that may be involved in major histocompatibility complex, allele-dependent, mate selection (Wedekind

*corresponding author, kate.prigge@gmail.com, phone: (201) 462-5770.

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et al. 1995). These studies point to the importance of understanding the factors that contribute to human odor production. Current evidence suggests that genetically based odor profiles play a role in individual identity, immune and stress responses, and that odor may be useful for monitoring physical, emotional, and disease states in humans (Dormont et al. 2013). For this potential to be fully realized, however, careful analytical studies, in well-characterized human populations, are needed. Indeed, recently NIH has urged ethnic/racial diversity and genetic analyses to be inclusion criteria in clinical/medical research (Green et al. 2011). Our approach, herein, is to study the influence of ethnic and genetic factors contributing to human odorant profiles.

Human body odor is a complex mixture of VOCs. Organoleptic and analytical chemistry methodologies have revealed that axillary odor derives from a complex mixture of C_2–C_{11} normal, branched, and unsaturated acids, with the main components being (*E*)-3-methyl-2-hexenoic acid (E-3M2H) (Pierce et al. 1995; Zeng et al. 1991, 1992, 1996a, b) and 3-hydroxy-3-methylhexanoic acid (3H3M) (Natsch et al. 2003), as well as volatile sulfur compounds, particularly (*S*)-3-methyl-3-sulfanylhexan-1-ol) (Hasegawa et al. 2004; Natsch et al. 2004; Troccaz et al. 2004). The latter sulfur-containing compounds often are present at very low levels but have high odor impact (i.e., low olfactory threshold). Volatile steroids, such as 5α-androst-16-en-3-one (androstenone) and 5α-androst-16-en-3β-ol (androstenol), originally were thought to play a role in axillary odor (Bird and Gower 1981), but later were found to be minor sensory and analytical contributors relative to the organic acids (Zeng et al. 1996a, b).

Apocrine secretions, which contain the precursors to axillary odor, are odorless upon secretion and become odorous after interaction with the axillary microbial communities residing on the skin's surface (Labows et al. 1979; Leyden et al. 1981; Natsch et al. 2003, 2006; Troccaz et al. 2009; Starkenmann et al. 2005; Zeng et al. 1992). In those studies that have collected and used sterile, pure apocrine secretions, the odorless precursors are proteins that contain the odorants within lipid-friendly calyxes (Spielman et al. 1995; Zeng et al. 1992, 1996a). The axillae support a dense bacterial population dominated by two types, *Staphylococcus* and *Corynebacterium*. A strong correlation has been found between a dense population of corynebacteria and robust axillary odor production (Barzantny et al. 2012; Leyden et al. 1981).

Recent studies have suggested that human axillary odor is influenced by genetic factors. The human adenosine triphosphate (ATP)-Binding Cassette transporter, sub-family C, member 11 (*ABCC11*), encodes an ATP-driven efflux transporter that is expressed and localized in human apocrine sweat glands. The ABCC11 protein is known to transport a variety of small molecules (Chen et al. 2005; Kruh et al. 2007) and has been shown to play a role in both the generation of axillary malodor (Baumann et al. 2014; Martin et al. 2010; Preti and Leyden 2010) and earwax (cerumen) phenotype (Toyoda et al. 2009; Yoshiura et al. 2006). A single nucleotide polymorphism (SNP, *rs17822931*) in *ABCC11* (538G→A) leads to a glycine-to-arginine substitution (G180R) in the resulting protein. The G180R variant of ABCC11 results in a dry, white earwax phenotype, which is predominant (80-95%) among East Asian populations (e.g., Japanese, Korean, and Chinese), but is quite rare (0-3%) among individuals of European and African descent. TT homozygous individuals for the G180R

variant produce significantly less characteristic axillary odor than both heterozygous (CT) and homozygous (CC) individuals (Harker et al. 2014; Inoue et al. 2010; Martin et al. 2010; Nakano et al. 2009). Previous findings from our laboratory highlighted marked ethnic differences in cerumen VOCs between individuals of Caucasian, East Asian, and African American descent (Prokop-Prigge et al. 2014, 2015). Our current work extends that of previous reports, both ours and that of others, and investigates the influence of ethnicity on the relative amounts of axillary VOCs produced. Based on the pattern of ethnic diversity that exists in *ABCC11*, we hypothesized that axillary odorants produced by East Asians will differ markedly from those obtained from individuals of European and African descent. Using gas chromatography/mass spectrometry [GC/MS], we examined differences in VOCs found in the axillary secretions of Caucasian, East Asian, and African-American individuals with respect to their *ABCC11* genotype.

METHODS AND MATERIALS

Collection of Axillary Secretions

Thirty, healthy males between the ages of 21-40 were enrolled in the study (mean age ± s.d. = 29 ± 1.1). Males belonged to one of the following donor groups: African-American (N = 10), Caucasian (N = 10), or East Asian (N = 10, Chinese, Korean, or Japanese), as self-reported on a questionnaire. All volunteers were informed about the aims of the study and were asked to provide written consent. Protocols were approved by the University of Pennsylvania Institutional Review Board (IRB) for Research Involving Human Subjects (IRB # 816983). Prior to collection of body odor, individuals were asked to fill out a confidential questionnaire assessing the following: medical history, medications, vitamins, personal care, and perfume/cologne product usage. For seven days prior to collection, as well as throughout the duration of collections, donors were asked to bathe/shower with a fragrance-free liquid soap (provided by Symrise Inc., Teterboro, NJ, USA). Donors also were asked to refrain from using deodorant/antiperspirant and perfume/cologne to lessen contamination from fragrance compounds typically found in personal care products.

Donors were provided with two newly purchased T-shirts. New, unwashed T-shirts were used to minimize exposure from additives found in laundry detergents, as we were able to identify exogenous compounds consistently found in the unwashed T-shirts and account for such compounds accordingly. The use of a washing machine adds variability and additional, unaccounted for contaminants. Following the 7 d period where donors bathed/showered with fragrance-free soap, each individual wore one of the T-shirts for approximately 12 h throughout the course of their normal, daily activity. Donors were instructed to store the worn T-shirt in a separate, gallon-sized, plastic bag (provided). This procedure of wear was repeated with the remaining T-shirt. The two worn T-shirts were then returned to the laboratory. A 4×4 in section from the axillary region of each T-shirt containing axillary sweat was removed and stored at 0°C until ready for further extraction and analysis.

Extraction of Axillary Secretions

Samples were prepared by extracting four, 4×4 in sections from the two axillary regions of two T-shirts provided by each individual. Squares were first soaked for 1 h in doubly

distilled ethanol (EtOH) along with an internal standard for the extraction process, viz., d-19 decanoic acid (50 μl of a 0.01 mg/ml solution) in chloroform ($CHCl_3$). The ethanol was collected and the same T-shirt samples were subsequently soaked in $CHCl_3$ for 1 h. The T-shirts then were squeezed in a Teflon® press to remove solvent; the EtOH and $CHCl_3$ extracts were combined with 1.5 ml of a saturated sodium bicarbonate solution to precipitate the organic acids. The mixture was concentrated to dryness on a rotary evaporator. The precipitate was re-dissolved in water and washed with $CHCl_3$ × 3. The aqueous solution was acidified with 6N HCl to pH = 2, and the organic acids were extracted into $CHCl_3$. The acidified solution was washed × 3 with water, and subsequently stored at −30°C until ready for analysis.

GC/MS Analysis of Axillary Volatiles

Immediately prior to analysis, extracts were concentrated to a total volume of approximately 75 μl. A Thermo Scientific ISQ single quadrupole GC/MS with Xcalibur software (Thermo Fisher Scientific, Waltham, MA, USA) was used for separation and analysis of the axillary VOCs. The GC/MS was equipped with a Stabilwax column, 30 m × 0.32 mm with 1.0 μm film thickness (Restek Corp., Bellefonte, PA, USA). The injection port was set at 230°C, and 5 μl of the concentrated extract were injected. The oven temperature was held at 60°C for 4 min, raised to 230°C at 6°C min^{-1}, and maintained at 230°C for 40 min. Helium carrier gas constantly flowed at 2.5 ml min^{-1}.

The mass spectrometer was operated at an ionizing energy of 70 eV with a 2 scans/sec rate over a range of *m/z* 40–400 and an ion source temperature of 200°C. Identification of structures/compounds was performed using the National Institute of Standards and Technology Library (NIST ’11), as well as comparisons with known literature compounds, synthetic (3-methyl-2-hexenoic acid, provided as a gift from Dr. David Blank), and commercially available standards. Standards were purchased from PharmBlock, Inc. (Middletown, NY, USA) (3-hydroxy-3-methyl-hexanoic acid), Sigma-Aldrich or Alfa Aesar at the highest available purity and used as received after purity determination by GC/MS. The peaks of interest were quantified using their major, characteristic ion, and normalized by both sample volume and an external standard (methyl stearate) measured daily. Compounds consistently seen in all donors were subjected to a multivariate analysis of variance and, where deemed appropriate, to non-parametric analyses (IBM SPSS Statistics, v. 20).

Genotyping

Saliva was collected from all individuals and DNA was isolated following kit manufacturer recommendations (DNA Genotek, Ottawa Canada). Individuals were genotyped for the SNP 538 C→T in *ABCC11* (*rs17822931*). This SNP is believed to play a key role in the function of apocrine gland secretion (Baumann et al. 2014; Harker et al. 2014; Martin et al. 2010). Genotyping was performed using a 5’-exonuclease reaction (TaqMan) from Applied Biosystems (Foster City, CA, USA) and read in a 96-well plate format on a StepOnePlus Real-Time PCR System (Applied Biosystems).

RESULTS

The *ABCC11* genotype (*rs17822931*) of each donor was analyzed (Fig. 1). Nine East Asian donors were identified as TT homozygotes, while one was found to be a CT heterozygote. The remaining 20 donors (Caucasian and African-American) were all CC homozygotes. These findings match the expected allele frequencies for these populations (Yoshiura et al. 2006).

We examined whether (a) the *ABCC11* genotype and (b) ethnicity contributed to variability in axillary sweat samples collected from all genotyped donors. The results revealed that all donor groups, at least qualitatively, produced the same volatile acid profile. However, subtle differences in the amounts of short, C_2-C_6, straight- and branched-chain organic acids were observed (Fig. 2). While these differences were not found to vary significantly across groups, it is interesting to note that relative differences were found for the branched-chain acids specifically. As a group, African-Americans produced relatively higher amounts of all straight-chain acids: acetic, propanoic, butyric, valeric, and hexanoic; however, when branch-chained acids (isobutyric, 2-methylbutyric, and isovaleric acid) were examined, Caucasian donors appeared to produce relatively higher amounts than East Asian and African-American donors. These shifts between Caucasians and other donor groups may have contributed to our non-significant statistical results across all compounds (see below).

All 12 compounds measured in all individuals (see Fig. 2-3) were subjected to a multivariate analysis of variance (MANOVA) with donor group as a between-subjects factor. Granted, many assumptions underlying this parametric analysis were violated, this statistical approach revealed no significant difference across donor group ($F_{(24,34)} = 1.03$, $P = 0.46$), although there were some suggestions of differences that were probed with ANOVA and non-parametric tests (see below).

While differences were marginal for short-chain volatile acids across donor groups (a MANOVA revealed $F_{(16,42)} = 1.76$, $P = 0.07$; Fig. 2), differences were noted for the longer-chain, characteristic axillary, odorants (e.g., 3-methyl-2-hexenoic acid, 7-octenoic acid, Fig. 3). Both isomers of 3M2H were subjected to repeated measures ANOVA with donor group as a between-subjects factor. The main effect of isomer was significant ($F_{(1,27)} = 8.62$, $P = 0.007$; *E* > *Z*), but so was the interaction between isomer and donor group ($F_{(2,27)} = 4.51$, $P = 0.02$; i.e., the pattern of results across donor groups was significantly different for the two isomers). We used the Kruskal-Wallis nonparametric test to explore further variation in the *E*-and *Z*-isomers of 3M2H. For the *Z*-isomer, there was no significant difference across groups ($P = 0.238$,); however, the *E*-isomer did vary ($P = 0.010$) with African-American > Caucasian > East Asian in the relative amounts produced. Mann-Whitney pairwise comparisons, using a Bonferroni-corrected $P = 0.017$, revealed a significant difference between samples from African-Americans vs. East Asians (U = 10.0, $P = 0.002$); no other pairwise comparison was significant. A similar trend also was observed for 3-hydroxy-3-methylhexanoic acid (3H3M) with African-American > Caucasian > East Asian in relative amounts observed. While difficult to quantitate using the GC/MS parameters employed, there was a significant difference across donor groups in the number of individuals who produced detectable levels of 3H3M (Fig. 4; $X^2 = 10.05$, $P = 0.007$). Post hoc tests using

adjusted residuals and a Bonferroni correction revealed a significant effect of African-American vs. East Asian donors.

DISCUSSION

The sources that contribute to human body odor and an individual's odor profile are diverse, and recent studies have suggested that there may be an underlying genetic factor that controls axillary odorant formation. A single gene, viz., *ACBCC11* (*rs17822931*), is believed to be a major component for predicting the level of axillary odorants and earwax phenotype (Baumann et al. 2014; Martin et al. 2010; Preti and Leyden 2010; Toyoda et al. 2009; Yoshiura et al. 2006). Our results, however, suggest that the control of odor production is not so straight forward. Examination of 30 male individuals of three diverse ethnic/racial backgrounds (African-American, Caucasian, and East Asian) revealed that key characteristic axillary odorants vary with respect to ethnic origin, not strictly *ABCC11* genotype, as previously reported.

The *ABCC11* genotype (*rs17822931*) of each donor was analyzed, and the findings are in excellent agreement with the expected allele frequencies for the three populations (Yoshiura et al. 2006). Nine East Asian donors were identified as TT homozygotes, while all Caucasian and African-American donors were CC homozygotes. Previous findings suggest that individuals homozygous for the SNP 538G→A produced significantly less characteristic axillary odorant precursors than both heterozygous (C/T) and wild-type (C/C) individuals (Harker et al. 2014; Inoue et al. 2010; Martin et al. 2010; Nakano et al. 2009). Based on these findings, and the marked ethnic diversity of the *ABCC11* allele frequencies, one would predict East Asian donors to exhibit lower levels of axillary odorants as compared to donors of Western descent. Our findings are consistent with these predictions. The results, however, also reveal that despite exhibiting the same *ABCC11* genotype, there were marked differences in the levels of characteristic axillary odors between African-American and Caucasian donors. For example, a major contributor to axillary odor, *E*-3M2H, was significantly higher in African-Americans when compared to Caucasians. In addition, there were significant differences across donor groups in the number of individuals who produced detectable levels of 3H3M, with African-American > Caucasian > East Asian. The lack of 3-methyl-3-sulfanylhexan-1-ol in any of our extracts is due most likely to the method of collection. Its oniony-sweaty odor was not evident in the extracts (though present on some T-shirts evaluated organoleptically), suggesting that it was not extracted efficiently under the extraction conditions employed. Previous studies (Hasegawa et al. 2004; Natsch et al. 2004; Troccaz et al. 2004) have isolated it from pooled, liquid sweat collected directly from the axillae of multiple donors.

Previous results suggest that the *ABCC11*-controlled transporter protein should not be functional in our cohort of East Asian donors with the TT genotype (Martin et al. 2010). In contrast, Harker et al. (2014) noted that their donors with TT genotype had measurable, albeit significantly lower, levels of axillary malodorant precursors (measured as both their N-acyl glutamine conjugates and the corresponding free acids). The findings also demonstrate that odorant molecules, like 3M2H, are still able to reach the skin's surface. Preti and Leyden (2010) noted that research groups examining the influence of *ABCC11* had

failed to consider the influence of the lipocalin-type proteins, namely apocrine apolipoprotein D (ApoD) (Spielman et al. 1998; Zeng et al. 1996a). Quantitative measures of this protein in both axillary and apocrine secretions demonstrate that it is present in Asian populations, albeit at significantly lower concentrations than in Caucasians or African-Americans (Jacoby et al. 2004). A second protein found in apocrine secretions also was shown by Spielman et al. to carry 3M2H, but its blocked N-terminus failed to provide structural identity by classical means (Spielman et al. 1995, 1998). Spielman and co-workers designated this protein ASOB1 (apocrine secretion odor binding protein 1; molecular weight approx. 45kD). Studies involving antibodies to apocrine ApoD as well as ASOB1 demonstrate that these proteins have wide-spread presence in various body fluids/secretions (Gallagher et al. 2008; Spielman et al. 1995). Consequently, these findings suggest that biochemical pathways involving protein carriers of odorants other than the protein made by the *ABCC11* gene are involved in the regulation of transport and/or release of volatile odorants in the axilla. Recent studies and reviews of axillary odor formation (Harker et al., 2014; Natsch 2015) appear to have neglected incorporating the ApoD protein precursor into their narrative, as noted by Preti and Leyden (2010). The isolation procedures used by these investigators (Harker et al., 2014; Natsch 2015) and others did not focus on sterile-collected, apocrine secretions as did the study by Zeng et al. (1996a). Instead, they used non-sterile axillary washings, thus providing ample time for the axillary bacteria to convert protein carriers to the N-acyl glutamine conjugates, as previously indicated (Preti and Leyden, 2010).

Odorous, volatile short-chain fatty acids, albeit more minor, are contributors to human axillary odor (Harker et al. 2014). Our results reveal a marginal effect on the relative amounts of these compounds across the ethnic groups studied. The reduced presence of these short-chain acids, in addition to low levels of *E*- and *Z*-3M2H documented here and by others (Akutsu et al. 2006; Harker et al. 2014), most likely contribute to the reduced malodor reported for individuals of Asian descent (typically TT homozygotes). In addition, interesting trends were revealed here for the relative amounts of branched chain vs. straight short-chain volatile acids. Individuals from the cohort of African-American donors produced slightly higher amounts of all straight-chain acids: acetic, propanoic, butyric, valeric, and hexanoic. When branched chain acids (isobutyric, 2-methylbutyric, and isovaleric acid) were examined, Caucasian donors appeared to produce relatively higher amounts than both Asian and African-American donors. Perhaps differences in dietary intake can account for this trend. The amino acids leucine and isoleucine are found in high levels in dairy products (Annigan 2014). The branched-chain volatile acids, isovaleric acid and 2-methylbutyric acid, stem from the metabolism of these two amino acids, respectively. East Asians and African-Americans experience higher levels of lactose intolerance than do Caucasians (ProCon.org 2010); hence we speculate that increased intake of dairy products by individuals of Caucasian descent results in increased levels of the branched chain amino acids in these individuals. There has been considerable speculation concerning the influence, if any, of diet on axillary odor, but little to no experimental data exists to date. However, Havlicek and Lenochova (2006) have shown that red meat consumption increases the negative hedonics of axillary odors (e.g., less attractive, more intense and unpleasant). While the measured differences in branched chain volatile acids in this study did not vary

significantly across donor groups; perhaps a larger sample size and a controlled study monitoring dietary intake would provide insight. Further studies on the effect of diet on axillary odorant profiles are warranted.

Another interesting trend was seen in the data from East Asian donors (as shown in Fig. 3a). The ratio of *E*-to *Z*-isomers for 3M2H appears different from that seen for African-Americans and Caucasian donors, and this appears to be the reason for the significant interaction between donor group and 3M2H isomer (see Results section). The *E*-to *Z*-isomer ratio for East Asian individuals favors the *Z*-isomer vs. the larger relative amount of the *E*-isomer seen in the other two donor groups (Zeng et al. 1991, 1996a). Hence, the biogenesis of the 3M2H may differ across the ethnic groups, where conditions in the apocrine glands of the East Asians energetically favor formation and/or retention of the *Z*-isomer.

Overall, our findings suggest that an individual's ethnicity has a significant impact on human axillary odor production. Ongoing sensory studies will address whether differences in ethnicity can be discriminated by human panelists. Furthermore, as advancements are made in studies of disease-related alterations in metabolism, some of which may affect qualitative/and or quantitative expression of odorous VOCs that emanate from the body or its excretions, e-nose technologies may prove to be an invaluable supplement to diagnostic protocols. When this occurs, differences in baselines across different groups will have to be taken into account.

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REFERENCES

Akutsu T, Sekiguchi K, Ohmori T, Sakurada K. Individual comparisons of the levels of (E)-3-methyl-2-hexenoic acid, an axillary odor-related compound. Japanese. Chem Senses. 2006; 31:557–563. [PubMed: 16690870]

Annigan, J. [24 October 2014] Foods that are highest in isoleucine & leucine. 2014. http://www.livestrong.com/article/275274-foods-that-are-highest-in-isoleucine-leucine/

Barzantny H, Brune I, Tauch A. Molecular basis of human body odour formation: Insights deduced from corynebacterial genome sequences. Int J Cosmetic Sci. 2012; 34:2–11.

Baumann T, Bergmann S, Schmidt-Rose T, Max H, Martin A, Enthaler B, Terstegen L, Schweiger D, Kalbacher H, Wenck H, et al. Glutathione-conjugated sulfanylalkanols are substrates for ABCC11 and gamma-glutamyl transferase 1: A potential new pathway for the formation of odorant precursors in the apocrine sweat gland. Exp Dermatol. 2014; 23:247–252. [PubMed: 24533866]

Bird S, Gower DB. The validation and use of a radioimmunoassay for 5 alpha-androst-16-en-3-one in human axillary collections. J Steroid Biochem. 1981; 14:213–219. [PubMed: 7193782]

Chen ZS, Guo Y, Belinsky MG, Kotova E, Kruh GD. Transport of bile acids, sulfated steroids, estradiol 17-beta-D-glucuronide, and leukotriene C4 by human multidrug resistance protein 8 (ABCC11). Mol Pharmacol. 2005; 67:545–557. [PubMed: 15537867]

Dormont L, Bessiere JM, Cohuet A. Human skin volatiles: A review. J Chem Ecol. 2013; 39(5):569–578. [PubMed: 23615881]

Gallagher M, Wysocki CJ, Leyden JJ, Spielman AI, Sun X, Preti G. Analyses of volatile organic compounds from human skin. Br J Dermatol. 2008; 159:780–791. [PubMed: 18637798]

Green ED, Guyer MS, et al. Charting a course for genomic medicine from base pairs to bedside. Nature. 2011; 470:204–213. [PubMed: 21307933]

Harker M, Carvell AM, Marti VP, Riazanskaia S, Kelso H, Taylor D, Grimshaw S, Arnold DS, Zillmer R, Shaw J, et al. Functional characterisation of a SNP in the ABCC11 allele - effects on axillary skin metabolism, odour generation and associated behaviours. J Dermatol Sci. 2014; 73:23–30. [PubMed: 24076068]

Hasegawa Y, Yabuki M, Matsukane M. Identification of new odoriferous compounds in human axillary sweat. Chem Biodivers. 2004; 1:2042–2050. [PubMed: 17191839]

Havlicek J, Lenochova P. The effect of meat consumption on body odor attractiveness. Chem. Senses. 2006; 31:747–752. [PubMed: 16891352]

Inoue Y, Mori T, Toyoda Y, Sakurai A, Ishikawa T, Mitani Y, Hayashizaki Y, Yoshimura Y, Kurahashi H, Sakai Y. Correlation of axillary osmidrosis to a SNP in the ABCC11 gene determined by the Smart Amplification Process (SmartAmp) method. J Plast Reconstr Aesthet Surg. 2010; 63:1369–1374. [PubMed: 19625231]

Jacoby RB, Brahms JC, Ansari SA, Mattai J. Detection and quantification of apocrine secreted odor-binding protein on intact human axillary skin. Int J Cosmet Sci. 2004; 26:37–46. [PubMed: 18494923]

Kruh GD, Guo Y, Hopper-Borge E, Belinsky MG, Chen ZS. ABCC10, ABCC11, and ABCC12. Pflugers Arch. 2007; 453:675–684. [PubMed: 16868766]

Labows JN, Preti G, Hoelzle E, Leyden J, Kligman A. Steroid analysis of human apocrine secretion. Steroids. 1979; 34:249–258. [PubMed: 158859]

Leyden JJ, McGinley KJ, Holzle E, Labows JN, Kligman AM. The microbiology of the human axilla and its relationship to axillary odor. J Invest Dermatol. 1981; 77:413–416. [PubMed: 7288207]

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 Dermatol. 2010; 130:529–540. [PubMed: 19710689]

Nakano M, Miwa N, Hirano A, Yoshiura K, Niikawa N. A strong association of axillary osmidrosis with the wet earwax type determined by genotyping of the ABCC11 gene. BMC genetics. 2009; 10:42. [PubMed: 19650936]

Natsch A. What makes us smell: The biochemistry of body odour and the design of new deodorant ingredients. Chimia. 2015; 69:414–420. [PubMed: 26507593]

Natsch A, Gfeller H, Gygax P, Schmid J, Acuna G. A specific bacterial aminoacylase cleaves odorant precursors secreted in the human axilla. J Biol Chem. 2003; 278:5718–5727. [PubMed: 12468539]

Natsch A, Schmid J, Flachsmann F. Identification of odoriferous sulfanylalkanols in human axilla secretions and their formation through cleavage of cysteine precursors by a C-S lyase isolated from axilla bacteria. Chem Biodivers. 2004; 1:1058–1072. [PubMed: 17191898]

Natsch A, Derrer S, Flachsmann F, Schmid J. A broad diversity of volatile carboxylic acids, released by a bacterial aminoacylase from axilla secretions, as candicate molecules for the determination of human-body odor type. Chem Biodivers. 2006; 3:1–20. [PubMed: 17193210]

Pierce JD Jr. Zeng XN, Aronov EV, Preti G, Wysocki CJ. Cross-adaptation of sweaty-smelling 3-methyl-2-hexenoic acid by a structurally-similar, pleasant-smelling odorant. Chem Senses. 1995; 20:401–411. [PubMed: 8590025]

Preti G, Leyden JJ. Genetic influences on human body odor: From genes to the axillae. J Invest Dermatol. 2010; 130:344–346. [PubMed: 20081888]

Preti G, Wysocki CJ, Barnhart KT, Sondheimer SJ, Leyden JJ. Male axillary extracts contain pheromones that affect pulsatile secretion of luteinizing hormone and mood in women recipients. Biol Reprod. 2003; 68:2107–2113. [PubMed: 12606409]

ProCon.org. [24 October 2014] Lactose intolorance by ethnicity and region. 2010. ProCon.orgProCon.orghttp://milk.procon.org/view.resource.php?resourceID=000661

Prokop-Prigge KA, Thaler E, Wysocki CJ, Preti G. Identification of volatile organic compounds in human cerumen. J Chromatogr B. 2014; 953-954:48–52.

Prokop-Prigge KA, Mansfield CJ, Parker MR, Thaler E, Grice EA, Wysocki CJ, Preti G. Ethnic/Racial and Genetic Influences on Cerumen Odorant Profiles. J Chem Ecol. 2015; 41:67–74. [PubMed: 25501636]

Spielman AI, Sunavala G, Harmony JA, Stuart WD, Leyden JJ, Turner G, Vowels BR, Lam WC, Yang S, Preti G. Identification and immunohistochemical localization of protein precursors to human axillary odors in apocrine glands and secretions. Arch Dermatol. 1998; 134:813–818. [PubMed: 9681344]

Spielman AI, Zeng XN, Leyden JJ, Preti G. Proteinaceous precursors of human axillary odor: Isolation of two novel odor-binding proteins. Experientia. 1995; 51:40–47. [PubMed: 7843330]

Starkenmann C, Niclass Y, Troccaz M, Clark AJ. Identification of the precursor of (S)-3-methyl-3-sulfanylhexan-1-ol, the sulfury malodour of human axilla sweat. Chem Biodivers. 2005; 2:705–715. [PubMed: 17192014]

Toyoda Y, Sakurai A, Mitani Y, Nakashima M, Yoshiura K, Nakagawa H, Sakai Y, Ota I, Lezhava A, Hayashizaki Y, et al. Earwax, osmidrosis, and breast cancer: Why does one SNP (538G>A) in the human ABC transporter ABCC11 gene determine earwax type? FASEB J. 2009; 23:2001–2013. [PubMed: 19383836]

Troccaz M, Starkenmann C, Niclass Y, van de Waal M, Clark AJ. 3-Methyl-3-sulfanylhexan-1-ol as a major descriptor for the human axilla-sweat odour profile. Chem Biodivers. 2004; 1:1022–1035. [PubMed: 17191896]

Troccaz M, Borchard G, Vuilleumier C, et al. Gender-specific differences between the concentrations of nonvolatile (R)/(S)-3-Methyl-3-Sulfanylhexan-1-Ol and (R)/(S)-3-Hydroxy-3-Methyl-Hexanoic acid odor precursors in axillary secretions. Chem Senses. 2009; 34:203–210. [PubMed: 19147808]

Wedekind C, Seebeck T, Bettens F, Paepke AJ. MHC-dependent mate preferences in humans. Proc Biol Sci. 1995; 260:245–249. [PubMed: 7630893]

Yoshiura K, Kinoshita A, Ishida T, Ninokata A, Ishikawa T, Kaname T, Bannai M, Tokunaga K, Sonoda S, Komaki R, et al. A SNP in the ABCC11 gene is the determinant of human earwax type. Nat Genet. 2006; 38:324–330. [PubMed: 16444273]

Zeng C, Spielman AI, Vowels BR, Leyden JJ, Biemann K, Preti G. A human axillary odorant is carried by apolipoprotein D. Proc Natl Acad Sci U S A. 1996a; 93:6626–6630. [PubMed: 8692868]

Zeng XN, Leyden JJ, Brand JG, Spielman AI, McGinley KJ, Preti G. An Investigation of Human Apocrine Gland Secetion for Axillary Odor Precursors. J Chem Ecol. 1992; 18:1039–1055. [PubMed: 24254146]

Zeng XN, Leyden JJ, Spielman AI, Preti G. Analysis of characteristic human female axillary odors: Qualitative comparison to males. J Chem Ecol. 1996b; 22:237–257. [PubMed: 24227407]

Zeng XN, Preti G, Leyden JJ, Lawley HJ, Sawano K, Nohara I. Analysis of the characteristic odors from the male axillae. J Chem Ecol. 1991; 17:1469–1492. [PubMed: 24257805]

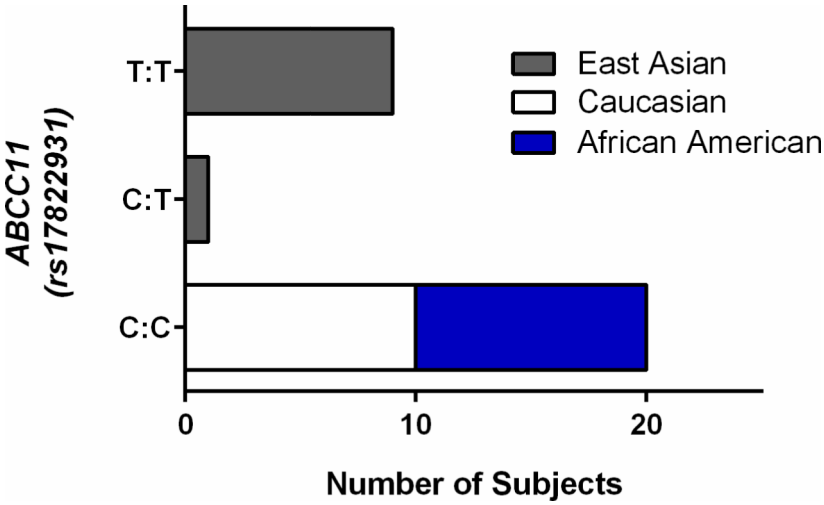

Fig. 1.
ABCC11 genotype (*rs17822931*) of 30 male donors with respect to ethnicity/race.

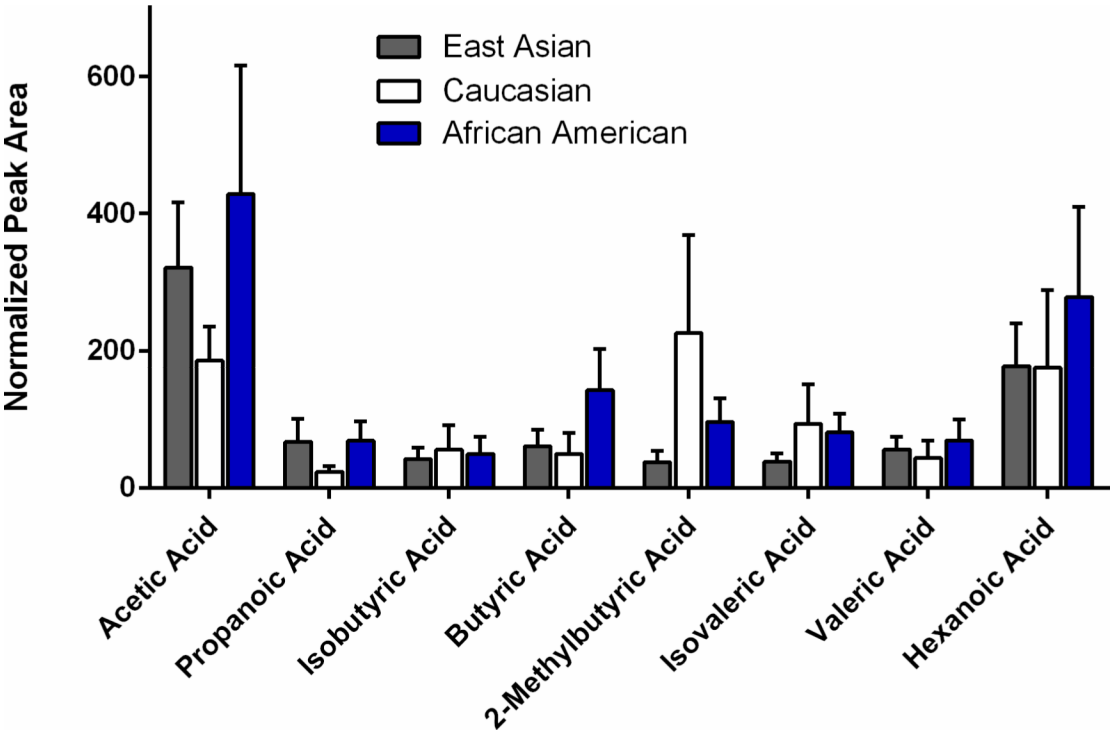

Fig. 2.

Comparison of short-chain volatile acids detected in axillary sweat samples collected from East Asian, Caucasian, and African-American donors. Variation across the three donor groups was nearly significant ($F_{(16,42)} = 1.76$, $P = 0.07$).

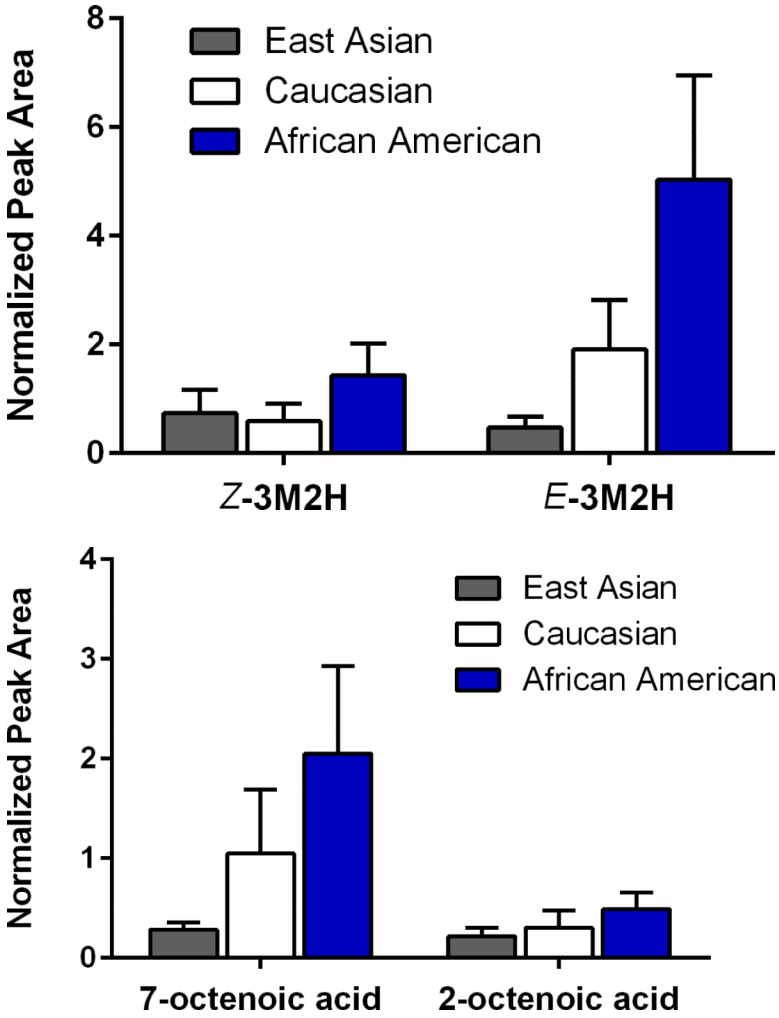

Fig. 3.

a 3-Methyl-2-hexenoic acid (3M2H) comparison revealing significant differences (P = 0.009, Kruskal-Wallis test) in the relative amounts of the characteristic axillary odorant, *E*-3M2H, among the three donor groups (also, see text for a significant interaction generated by a repeated measures ANOVA). **b** Comparison of 7- and 2-octenoic acid detected in axillary sweat samples from East Asian, Caucasian, and African-American donors. For 7-octenoic acid, differences in the distributions across the three groups of donors was suggestive (Jonckheere-Terpstra test for ordered alternatives; P = 0.065; across the three groups, this test has more statistical power than the Kruskal–Wallis test).

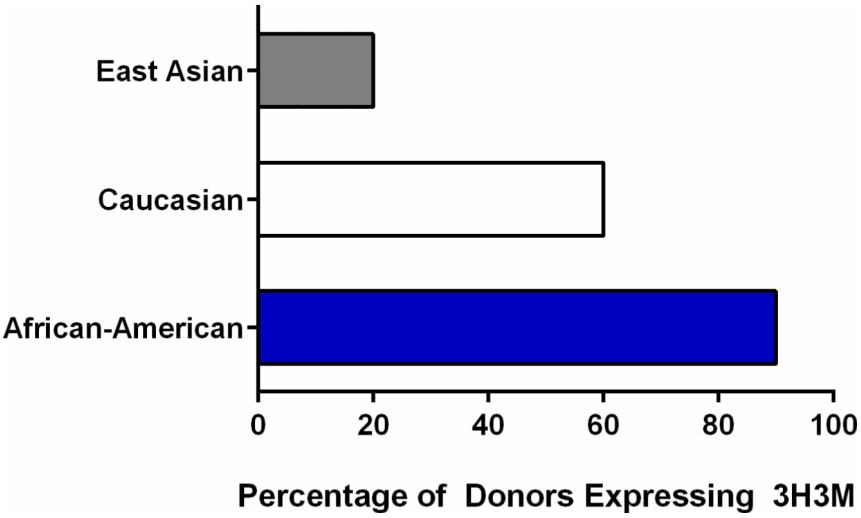

Fig. 4.

Percentage of donors from whom 3H3M was detected in axillary secretions. *Chi Square* analysis revealed a significant difference across groups (X^2 = 10.05, P = 0.007).