

# A Genome-Wide Scan on Individual Typology Angle Found Variants at *SLC24A2* Associated with Skin Color Variation in Chinese Populations

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## TO THE EDITOR

Skin pigmentation functions as a shield to prevent UV damage to the DNA of epidermal cells. A good number of GWASs on skin color variation or skin photosensitivity have been conducted that discovered a large number of associated loci (Ganguly et al., 2019). Polymorphisms/mutations at these loci have been used to study the molecular type of skin color for individuals from different continental groups (Chen et al., 2021) and have been associated with various forms of albinism (Marçon and Maia, 2019), loss of photo-protection, and increased rates of photo-aging (Liu et al., 2016). However, there have been surprisingly few GWASs conducted in East Asian populations, likely owing to the presumption of a low skin color variation in East Asians (Rawofi et al., 2017). The question regarding the presence of East Asian-specific skin color alleles remains to be answered. Individual typology angle (ITA°) is a quantitative skin color measurement based on the colorimetric parameters of the L\*a\*b\* system (Chardon et al., 1991). The validity of ITA° in serving as an objective skin color measurement has been extensively evaluated with regard to its correlations with constitutive pigmentation, the geographical distribution of skin pigmentation, and biological markers of UV-induced erythema (Del Bino and Bernerd, 2013). Despite the wide use of ITA° in clinical dermatology, few genetic studies had adopted it as the measurement of skin color.

In this study, we report a GWAS of ITA° in Chinese, followed by replications in Chinese and Latin Americans. The discovery sample included a total of 6,964

individuals of Chinese origin from two cohorts: the Jidong cohort (n = 5,034) and the National Survey of Physical Traits cohort (n = 1,930). Studies in these cohorts were approved by the Ethics Committee of Kailuan General Hospital of Tangshan City and the Medical Ethics Committee, Staff Hospital, Jidong Oil-field Branch, China National Petroleum Corporation in July 2013 (approval number 2013 YILUNZI1) as well as the Ethics Committees of Fudan University (14117) and the Shanghai Institutes for Biological Sciences (ER-SIBS-261410). The replication sample included a total of 2,053 individuals from two cohorts: the Taizhou longitudinal cohort of Chinese origin (n = 1,787) and the Colombian cohort of Latin American origin (n = 266). The Taizhou longitudinal cohort study was conducted with the approval of the Ethics Committee of Fudan University (Ethics Research Approval 85), Shanghai, China, and the Colombian cohort study was conducted with the approval of the bioethics committee of the Odontology Faculty at the University of Antioquia (CONCEPTO 01-2013). All participants provided written informed consent. For the discovery cohorts, sample characteristics and phenotyping details are provided in Supplementary Materials and Methods (Supplementary Table S1 and Figure 1a and b). In brief, we derived ITA° from high-resolution portrait photos, which were processed using an in-house pipeline, involving a face detector, automated facial landmarking, cheek segmentation, and color analysis. In a subgroup of 50 randomly selected samples, the ITA° derived from the portrait photos was highly correlated with the ITA° measured by a spectrophotometer ( $r = 0.94$ ,  $P =$

$4.42 \times 10^{-24}$ , Supplementary Figure S1). The Chardon skin color type (Chardon et al., 1991), as defined by ITA° cutoffs, was fairly concordant with human perception (Kappa = 0.47). Although dark skins were not seen and very light (1.51%) and brown (0.27%) skins were rarely seen in our Chinese samples, ITA° did show a substantial variance (Var = 8.03, mean = 35.95, minimum = -26.36, maximum = 68.42) across light (23.41%), intermediate (59.69%), and tan (15.12%) categories. Females had significant lighter skin than males ( $\beta = 6.18$ ,  $P = 9.22 \times 10^{-270}$ ) and aging increased coloration ( $\beta = -0.22$ ,  $P = 8.08 \times 10^{-244}$ ), which were consistent with previous observations (Tan et al., 2020). Z-transformed ITA° was used in the subsequent genetic association analysis (Supplementary Figure S2).

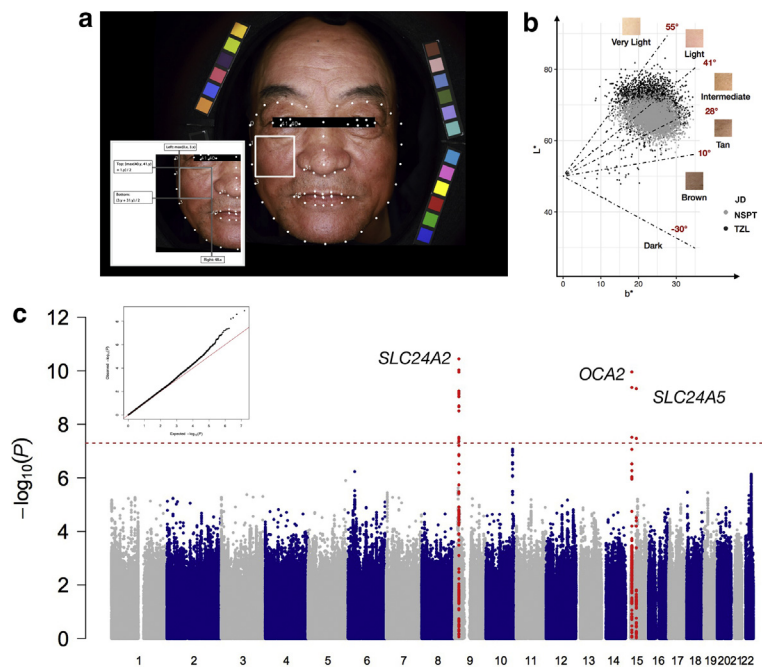
In the discovery stage of the study, we conducted a genome-wide inverse variance, a fixed-effect meta-analysis of two GWASs, which were independently conducted in the Jidong cohort and the National Survey of Physical Traits cohort, totaling 6,964 Chinese individuals. No evidence of population substratification or genome inflation was detected ( $\lambda = 0.99$ , Figure 1c). The meta-analysis identified a total of 19 SNPs at three genomic loci showing genome-wide significant association with z-transformed ITA° (Supplementary Table S2), including one previously unreported locus on 9p21.3 (*SLC24A2*) and two previously known loci on 15q12.6 (*OCA2*) and 15p21.1 (*SLC24A5*).

The locus at 9p21.3, as the most significant signal over the genome, contained a total of 14 significant SNPs, where the lead SNP (rs10122939) was an intron variant of *SLC24A2* (Figure 2a). The derived G allele showed a skin darkening effect reaching genome-wide significance in the Jidong cohort ( $\beta = -0.10$ ,  $P = 1.29 \times 10^{-9}$ ), nominal significance in the National Survey of

Abbreviation: ITA°, individual typology angle

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**Figure 1. GWASs for skin color in Chinese populations.** (a) The face detection module returned the locations of 68 facial landmarks (white points), and a fixed area on the cheek (white rectangle) was detected on the basis of seven facial landmarks. The participant has consented to the publication of his image. (b)  $ITA^\circ$  was derived from the fixed area. Samples were classified into five skin color types on the basis of  $ITA^\circ$  according to Chardon's definition. (c) Manhattan plot of the meta-analysis results for facial skin color from the GWASs (JD and NSPT, total N = 6,964). The  $-\log_{10} P$ -values for association were plotted for all SNPs according to their physical positions (genome-build GRCh38.p13). The red line was corresponding to the threshold for genome-wide significance ( $P = 5 \times 10^{-8}$ ). Genome-wide significant and nominal significant ( $P = 1 \times 10^{-6}$ ) SNPs were shown in [Supplementary Tables S2](#) and [S3](#), respectively.  $ITA^\circ$ , individual typology angle; JD, Jidong cohort; NSPT, National Survey of Physical Traits cohort.

Physical Traits cohort ( $\beta = -0.07$ ,  $P = 4.71 \times 10^{-3}$ ), and further enhanced significance in the meta-analysis ( $\beta = -0.09$ ,  $P = 3.61 \times 10^{-11}$ ). This association was also genome-wide significant for the original  $ITA^\circ$  without z-transformation ( $\beta = -1.89$ ,  $P = 7.28 \times 10^{-10}$ ). No genome-wide significant association signal was observed at 9p21.3 after conditioning on the genotype of the lead SNP rs10122939 ([Supplementary Figure S3](#)). The G allele of rs10122939 was highly prevalent in East Asians (our sample:  $f = 0.34$ ; in CHB of the 1000 Genomes Project:  $f = 0.29$ ) but was rare in Europeans (in EUR of 1000 Genomes Project,  $f = 0.004$ , [Figure 2b](#)), which may explain the failure of previous European GWASs in detecting its effect (other SNPs in linkage disequilibrium showed the same pattern, [Supplementary Table S2](#)). A series of population genetic analyses did not reveal significant evidence for positive selection surrounding rs10122939 at 9p21.3 ([Supplementary Figure S4](#)).

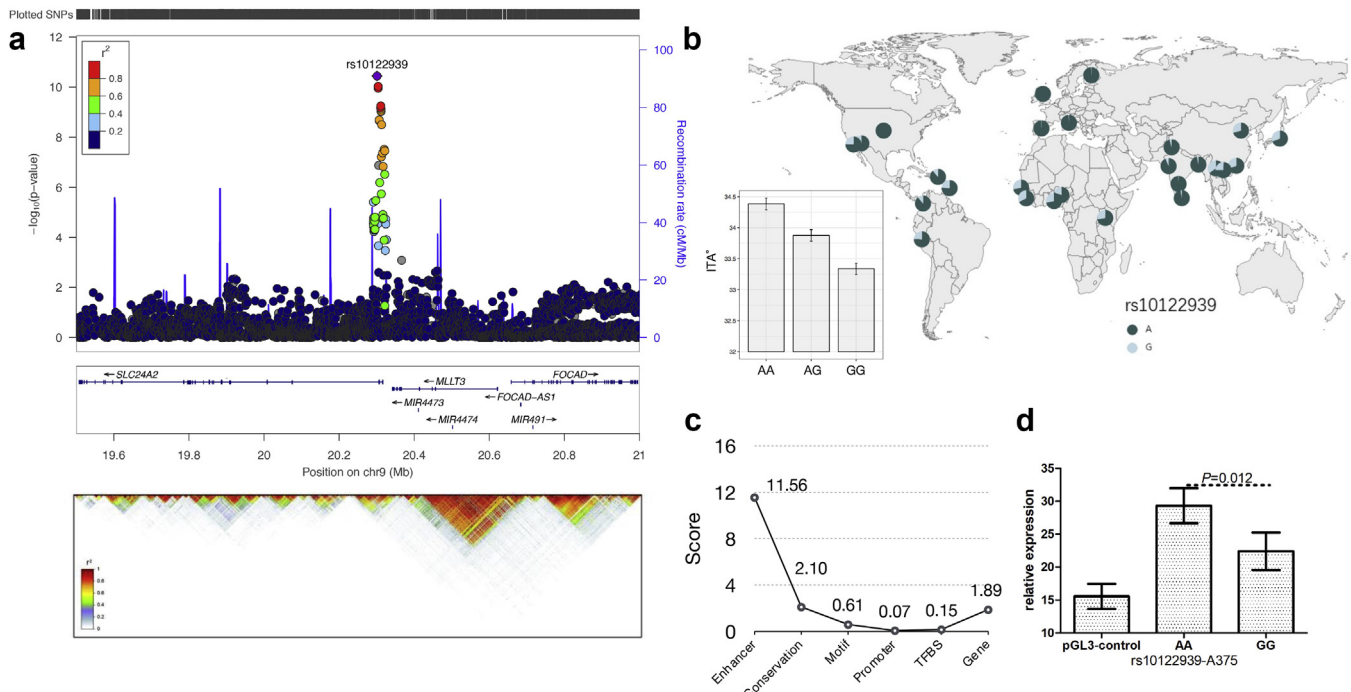
The other two loci have been previously associated with skin color. On chromosome 15q12.6, two well-known East Asian-specific missense variants rs1800414 (His615Arg) and rs74653330

(Ala481Thr) of *OCA2* ([Edwards et al., 2010](#); [Yang et al., 2016](#)) showed genome-wide significant association with  $ITA^\circ$ , where the derived C allele of rs1800414 and T allele of rs74653330 had a skin-lightening effect ( $P = 1.11 \times 10^{-10}$  and  $P = 3.05 \times 10^{-8}$ , respectively; [Supplementary Table S2](#) and [Supplementary Figure S5a](#) and [b](#)). Both alleles were nearly absent outside of East Asia ([Supplementary Figure S5c](#) and [d](#)). On chromosome 15p21.1, we confirmed the well-known effect of a missense variant rs1426654 of *SLC24A5*, of which the derived A allele had low frequency but a large skin-lightening effect ( $P = 4.64 \times 10^{-10}$ , [Supplementary Table S2](#) and [Supplementary Figure S6](#)).

We then looked up a total of 9,183 SNPs from four recently published large GWASs of skin/hair/eye pigmentation traits ([Adhikari et al., 2019](#); [Hysi et al., 2018](#); [Simcoe et al., 2021](#); [Visconti et al., 2018](#)). A total of 151 SNPs at 13 loci showed nominally significant ( $P < 0.01$ ) association, but except those in or close to *OCA2* and *SLC24A5* genes, none survived strict Bonferroni correction of multiple testing ( $P < 0.05/9,183$ ; [Supplementary Table S4](#)).

To replicate the finding at 9p21.3, we tested the association between rs10122939 and  $ITA^\circ$  in an additional Chinese cohort from Taizhou (Taizhou longitudinal cohort,  $n = 1,787$ ) and in a Latin American cohort from Colombia ( $n = 266$ ). The effect of rs10122939 was successfully replicated at nominal significance, and the G allele also showed a skin-darkening effect in both replication cohorts (Taizhou longitudinal cohort:  $\beta = -0.09$ ,  $P = 5.96 \times 10^{-3}$ , Colombian:  $\beta = -0.26$ ,  $P = 3.89 \times 10^{-2}$ ). A meta-analysis of all samples further enhanced the significance level of this association ( $P = 2.13 \times 10^{-13}$ ).

To further investigate the potential functions of rs10122939, we conducted a function annotation analysis using the quantitative scoring system embedding the 3DSNP database ([Lu et al., 2017](#)), which revealed significant evidence for rs10122939 serving as an enhancer of *SLC24A2* ([Figure 2c](#)). We further performed the luciferase report assays to experimentally validate this finding. The transcriptional activity of the enhancer containing the rs10122939 ancestral A allele was significantly



**Figure 2. A locus at 9p21.3 was associated with skin color in Chinese populations.** (a) Regional association plot for the significantly associated region on chromosome 9p21.3 consisting of *SLC24A2*. Increasing color intensities represented higher levels of linkage disequilibrium ( $r^2$ ) with rs10122939. (b) Geographical distribution of the minor allele frequencies for rs10122939 in 2,504 multiethnic individuals from the 1000 Genome Project. The effect allele (G) showed a skin-darkening effect. (c) The top SNP rs10122939 was annotated as an enhancer using 3DSNP. (d) Luciferase reporter assays confirmed that the transcriptional activity of the enhancer containing the rs10122939 ancestral A allele was significantly higher than that of the corresponding-derived G allele in the A375 cell line. A similar trend was observed but did not reach the significant level in HEK293 (Supplementary Figure S7). chr, chromosome; HEK293, human embryonic kidney 293; ITA°, individual typology angle; TFBS, transcription factor binding sites.

higher than that of the corresponding derived G allele in the A375 cell line ( $t$ -test  $P = 0.012$ , Figure 2d). This pattern would predict less *SLC24A2* production for the derived G allele carriers. Future studies may consider in vivo gene editing experiments to further investigate the pigmentation effect of *SLC24A2*. Unlike the well-known skin color genes *SLC24A5* and *SLC45A2*, this SLC family gene *SLC24A2* is not expressed in the skin but rather in the brain and adrenal, mainly involved in neuronal activity (Haque and Moon, 2018; Zhou et al., 2020). It has been recently reported that neuronal activity induced by acute stress can drive a rapid and permanent loss of melanocyte stem cells, which leads up to stress-induced hair greying (Zhang et al., 2020). A possible hypothesis could be that *SLC24A2* moderates neuronal activity that influences melanocyte stem cells, eventually causing changes in skin color. Alternatively, *SLC24A2* may change the innervation of the skin and affect ITA° through altered skin thickness or other relevant characteristics. This hypothesis is particularly attractive because we did observe a positive correlation

between ITA° and transepidermal water loss ( $P = 4.12 \times 10^{-9}$ ), a phenotype thought to be strongly associated with skin thickness (Bargo et al., 2013). The rs10122939 SNP is also associated with transepidermal water loss ( $P = 0.01$ ) (Supplementary Figure S8 and Supplementary Materials and Methods).

In conclusion, this is a meaningful skin color GWAS in well-sized Chinese populations. We identified an intron variant of *SLC24A2* (rs10122939) as a previously unreported East Asian–European differentiating polymorphism involved in skin color variation. The underlying cellular mechanism is to be explored.

#### Data availability statement

Summary statistics for all analyzed variants for the Jidong Study and the National Survey of Physical Traits can be viewed at NODE under accession number OEP001341 or directly at <http://www.biosino.org/node/project/detail/OEP001341> and accessed by submitting a request for data access. Data usage shall be in full compliance with the Regulations on Management of Human Genetic Resources in China. Individual

genotype and phenotype data cannot be shared owing to Institutional Review Board restrictions on privacy concerns. All other relevant data supporting the key findings of this study are available within the letter and Supplementary Materials or from the corresponding author on reasonable request.

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**CONFLICT OF INTEREST**

The authors state no conflict of interest.

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**SUPPLEMENTARY MATERIAL**

Supplementary material is linked to the online version of the paper at [www.jidonline.org](http://www.jidonline.org), and at <https://doi.org/10.1016/j.jid.2021.07.186>.

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## SUPPLEMENTARY MATERIALS AND METHODS

### Study populations

**The Jidong cohort.** The Jidong cohort is a community-based, long-term observational cohort study to evaluate health-related risk factors. The baseline data were collected from 2013 to 2014 in the Staff Hospital, Jidong Oilfield Branch, China. Approval was obtained from the Ethics Committee of Kailuan General Hospital of Tangshan City and the Medical Ethics Committee, Staff Hospital, Jidong Oilfield Branch, China National Petroleum Corporation in July 2013 (approval number 2013 YILUNZ11). The approval had been renewed in 2018. To date, 9,078 individuals aged >18 years have been enrolled after excluding individuals who were unable or unwilling to participate. Written informed consent was obtained from all participants. This study included a total of 5,601 individuals (2,512 men and 3,089 women, aged 31–87 years) who paid the return visit in 2018. The facial photograph and blood samples were collected in the Staff Hospital at the same time.

**The National Survey of Physical Traits cohort.** The National Survey of Physical Traits cohort (NSPT) is a population-based prospective cohort study to explore the environmental and genetic factors associated with physical traits and diseases. The NSPT cohort study was conducted with the official approval of the Ethics Committees of Fudan University (14117) and the Shanghai Institutes for Biological Sciences (ER-SIBS-261410). The NSPT totally collected samples of 3,565 Han Chinese individuals (1,320 men and 2,245 women, aged 17–83 years) in 2015–2018 from three sites (i.e., Taizhou, Nanning, and Zhengzhou). All individuals provided written informed consent. Portrait photos of 1,930 individuals (705 men and 1,225 women, aged 18–79 years) were collected in accordance with phenotyping standard operating procedure. Therefore, only 1,930 individuals were included in this study.

**The Taizhou longitudinal cohort.** The Taizhou longitudinal cohort study is a long-term observational cohort study to explore the environmental and genetic risk factors for common and non-communicable diseases. This research program was conducted with the approval of the Ethics Committee of

Fudan University (Ethics Research Approval 85), Shanghai, China. The detailed characteristics have been described before (Wang et al., 2009). Our replication set included 1,787 healthy Han Chinese with portrait photos, aged 31–85 years.

**Colombian cohort.** The Colombian cohort collected data from participants of several Latin American countries to study the genetics of normal variation in physical appearance. For the genetic analysis of individual typology angle (ITA°), 266 participants were recruited in the city of Medellin, Colombia. Ethical approval was obtained from the bioethics committee of the Odontology Faculty at the University of Antioquia (Medellin, Colombia) (CONCEPTO 01-2013). The age of the participants was between 18–50 years, with an average of 27 years.

### Phenotyping

All participants were asked not to take part in vigorous exercise an hour before their study visit, not to wear make-up, and to refrain from alcohol and tobacco use 24 hours before the visit. All photographs were taken in a confined space with stabilized light-emitting diode light source. Besides, all participants wore a shawl to help give consistent light illumination. A Canon 70D digital camera (lens: Canon EF 40 mm f/2.8; Canon, Tokyo, Japan) was used for all subjects without the flash. The facial photograph for each participant consisted of a frontal facial shot with the eyes closed and no facial expression. The resolution of the photographs was 300 dpi.

This study adopted ITA° as a quantitative measurement of skin color, which was derived from high-resolution portrait photos. ITA° is a quantitative variable designed for measuring skin pigmentation on the basis of colorimetric parameters. ITA° could be used to classify skin types, that is, very light (ITA° > 55), light (41 ~ 55), intermediate (28 ~ 41), tan (10 ~ 28), brown (−30 ~ 10), and dark (<−30) (Chardon et al., 1991). It has been shown that the ITA°-based skin color classification is physiologically relevant (Del Bino and Bernerd, 2013).

Portrait photos were processed using an in-house developed facial skin color quantification pipeline, which involves a face detector, automated facial

landmarking, cheek segmentation, and color analysis.

The face detection was achieved by the `get_frontal_face_detector` function from the C++ library Dlib (King, 2009). This function returns an object detector that is configured to find human faces that are looking more or less toward the camera, and the detector is composed of a linear classifier combined with classic Histogram of Oriented Gradients features (Dalal and Triggs, 2005), an image pyramid, and the sliding window detection scheme (Sullivan and Su, 2014). The face landmarking was achieved by the `shape_predictor` function from the C++ library Dlib on the basis of the face region detected by the `get_frontal_face_detector`. This predictor was created by training an ensemble of regression trees for face alignment on the iBUG 300-W face landmark dataset (Sagonas et al., 2016; Sagonas et al., 2013a, 2013b). It takes an image of a human face as input and identifies the locations of 68 facial landmarks including, the corners of the mouth and eyes, the tip of the nose, and edges of cheeks (Figure 1a).

For each side of the face, the pipeline automatically outlines a rectangle to segment the cheek part according to preselected anatomical landmarks in such a way that the rectangle contains the cheek-surrounding landmarks with the minimal horizontal and vertical distances between the landmarks (Figure 1a). After the segmentation, we manually examined the scope of the rectangles to exclude the confounding margins that incorporate photographing background and human hair. For the right cheek, the CIELAB (ISO, 2007) L, a and b values of all segmented pixels were obtained and converted to ITA° as  $ITA^\circ = \arctan \frac{L-50}{b} \times \frac{180}{\pi}$ , and the mean ITA° was calculated to represent the facial skin color of a portrait. Because ITA° values were not subject to the normal distribution both in the Jidong cohort and the NSPT cohort (Supplementary Figure S2a and b), we applied Z-transformed ITA° in further analysis.

For quality control purposes, additional measures were obtained in a subgroup of 50 randomly selected photographs. These included accessing skin colorimetric parameters on the right cheek using a spectrophotometer



(Skin Colorimeter CL 400, Courage+Khazaka Electronics GmbH, Cologne, Germany) and four skin color types (very light, light, intermediate, and tan) perceived by an investigator according to the Chardon skin color type (Chardon et al., 1991). Note that dark skin color types were absent in our Chinese sample. Intermethod reliability was evaluated with the Kappa statistic. No significant difference in ITA° was detected between the left and right cheeks ( $t$ -test  $P = 0.13$ ). Chardon's skin color type showed a high degree of concordance with the perceived skin color type as well as with the spectrophotometer values (Supplementary Figure S1b–d).

For phenotyping in the Taizhou longitudinal cohort, the photos were taken with a Canon 70D digital camera (lens: Canon EF 40 mm f/2.8). The rest of the procedures (i.e., automated facial landmarking, cheek segmentation, and color analysis) were the same as those used in the discovery cohorts.

For the Colombian cohort, ITA° was measured on the forehead. Owing to the smaller sample size, outlier values on either tail of the ITA° were excluded (values  $\leq -3$  or  $\geq 54$ ). Z-transformed ITA° was used for the analysis.

Among 1,887 subjects in the NSPT cohort, we also collected the transepidermal water loss measurement. Transepidermal water loss was measured on the cheek using Tewameter TM 300 of Courage+Khazaka Electronics GmbH (median [interquartile range], g/h/m<sup>2</sup> = 10.60 [8.20–13.90]).

### Genotyping

For both the Jidong and NSPT cohorts, genomic DNA was extracted from blood samples using the MagPure Blood DNA KF Kit. All samples were genotyped using the Illumina Infinium Global Screening Array (Illumina, San Diego, CA) consisting of about 710,000 SNPs. We implemented exclusion criteria for quality control using PLINK, version 1.9 (Chang et al., 2015). In detail, we excluded subjects with >5% missing data, the duplicated subjects, and subjects that failed the X-chromosome sex concordance check or had ethnic information incompatible with their genetic information. We excluded SNPs that had >2% missing data, SNPs

with a minor allele frequency <1%, and the ones that failed the Hardy–Weinberg deviation test ( $P < 1 \times 10^{-5}$ ). Imputation was performed using the 1000 Genomes Project phase 3 as the reference panel. The chip genotype data were firstly phased using SHAPEIT3 (O'Connell et al., 2016), and IMPUTE2 was then used to impute genotypes (Howie et al., 2009). SNPs with an imputation quality score (INFO) <0.6, minor allele frequency <0.01, or a missing rate >0.01 were eliminated from further analyses. Finally, 8,039,700 SNPs passed quality control and were used for further analyses.

For Taizhou longitudinal cohort, blood samples were collected, and DNA was extracted. All samples were genotyped using the Illumina HumanOmniZhongHua-8 chip (Illumina), which interrogates 894,517 SNPs. After quality control with PLINK, version 1.9, the genotype data were phased using SHAPEIT and were imputed using IMPUTE2 with the 1000 Genomes Project phase 3.

Blood samples were collected from the participants in the Colombian cohort. DNA was extracted and genotyped on the Illumina Infinium Global Screening Array. After quality control using PLINK, version 1.9, 511,848 SNPs were retained. The genotype data were then phased using SHAPEIT2 and imputed using IMPUTE2, with the 1000 Genomes Project phase 3 as the reference panel. Genotype data for SNP rs10122939 were obtained from the imputed dataset.

### Statistical analysis

**GWASs and meta-analysis.** GWASs were separately conducted in the Jidong and NSPT cohorts on Z-transformed ITA° values using software package PLINK (Chang et al., 2015) where additive allele effects were tested in linear models adjusted for covariates (age, sex, sampling locations, and the top four genomic principal components). GWAS outputs were combined using inverse variance fixed-effect meta-analysis as implemented in METAL (Willer et al., 2010).  $P$ -values  $\leq 5 \times 10^{-8}$  from the meta-analysis were considered genome-wide significant. The inflation factor was estimated close to 1.0 ( $\lambda = 0.995$ ) and not further considered. GWAS results were visualized using Manhattan plots, Q–Q plots.

Regional linkage disequilibrium plots and association plots were generated using Haploview and LocusZoom (Barrett et al., 2005; Pruim et al., 2010). For the association analysis in the replication cohorts, additive models were used, with age, sex, and five principal components of genotypes as covariates.

In the Taizhou longitudinal cohort and the Colombian cohort, genetic principal components were calculated from the chip genotype data. After quality control, an association test between SNP rs10122939 and Z-transformed ITA° values was conducted using PLINK, including age, sex, and five genetic principal components as covariates.

**Candidate gene analysis.** To compare our GWAS results with previous GWAS findings related to skin color, we conducted an examination for a list of 11,384 SNPs identified by recently large sample GWAS for tanning response to sun exposure (Visconti et al., 2018), skin pigmentation (Adhikari et al., 2019), hair color (Hysi et al., 2018), and eye color (Simcoe et al., 2021). Of 11,384 SNPs, 9,183 were available in our GWAS results. SNPs with  $P$ -values smaller than the Bonferroni-corrected threshold of 0.05/9,183 ( $1.09 \times 10^{-6}$ ) in our GWAS results were considered significant.

### Genetic diversity and signatures of positive selection

To detect the signatures of positive selection, we used two statistics commonly adopted in population genetics, including the fixed index ( $F_{ST}$ ) and integrated haplotype score (iHS).  $F_{ST}$  measures the proportion of genetic diversity caused by differences in allele frequencies between populations that is potentially resulted from divergent natural selection (Holsinger and Weir, 2009). We used genome-wide complex trait analysis (Yang et al., 2011) to derive genome-wide  $F_{ST}$  analysis for 10 pairs of groups—pairwise among African, East Asian, European, American, and South Asian—on the basis of the genotype data of samples from the 1000 Genome Project. The empirical significance cutoff was set to the values of the top 1% and top 5% of  $F_{ST}$  in the corresponding pairs of the population in the whole genome. iHS is an integration of extended haplotype homozygosity statistics to highlight the recent positive selection mutations that have not yet reached a fixed level. Larger

values indicated adaptation to selection pressure in the most recent stage of evolution (Sabeti et al., 2002; Voight et al., 2006). First, We used the selscan software (Szpiech and Hernandez, 2014) to calculate the iHS scores of SNPs on the basis of genotype data from the five populations, including African, East Asian, European, American, and South Asian of the 1000 Genome Project. The absolute iHS scores of the top 1% and 5% of all SNPs in these 22 randomly selected regions for each population were used as the empirical significance cutoff of the corresponding population. Then, we calculated the iHS scores of SNPs within 200 kb upstream and downstream of the lead SNP we identified, and the iHS absolute score represents the selection intensity.

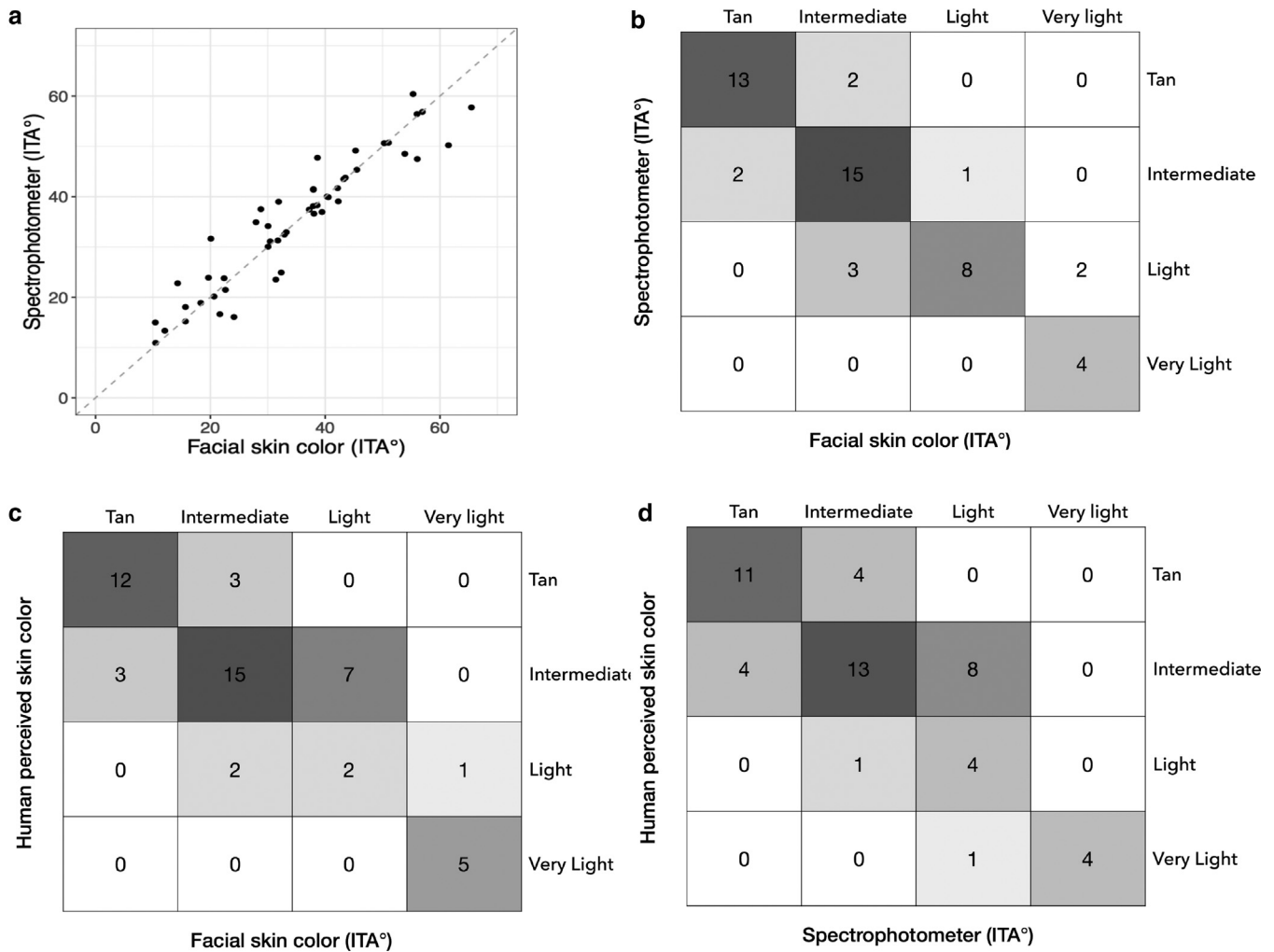
#### Functional test using a dual-luciferase reporter assay

We amplified a 115 bp fragment (GRCh38.p13) of *SLC24A2* by PCR from genomic DNA of two homozygous individuals with respect to the corresponding genotypes rs10122939 (AA and GG) using primers tailed with *Kpn* I and *Xho* I restriction sites for rs10122939 and directionally subcloned them into the pGL3-promoter expression vector (Promega, Madison, WI). We verified all recombinant clones by sequencing. A375 melanoma cells lines and human embryonic kidney 293 cell lines were routinely cultured, transfected, and incubated overnight at 37 °C in 5% carbon dioxide. A375 and human embryonic kidney 293 cells were cultured in high-glucose DMEM (Corning, Corning, NY) with 10% fetal bovine serum (Gibco, Waltham, MA). Transient transfection assays were conducted in these cells using the Lipofectamine 2000 transfection reagent (Invitrogen, Waltham, MA). All assays were performed with a minimum of four replicates. After 48 hours of incubation, we collected the

cells and measured luciferase activity using the Dual-Luciferase Reporter Assay System (Beyotime, Shanghai, China).

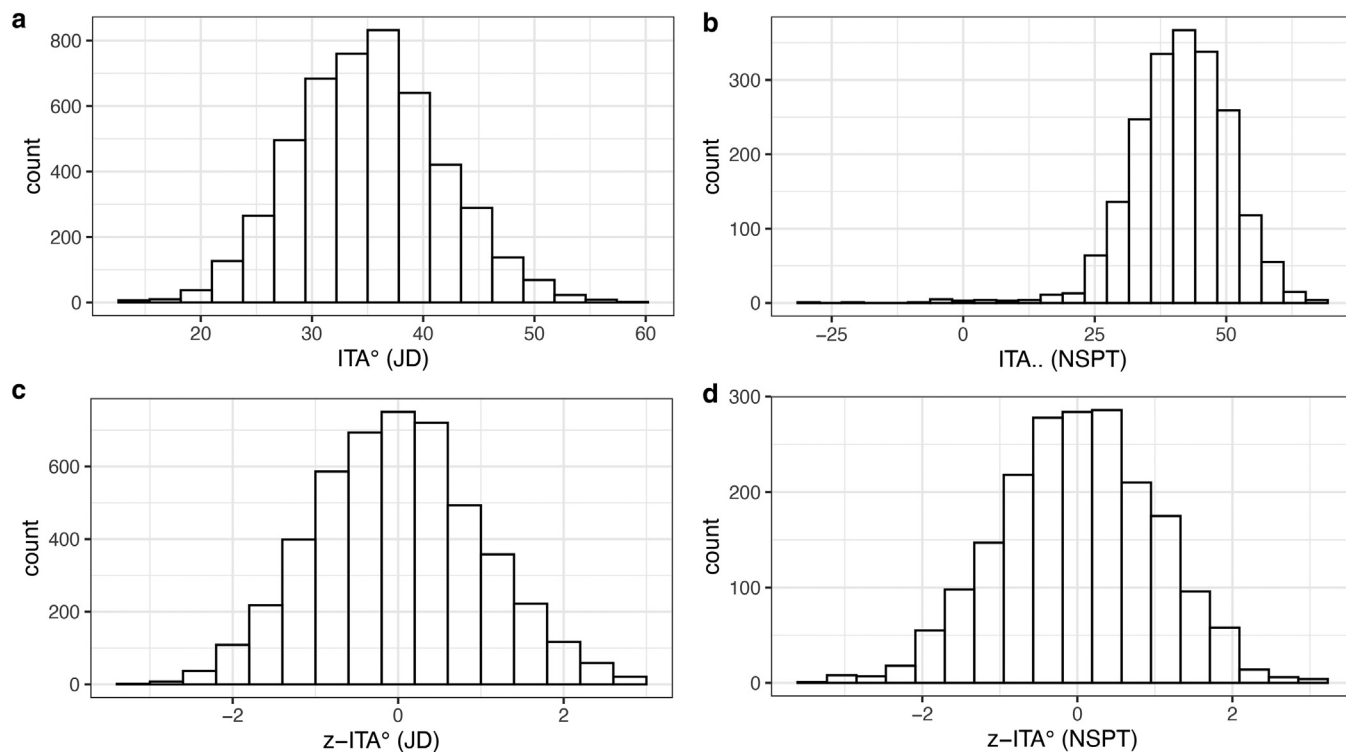
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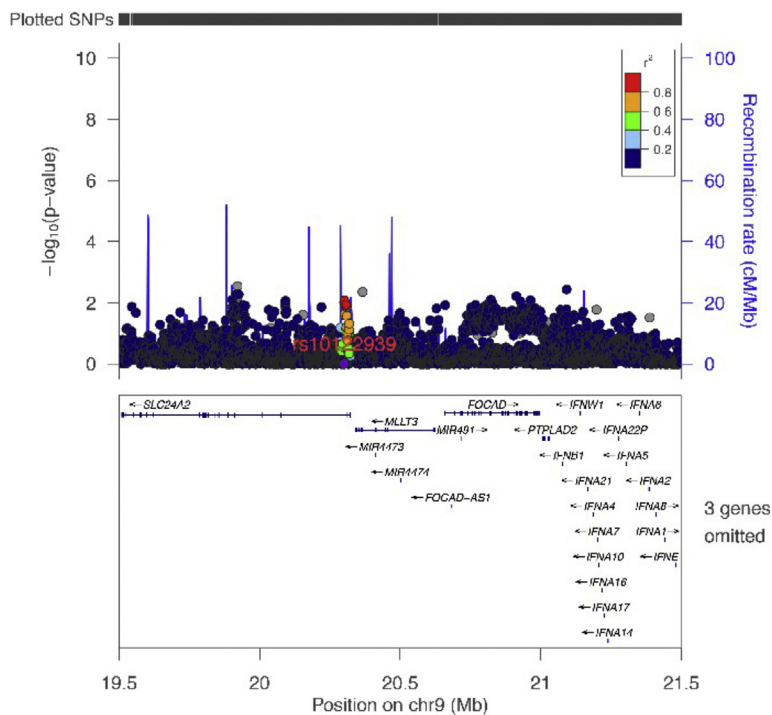


**Supplementary Figure S1. Scatter plot and confusion matrices of skin color measurements.** (a) Scatter plot of portrait-based ITA° and spectrophotometer ITA°. (b) Confusion matrices of Chardon skin color types derived from portrait-based ITA° versus those derived from spectrophotometer ITA°. (c) Chardon skin color types derived from portrait-based ITA° versus human perceived skin color and (d) human perceived skin color versus Chardon skin color types derived from spectrophotometer ITA°. ITA°, individual typology angle.

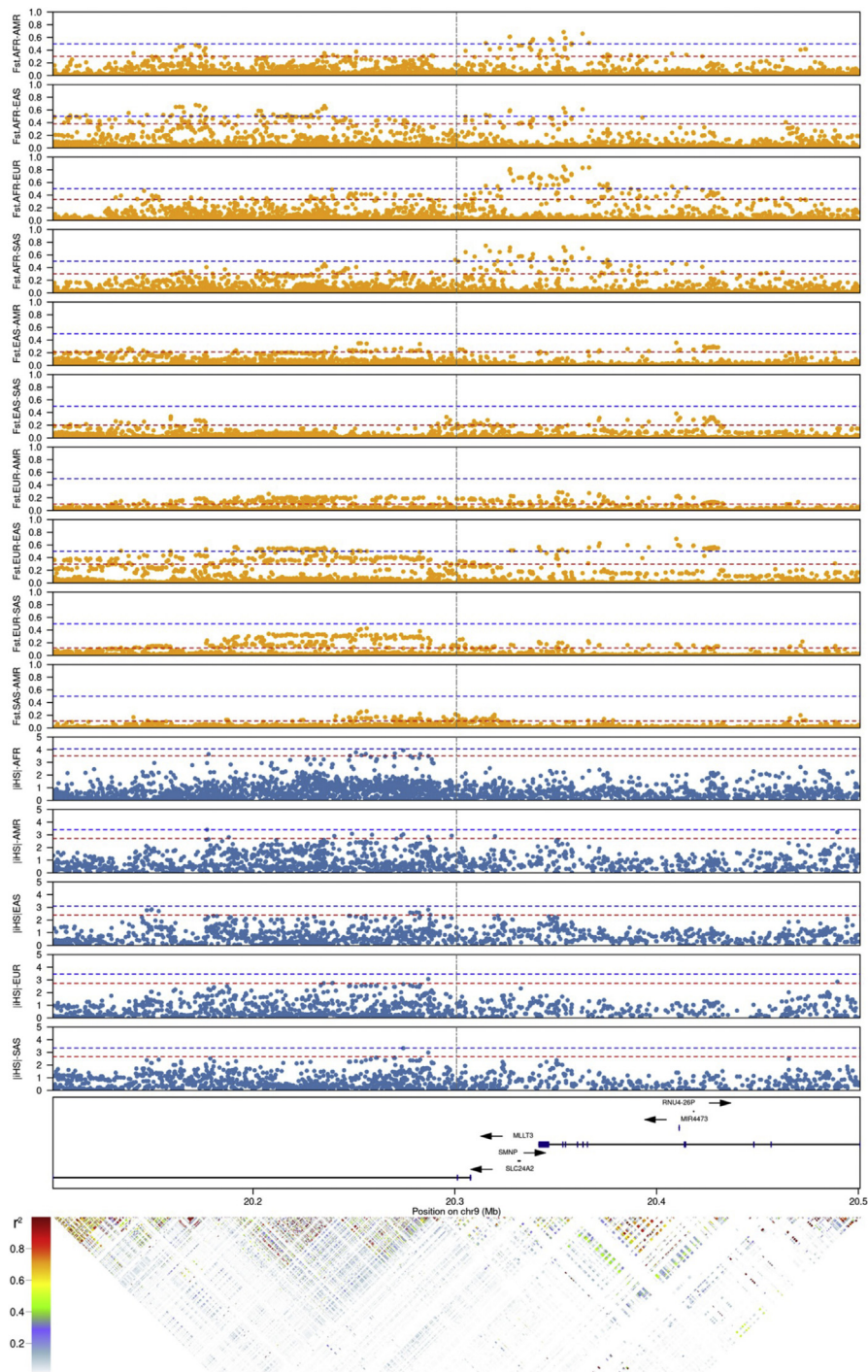




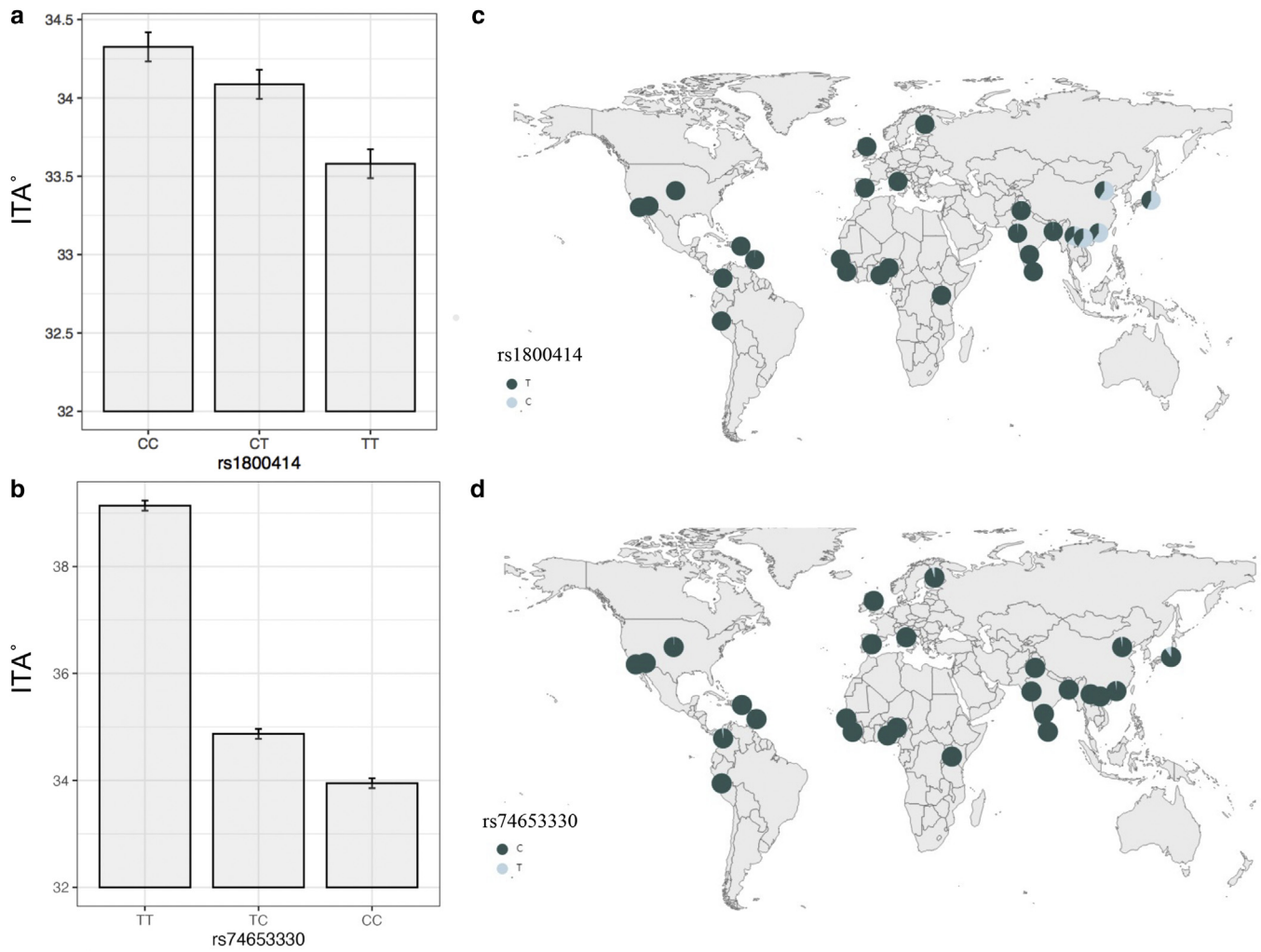
**Supplementary Figure S2. Histogram of ITA° in JD and NSPT.** (a, b) ITA° values were not subject to the normal distribution both in JD and NSPT. (c, d) Histogram of z-ITA° in JD and NSPT, respectively. ITA°, individual typology angle; JD, Jidong cohort; NSPT, National Survey of Physical Traits cohort.



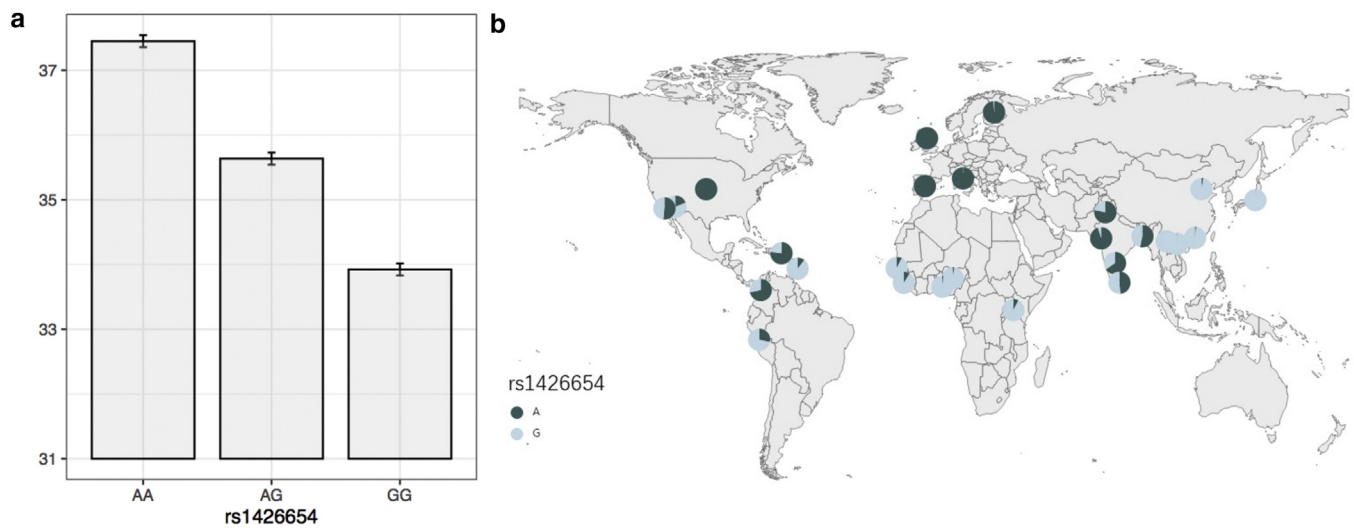
**Supplementary Figure S3. Regional association for the significantly associated region on *SLC24A2* after conditioning the leading SNP.**



**Supplementary Figure S4. Lack of signals of local positive selection for the genome region within 200 kb upstream and downstream of the lead SNP rs10122939.** We used  $F_{ST}$  and  $|iHS|$  statistics between and within EUR, AFR, AMR, SAS, and EAS population samples from the 1000 Genomes Project. Top 1% and 5% statistics cutoff were displayed using dotted lines with corresponding blue and red colors. The location of lead SNP rs10122939 was shown with vertical dotted lines. The gene annotations were based on the latest annotation for hg38 version of the genomic data from the NCBI database. The genomic region of LD plot was consistent with the upside plots. LD ( $r^2 > 0.05$ ) was calculated using the genodata of Europeans obtained from the 1000 Genome Project. AFR, African; AMR, American; EAS, East Asian; EUR, European;  $F_{ST}$ , fixed index;  $iHS$ , integrated haplotype score; LD, linkage disequilibrium; NCBI, National Center for Biotechnology Information; SAS, South Asian.

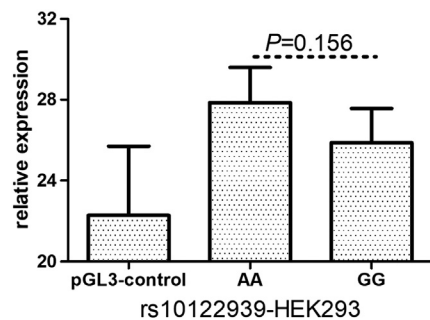


**Supplementary Figure S5. Difference in skin color and allele frequencies.** (a) The effect allele (C allele) of rs1800414 and (b) T allele of rs74653330 showed a lighting effect on skin color. Allele frequency data from 26 populations were taken from the 1000 Genome Project. For (c) rs1800414 and (d) rs74653330, ancestral alleles were represented in deep blue, derived alleles in water blue. ITA°, individual typology angle.

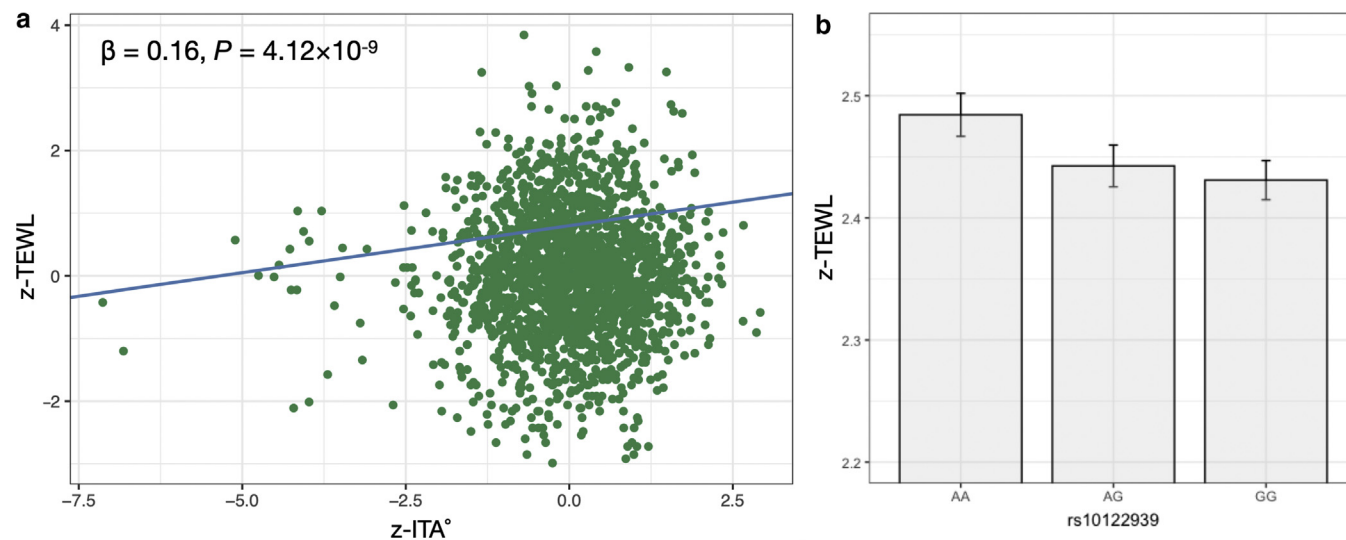


**Supplementary Figure S6. Difference in skin color and allele frequencies of rs1426654.** (a) The effect allele A of rs1426654 showed a lighting effect on skin color. (b) Geographical distribution of the allele frequencies for rs1426654.





**Supplementary Figure S7. Luciferase reporter assays in HEK293 cell line.** The transcriptional activity of the enhancer containing the rs10122939 ancestral A allele was higher than that of the corresponding derived G allele in the HEK293 cell line.



**Supplementary Figure S8. The association analyses related to TEWL.** (a) TEWL is positively associated with  $ITA^\circ$  after controlling for age and sex, meaning better barrier function (thicker skin) is associated with darker skin. (b)  $ITA^\circ$ -associated lead SNP rs10122939 was associated with TEWL. The darker skin (lower  $ITA^\circ$ )-associated G allele has lower TEWL (thicker skin).  $ITA^\circ$ , individual topology angle; TEWL, transepidermal water loss.

### Supplementary Table S1. Sample Characteristics

Characteristic <sup>1</sup>	JD	NSPT	$P^2$
Subjects, n	5,034	1,930	
Male sex, n (%)	2,501 (49.68)	705 (36.53)	$7.09 \times 10^{-23}$
Age in y, median (IQR)	44.00(34.00–56.00)	51.00(40.00–58.00)	$3.09 \times 10^{-16}$
$ITA^\circ$ , median (IQR)	36.59(32.42–40.89)	41.69(36.06–47.80)	$1.31 \times 10^{-151}$
Skin color type, n (%)			
Very light ( $ITA^\circ > 55^\circ$ )	3 (0.06)	138 (7.15)	$2.63 \times 10^{-233}$
Light ( $41^\circ < ITA^\circ < 55^\circ$ )	1,214 (24.12)	897 (46.48)	
Intermediate ( $28^\circ < ITA^\circ < 41^\circ$ )	3,439 (68.32)	804 (41.66)	
Tan ( $10^\circ < ITA^\circ < 28^\circ$ )	378 (7.51)	73 (3.78)	
Brown ( $-30^\circ < ITA^\circ < 28^\circ$ )	0 (0)	18 (0.93)	

Abbreviations: IQR, interquartile range;  $ITA^\circ$ , individual topology angle; JD, Jidong cohort; NSPT, National Survey of Physical Traits cohort.

<sup>1</sup>Baseline characteristics were compared between the discovery dataset and the JD dataset.

<sup>2</sup> $P$ -value of  $t$ -tests for continuous variables and  $\chi^2$  tests for categorical variables.

Supplementary Table S2. SNPs the Showing Genome-Wide Significant Association ( $P < 5e-8$ ) with Skin Color ITA<sup>o</sup> in 6,964 Chinese Individuals

SNP	Gene	CHR	MB	EA	OA	AA	JD (n = 5,034)				NSPT (n = 1,930)				META (n = 6,964)		EAF 1KGP		
							EAF	Beta	SE	P	EAF	Beta	SE	P	Beta	P	EAS	EUR	AFR
rs10122939	SLC24A2	9	20.30	G	A	A	0.34	-0.10	0.02	1.29E-09	0.33	-0.07	0.02	4.71E-03	-0.09	3.61E-11	0.30	0.00	0.27
rs10116858	SLC24A2	9	20.30	T	G	T	0.34	-0.10	0.02	6.35E-09	0.32	-0.07	0.03	3.61E-03	-0.09	1.12E-10	0.30	0.00	0.24
rs10117511	SLC24A2	9	20.30	A	G	G	0.33	-0.10	0.02	5.03E-09	0.32	-0.07	0.03	3.65E-03	-0.09	9.34E-11	0.29	0.00	0.13
rs7033540	SLC24A2	9	20.30	T	C	C	0.29	-0.10	0.02	4.19E-08	0.28	-0.07	0.03	0.01	-0.09	2.21E-09	0.26	0.00	0.21
rs7037385	SLC24A2	9	20.30	A	G	G	0.30	-0.09	0.02	9.59E-08	0.28	-0.07	0.03	5.23E-03	-0.09	2.06E-09	0.27	0.00	0.26
rs12551950	SLC24A2	9	20.31	G	A	A	0.31	-0.09	0.02	6.37E-08	0.30	-0.08	0.03	2.62E-03	-0.09	6.62E-10	0.29	0.01	0.18
rs7851959	SLC24A2	9	20.31	C	G	G	0.31	-0.10	0.02	4.44E-08	0.30	-0.08	0.03	3.10E-03	-0.09	5.68E-10	0.71	0.99	0.62
rs58951095	SLC24A2	9	20.31	A	G	G	0.30	-0.09	0.02	8.63E-08	0.29	-0.08	0.03	2.74E-03	-0.09	9.29E-10	0.27	0.00	0.19
rs57500604	SLC24A2	9	20.31	A	C	C	0.30	-0.10	0.02	5.77E-08	0.29	-0.08	0.03	3.78E-03	-0.09	8.98E-10	0.27	0.01	0.31
rs16938009	SLC24A2	9	20.31	G	A	A	0.31	-0.09	0.02	6.54E-08	0.30	-0.08	0.03	2.87E-03	-0.09	7.54E-10	0.29	0.01	0.32
rs12555331	SLC24A2	9	20.31	G	C	C	0.30	-0.09	0.02	1.56E-07	0.29	-0.07	0.03	5.04E-03	-0.09	3.17E-09	0.73	1.00	0.81
rs1456966	SLC24A2	9	20.31	G	A	A	0.33	-0.08	0.02	2.37E-06	0.31	-0.07	0.03	5.23E-03	-0.08	4.27E-08	0.31	0.01	0.49
rs2383137	SLC24A2	9	20.32	C	G	G	0.32	-0.08	0.02	1.27E-06	0.30	-0.07	0.03	6.71E-03	-0.08	3.04E-08	0.70	0.99	0.82
rs7023559	SLC24A2	9	20.32	C	A	A	0.33	-0.08	0.02	2.00E-06	0.32	-0.07	0.03	5.02E-03	-0.08	3.48E-08	0.31	0.07	0.31
rs1800414	OCA2	15	28.19	T	C	T	0.48	-0.08	0.02	1.96E-06	0.46	-0.10	0.02	9.55E-06	-0.09	1.11E-10	0.40	1.00	1.00
rs76930569	OCA2	15	28.20	C	T	C	0.48	-0.08	0.02	1.96E-06	0.43	-0.10	0.02	9.55E-06	-0.09	1.11E-10	0.40	1.00	1.00
rs76470826	OCA2	15	28.22	AT	A	AT	0.48	-0.07	0.02	5.19E-06	0.43	-0.10	0.02	1.32E-05	-0.08	4.22E-10	0.59	0.00	0.00
rs74653330	OCA2	15	28.23	T	C	C	0.04	0.18	0.04	7.93E-06	0.02	0.21	0.06	9.88E-04	0.19	3.05E-08	0.03	0.01	0.00
rs1426654	SLC24A5	15	48.42	A	G	G	0.03	0.27	0.03	2.55E-09	0.03	0.16	0.03	3.00E-02	0.24	4.64E-10	0.01	1.00	0.07
rs2413887	CTNX2	15	48.49	C	T	T	0.04	0.22	0.04	2.93E-07	0.02	0.15	0.07	0.03	0.20	3.36E-08	0.02	1.00	0.08

Abbreviations: AA, ancestral allele; AFR, African; CHR, chromosome; EA, effect allele; EAF, effect allele frequency; EAS, East Asian; EUR, European; ITA<sup>o</sup>, individual topology angle; JD, Jidong cohort; NSPT, National Survey of Physical Traits cohort; OA, other allele; 1KGP, 1000 Genome Project.

**Supplementary Table S3. SNPs Showing the Suggestive Association ( $5e-8 < P < 1e-6$ ) with ITA<sup>o</sup> in the Meta-Analysis of 6,964 Chinese Individuals**

SNP	Gene	CHR	MB	EA	OA	AA	JD (n = 5,034)				NSPT (n = 1,930)				META (n = 6,964)		EAF 1KGP		
							EAF	Beta	SE	P	EAF	Beta	SE	P	Beta	P	EAS	EUR	AFR
rs201197089	GABBR1	6	29.57	C	CT	CT	0.14	-0.10	0.02	1.08E-05	0.16	-0.08	0.04	0.02	-0.10	5.81E-07	0.30	0.00	0.27
rs11304792	SLC24A2	9	20.31	C	CT	CT	0.40	-0.07	0.02	8.16E-06	0.38	-0.07	0.02	5.02E-03	-0.07	1.34E-07	0.37	0.16	0.53
rs6475429	SLC24A2	9	20.31	C	A	C	0.47	-0.06	0.02	2.17E-04	0.43	-0.08	0.02	6.77E-04	-0.07	6.40E-07	0.41	0.50	0.94
rs28641053	SLC24A2	9	20.31	A	C	C	0.40	-0.07	0.02	1.85E-05	0.37	-0.08	0.02	9.09E-04	-0.07	6.15E-08	0.35	0.01	0.47
rs7021984	SLC24A2	9	20.31	A	T	T	0.33	-0.08	0.02	2.40E-06	0.31	-0.06	0.03	0.02	-0.08	1.47E-07	0.69	0.98	0.76
rs7023747	SLC24A2	9	20.32	T	G	T	0.34	-0.08	0.02	3.73E-06	0.34	-0.06	0.03	0.02	-0.07	3.05E-07	0.35	0.08	0.38
rs3915945	RAB11FIP2	10	119.75	A	G	G	0.15	0.10	0.02	4.03E-06	0.12	0.08	0.03	0.02	0.10	2.70E-07	0.13	0.01	0.00
rs116921893	RAB11FIP2	10	119.76	C	T	T	0.15	0.10	0.02	4.03E-06	0.12	0.08	0.03	0.02	0.10	2.70E-07	0.13	0.01	0.00
rs74638723	RAB11FIP2	10	119.77	G	A	A	0.15	0.10	0.02	5.03E-06	0.12	0.08	0.03	0.02	0.10	3.04E-07	0.13	0.01	0.01
rs3740550	RAB11FIP2	10	119.77	A	G	G	0.15	0.10	0.02	5.03E-06	0.12	0.08	0.03	0.02	0.10	3.04E-07	0.13	0.01	0.01
rs60424173	RAB11FIP2	10	119.78	G	T	T	0.16	0.10	0.02	9.13E-06	0.12	0.07	0.03	0.03	0.09	8.20E-07	0.13	0.01	0.01
rs79852633	CASC2	10	119.84	A	G	G	0.15	0.10	0.02	8.87E-06	0.12	0.10	0.03	3.28E-03	0.10	9.64E-08	0.13	0.01	0.00
rs79250499	CASC2	10	119.86	A	C	C	0.15	0.10	0.02	1.03E-05	0.12	0.10	0.03	4.22E-03	0.10	1.42E-07	0.13	0.01	0.01
rs7077320	CASC2	10	119.87	C	T	T	0.15	0.10	0.02	1.02E-05	0.11	0.10	0.03	3.23E-03	0.10	1.09E-07	0.13	0.01	0.01
rs61507658	CASC2	10	119.88	G	A	A	0.14	0.10	0.02	1.44E-05	0.10	0.11	0.04	1.67E-03	0.11	8.48E-08	0.11	0.01	0.00
rs201658840	CASC2	10	119.90	T	TG	TG	0.15	0.09	0.02	4.51E-05	0.12	0.10	0.03	3.15E-03	0.10	4.71E-07	0.13	0.01	0.01
rs75295597	OCA2	15	28.23	A	T	A	0.49	-0.06	0.02	1.88E-04	0.43	-0.09	0.02	6.76E-05	-0.07	8.67E-08	0.39	1.00	1.00
rs12442916	OCA2	15	28.23	G	A	G	0.37	-0.06	0.02	2.81E-04	0.35	-0.09	0.02	1.82E-04	-0.07	3.00E-07	0.30	0.94	1.00
rs10775262	OCA2	15	28.23	T	C	C	0.36	-0.06	0.02	6.46E-04	0.34	-0.09	0.02	2.37E-04	-0.07	9.21E-07	0.29	0.87	0.80
rs10775263	OCA2	15	28.23	C	T	C	0.36	-0.06	0.02	6.46E-04	0.34	-0.09	0.02	2.37E-04	-0.07	9.21E-07	0.29	0.87	0.80
rs730502	OCA2	15	28.23	G	T	G	0.36	-0.06	0.02	5.01E-04	0.34	-0.09	0.02	1.70E-04	-0.07	5.39E-07	0.29	0.87	0.80
rs2267434	ACO2	22	41.88	T	C	C	0.41	0.07	0.02	1.79E-05	0.51	0.06	0.02	0.01	0.07	8.59E-07	0.51	0.01	0.26
rs5751114	ACO2	22	41.88	G	A	G	0.41	0.07	0.02	1.24E-05	0.51	0.06	0.02	0.02	0.07	7.27E-07	0.51	0.02	0.52
rs2267435	ACO2	22	41.88	G	A	A	0.41	0.07	0.02	1.85E-05	0.51	0.06	0.02	0.01	0.07	8.83E-07	0.51	0.01	0.21
rs2284080	ACO2	22	41.89	C	G	G	0.41	0.07	0.02	1.85E-05	0.51	0.06	0.02	0.01	0.07	8.83E-07	0.49	0.99	0.79
rs5751123	POLR3H	22	41.93	A	C	C	0.42	0.07	0.02	2.83E-05	0.52	0.06	0.02	9.28E-03	0.07	8.36E-07	0.52	0.01	0.22
rs5758384	POLR3H	22	41.93	T	G	G	0.42	0.07	0.02	2.83E-05	0.52	0.06	0.02	9.28E-03	0.07	8.36E-07	0.52	0.01	0.22
rs5758386	POLR3H	22	41.94	A	G	G	0.42	0.07	0.02	3.01E-05	0.52	0.06	0.02	9.82E-03	0.07	9.42E-07	0.52	0.01	0.57
rs5758388	POLR3H	22	41.94	T	C	C	0.42	0.07	0.02	2.83E-05	0.52	0.06	0.02	9.28E-03	0.07	8.36E-07	0.52	0.01	0.22
rs8138232	POLR3H	22	41.94	T	C	C	0.42	0.07	0.02	2.83E-05	0.52	0.06	0.02	9.28E-03	0.07	8.36E-07	0.52	0.01	0.23

Abbreviations: AA, ancestral allele; AFR, African; CHR, chromosome; EA, effect allele; EAF, effect allele frequency; EAS, East Asian; EUR, European; ITA<sup>o</sup>, individual topology angle; JD, Jidong cohort; NSPT, National Survey of Physical Traits cohort; OA: other allele; 1KGP: 1000 Genome Project.



**Table S4. Replication of a Total of 9,183 SNPs Associated with Skin Tanning, Skin Pigmentation, Hair Color, and Eye Color From Viscont et al., Adhikari et al., Hysi et al., and Simcoe et al. in META Results**

SNP	Gene	CHR	MB	EA	OA	JD (N = 5,034)				NSPT (N = 1,930)				META (N = 6,964)		EAF			Related Trait
						EAF	Beta	SE	P	EAF	Beta	SE	P	Beta	P	EAS	EUR	AFR	
rs1426654	SLC24A5	15	48.43	G	A	0.97	0.27	0.05	2.55E-09	0.98	0.16	0.07	2.71E-02	0.24	4.64E-10	0.99	0.00	0.93	Skin, hair and eye color; skin tanning
rs2413887	SLC24A5	15	48.49	T	C	0.96	0.22	0.04	2.93E-07	0.98	0.15	0.07	2.70E-02	0.20	3.36E-08	0.98	0.00	0.92	Skin tanning
rs12442916	OCA2	15	28.23	A	G	0.63	-0.06	0.02	2.81E-04	0.65	-0.09	0.02	1.82E-04	-0.07	3.00E-07	0.70	0.06	0.00	Skin tanning
rs730502	OCA2	15	28.23	T	G	0.64	-0.06	0.02	5.01E-04	0.66	-0.09	0.02	1.70E-04	-0.07	5.39E-07	0.71	0.13	0.20	Skin tanning
rs10775262	OCA2	15	28.23	C	T	0.64	-0.06	0.02	6.46E-04	0.66	-0.09	0.02	2.37E-04	-0.07	9.21E-07	0.71	0.13	0.20	Skin tanning
rs10775263	OCA2	15	28.23	T	C	0.64	-0.06	0.02	6.46E-04	0.66	-0.09	0.02	2.37E-04	-0.07	9.21E-07	0.71	0.13	0.20	Skin tanning
rs12438490	OCA2	15	28.26	T	C	0.60	-0.04	0.02	1.11E-02	0.67	-0.08	0.02	7.67E-04	-0.05	6.36E-05	0.69	0.03	0.06	Skin tanning
rs113769342	DEF8	16	89.98	T	C	0.06	0.15	0.03	1.21E-05	0.05	0.03	0.05	5.85E-01	0.11	8.41E-05	0.04	0.01	0.00	Skin tanning
rs112597872	DEF8	16	89.97	C	G	0.06	0.17	0.04	3.49E-06	0.04	0.00	0.05	9.94E-01	0.11	1.21E-04	0.96	0.99	1.00	Skin tanning
rs4778136	OCA2	15	28.25	C	T	0.54	-0.04	0.02	2.80E-02	0.59	-0.08	0.02	7.28E-04	-0.05	1.86E-04	0.62	0.10	0.38	Skin tanning
rs1800404	OCA2	15	28.24	T	C	0.00	0.04	0.02	2.00E-02	0.00	0.07	0.02	1.60E-03	-0.05	2.08E-04	0.42	0.79	0.12	Skin color
rs12440330	OCA2	15	28.25	T	C	0.52	-0.04	0.02	1.95E-02	0.58	-0.07	0.02	1.88E-03	-0.05	2.20E-04	0.61	0.03	0.01	Skin tanning
rs116848174	FANCA	16	89.90	T	A	0.06	0.16	0.04	6.62E-06	0.04	-0.01	0.05	8.65E-01	0.11	2.73E-04	0.95	0.99	1.00	Skin tanning
rs4778224	OCA2	15	28.24	G	A	0.00	-0.04	0.02	2.93E-02	0.44	-0.07	0.02	1.89E-03	-0.05	3.62E-04	0.39	0.85	0.47	Eye color
rs1868333	OCA2	15	28.24	A	G	0.00	-0.04	0.02	2.49E-02	0.43	-0.07	0.02	2.67E-03	-0.05	3.70E-04	0.39	0.79	0.13	Eye color
rs735066	OCA2	15	28.24	G	A	0.00	-0.04	0.02	2.49E-02	0.43	-0.07	0.02	2.67E-03	-0.05	3.70E-04	0.39	0.79	0.13	Eye color
rs11630828	OCA2	15	28.24	A	G	0.00	-0.04	0.02	2.77E-02	0.43	-0.07	0.02	2.67E-03	-0.05	4.22E-04	0.39	0.79	0.21	Eye color
rs7178315	OCA2	15	28.24	C	T	0.00	-0.04	0.02	2.77E-02	0.43	-0.07	0.02	2.67E-03	-0.05	4.22E-04	0.39	0.78	0.21	Eye color
rs1868332	OCA2	15	28.24	A	G	0.00	-0.04	0.02	2.77E-02	0.43	-0.07	0.02	2.67E-03	-0.05	4.22E-04	0.38	0.79	0.21	Eye color
rs1868334	OCA2	15	28.24	A	C	0.00	-0.04	0.02	2.77E-02	0.43	-0.07	0.02	2.67E-03	-0.05	4.22E-04	0.39	0.79	0.21	Eye color
rs12595216	OCA2	15	28.24	G	A	0.00	-0.04	0.02	2.77E-02	0.43	-0.07	0.02	2.67E-03	-0.05	4.22E-04	0.39	0.79	0.21	Eye color
rs136402	EP300	22	41.60	A	G	0.31	0.06	0.02	1.32E-03	0.38	0.04	0.02	1.01E-01	0.05	4.52E-04	0.41	0.31	0.38	Hair color
rs112225320	VPS9D1	16	89.85	C	A	0.06	0.14	0.03	3.34E-05	0.04	0.00	0.05	9.28E-01	0.10	4.89E-04	0.05	0.01	0.00	Skin tanning
rs113234026	ZNF276	16	89.88	G	A	0.06	0.16	0.04	7.93E-06	0.04	-0.02	0.05	6.75E-01	0.10	5.52E-04	0.05	0.01	0.00	Skin tanning
rs2302161	SPATA2L	16	89.85	T	C	0.06	0.14	0.03	6.09E-05	0.04	0.01	0.05	9.07E-01	0.10	7.30E-04	0.04	0.01	0.00	Skin tanning
rs4778219	OCA2	15	28.21	C	T	0.00	0.05	0.02	2.10E-02	0.00	0.08	0.03	1.11E-02	-0.06	8.16E-04	0.12	0.87	0.81	Skin color
rs8035315	OCA2	15	28.21	T	G	0.00	-0.05	0.02	2.12E-02	0.16	-0.08	0.03	1.42E-02	-0.06	9.72E-04	0.16	0.67	0.11	Eye color
rs7349397	PRKCE	2	46.25	T	C	0.00	0.07	0.02	3.67E-03	0.13	0.05	0.04	1.55E-01	0.06	1.36E-03	0.14	0.25	0.37	Eye color
rs7274168	ZNF341	20	32.44	T	C	0.90	-0.07	0.03	1.24E-02	0.91	-0.09	0.04	4.58E-02	-0.07	1.45E-03	0.90	0.54	0.37	Skin tanning
rs1810534	ZNF341	20	32.44	T	C	0.90	-0.07	0.03	1.38E-02	0.91	-0.09	0.04	4.48E-02	-0.07	1.60E-03	0.90	0.54	0.36	Skin tanning
rs13041078	ZNF341	20	32.44	T	G	0.90	-0.07	0.03	1.18E-02	0.91	-0.08	0.04	5.67E-02	-0.07	1.63E-03	0.90	0.51	0.34	Skin tanning
rs75092208	SPATA33	16	89.81	C	T	0.07	0.10	0.03	1.22E-03	0.06	0.03	0.05	4.72E-01	0.08	2.02E-03	0.05	0.01	0.00	Skin tanning
rs535070	PIEZO1	16	88.88	G	A	0.74	-0.06	0.02	2.56E-03	0.69	-0.03	0.03	2.82E-01	-0.05	2.03E-03	0.69	0.36	0.80	Skin tanning
rs2788222	EXOC2	6	0.72	G	T	0.11	-0.08	0.03	4.42E-03	0.10	-0.05	0.04	1.89E-01	-0.07	2.04E-03	0.13	0.34	0.58	Skin tanning
rs530782	GRM5	11	88.57	G	T	0.59	0.06	0.02	3.03E-04	0.60	0.00	0.02	8.83E-01	0.04	2.23E-03	0.62	0.28	0.79	Skin tanning
rs112992887	VPS9D1	16	89.86	A	G	0.07	0.13	0.03	6.80E-05	0.05	-0.02	0.05	6.59E-01	0.08	2.24E-03	0.05	0.01	0.00	Skin tanning
rs2804737	EXOC2	6	0.72	G	A	0.11	-0.07	0.03	5.50E-03	0.10	-0.05	0.04	1.75E-01	-0.07	2.27E-03	0.13	0.34	0.70	Skin tanning
rs7928319	TPCN2	11	68.91	A	G	0.15	-0.05	0.02	2.50E-02	0.13	-0.07	0.03	3.44E-02	-0.06	2.33E-03	0.11	0.30	0.23	Skin tanning
rs6120392	ZNF341	20	32.45	A	G	0.91	-0.07	0.03	1.06E-02	0.92	-0.07	0.04	1.05E-01	-0.07	2.46E-03	0.91	0.51	0.84	Skin tanning

(continued)

Table S4. Continued

SNP	Gene	CHR	MB	EA	OA	JD (N = 5,034)				NSPT (N = 1,930)				META (N = 6,964)		EAF			Related Trait
						EAF	Beta	SE	P	EAF	Beta	SE	P	Beta	P	EAS	EUR	AFR	
rs57995073	ZNF341	20	32.45	A	C	0.91	-0.07	0.03	1.06E-02	0.92	-0.07	0.04	1.05E-01	-0.07	2.46E-03	0.91	0.51	0.90	Skin tanning
rs4911133	ZNF341	20	32.45	A	G	0.91	-0.07	0.03	1.06E-02	0.92	-0.07	0.04	1.05E-01	-0.07	2.46E-03	0.91	0.51	0.90	Skin tanning
rs6059501	ZNF341	20	32.45	A	T	0.91	-0.07	0.03	1.06E-02	0.92	-0.07	0.04	1.05E-01	-0.07	2.46E-03	0.09	0.49	0.19	Skin tanning
rs4961760	BNC2	9	16.79	C	T	0.12	-0.08	0.03	1.10E-03	0.13	-0.02	0.03	5.20E-01	-0.06	2.56E-03	0.12	0.06	0.20	Skin tanning
rs6059496	ZNF341	20	32.45	C	T	0.91	-0.07	0.03	1.14E-02	0.92	-0.07	0.04	1.03E-01	-0.07	2.61E-03	0.91	0.50	0.84	Skin tanning
rs6059497	ZNF341	20	32.45	G	C	0.91	-0.07	0.03	1.14E-02	0.92	-0.07	0.04	1.03E-01	-0.07	2.61E-03	0.09	0.49	0.16	Skin tanning
rs116953717	CDK10	16	89.83	G	A	0.08	0.11	0.03	2.72E-04	0.07	0.00	0.04	9.91E-01	0.07	2.62E-03	0.06	0.01	0.00	Skin tanning
rs555464	GRM5	11	88.57	T	A	0.59	0.06	0.02	3.16E-04	0.60	0.00	0.02	9.60E-01	0.04	2.75E-03	0.38	0.72	0.22	Skin tanning
rs6059498	ZNF341	20	32.45	C	T	0.91	-0.07	0.03	1.18E-02	0.92	-0.07	0.04	1.11E-01	-0.07	2.88E-03	0.91	0.51	0.84	Skin tanning
rs6059499	ZNF341	20	32.45	C	T	0.91	-0.07	0.03	1.18E-02	0.92	-0.07	0.04	1.11E-01	-0.07	2.88E-03	0.91	0.51	0.84	Skin tanning
rs530975	GRM5	11	88.57	T	C	0.59	0.06	0.02	3.35E-04	0.60	0.00	0.02	9.79E-01	0.04	2.98E-03	0.62	0.28	0.66	Skin tanning
rs2378024	ZNF341	20	32.44	G	C	0.90	-0.07	0.03	1.35E-02	0.92	-0.07	0.04	1.00E-01	-0.07	2.99E-03	0.09	0.49	0.61	Skin tanning
rs79361800	MIR200B	1	1.18	C	G	0.25	-0.04	0.02	2.00E-02	0.24	-0.05	0.03	8.17E-02	-0.05	3.07E-03	0.17	0.09	0.15	Hair color
rs2293585	FANCA	16	89.89	T	C	0.07	0.13	0.03	2.75E-05	0.05	-0.04	0.05	3.59E-01	0.08	3.07E-03	0.06	0.01	0.00	Skin tanning
rs117555146	CDK10	16	89.83	T	C	0.08	0.11	0.03	3.48E-04	0.07	0.00	0.04	9.96E-01	0.07	3.12E-03	0.06	0.01	0.00	Skin tanning
rs11021369	GRM5	11	88.54	C	G	0.59	0.06	0.02	4.89E-04	0.60	0.00	0.02	9.24E-01	0.04	3.43E-03	0.38	0.77	0.24	Skin tanning
rs118066878	SPG7	16	89.65	A	G	0.11	0.04	0.03	9.10E-02	0.12	0.10	0.04	7.49E-03	0.06	3.70E-03	0.13	0.10	0.00	Skin tanning
rs6120395	ZNF341	20	32.45	G	A	0.91	-0.07	0.03	1.59E-02	0.92	-0.07	0.04	1.13E-01	-0.07	3.90E-03	0.91	0.51	0.97	Skin tanning
rs2788224	EXOC2	6	0.72	G	A	0.10	-0.07	0.03	6.30E-03	0.10	-0.04	0.04	2.71E-01	-0.06	4.12E-03	0.13	0.34	0.57	Skin tanning
rs6088301	PXMP4	20	32.37	C	A	0.38	0.03	0.02	8.66E-02	0.36	0.06	0.02	1.02E-02	0.04	4.24E-03	0.32	0.34	0.24	Skin tanning
rs17226764	CDK10	16	89.83	G	GAC	0.08	0.10	0.03	8.50E-04	0.07	0.01	0.04	8.67E-01	0.07	4.25E-03	0.06	0.01	0.00	Skin tanning
rs2804738	EXOC2	6	0.73	G	A	0.10	-0.07	0.03	8.41E-03	0.10	-0.05	0.04	2.28E-01	-0.06	4.39E-03	0.13	0.34	0.40	Skin tanning
rs2804739	EXOC2	6	0.73	G	A	0.10	-0.07	0.03	8.41E-03	0.10	-0.05	0.04	2.28E-01	-0.06	4.39E-03	0.13	0.34	0.40	Skin tanning
rs6088300	PXMP4	20	32.37	C	T	0.38	0.03	0.02	8.11E-02	0.36	0.06	0.02	1.27E-02	0.04	4.48E-03	0.32	0.34	0.25	Skin tanning
rs7187583	ACSF3	16	89.17	G	A	0.68	-0.04	0.02	2.05E-02	0.71	-0.04	0.03	1.03E-01	-0.04	4.61E-03	0.68	0.29	0.47	Skin tanning
rs12221717	GRM5	11	88.54	T	G	0.59	0.06	0.02	6.77E-04	0.60	0.00	0.02	9.69E-01	0.04	4.83E-03	0.61	0.28	0.76	Skin tanning
rs6059462	PXMP4	20	32.36	T	C	0.38	0.03	0.02	8.26E-02	0.36	0.06	0.02	1.42E-02	0.04	4.92E-03	0.32	0.34	0.27	Skin tanning
rs7202996	ACSF3	16	89.17	G	A	0.68	-0.04	0.02	2.01E-02	0.71	-0.04	0.03	1.20E-01	-0.04	5.13E-03	0.68	0.30	0.47	Skin tanning
rs736953	ZNF341	20	32.42	T	G	0.90	-0.06	0.03	2.41E-02	0.91	-0.07	0.04	9.91E-02	-0.06	5.29E-03	0.90	0.50	0.36	Skin tanning
rs11478076	PXMP4	20	32.38	C	CT	0.38	0.03	0.02	1.17E-01	0.36	0.06	0.02	7.73E-03	0.04	5.29E-03	0.32	0.34	0.32	Skin tanning
rs7202765	ACSF3	16	89.17	G	A	0.68	-0.04	0.02	2.08E-02	0.71	-0.04	0.03	1.20E-01	-0.04	5.30E-03	0.68	0.30	0.42	Skin tanning
rs2626558	ZNF341	20	32.43	A	G	0.91	-0.07	0.03	1.64E-02	0.92	-0.06	0.04	1.63E-01	-0.07	5.52E-03	0.90	0.51	0.71	Skin tanning
rs10741523	GRM5	11	88.52	C	T	0.59	0.05	0.02	1.06E-03	0.60	0.00	0.02	9.04E-01	0.04	5.77E-03	0.62	0.28	0.72	Skin tanning
rs319032	NOX4	11	89.17	T	G	0.54	0.04	0.02	2.67E-02	0.53	0.04	0.02	1.00E-01	0.04	5.82E-03	0.53	0.35	0.52	Skin tanning
rs2103804	ZNF341	20	32.43	T	C	0.90	-0.06	0.03	2.41E-02	0.92	-0.07	0.04	1.17E-01	-0.06	6.06E-03	0.90	0.51	0.37	Skin tanning
rs11493150	GRM5	11	88.61	T	C	0.07	0.11	0.03	5.21E-04	0.07	0.00	0.04	9.30E-01	0.07	6.19E-03	0.05	0.02	0.01	Skin tanning
rs2788219	EXOC2	6	0.71	C	T	0.08	-0.07	0.03	1.81E-02	0.08	-0.06	0.04	1.63E-01	-0.07	6.22E-03	0.10	0.23	0.47	Skin tanning
rs35965351	PXMP4	20	32.37	A	AC	0.38	0.03	0.02	1.04E-01	0.35	0.06	0.02	1.33E-02	0.04	6.24E-03	0.31	0.34	0.31	Skin tanning
rs4105582	GRM5	11	88.53	C	A	0.59	0.05	0.02	1.16E-03	0.60	0.00	0.02	9.21E-01	0.04	6.39E-03	0.62	0.28	0.67	Skin tanning
rs11908486	MANBAL	20	35.98	T	G	0.03	-0.09	0.05	7.49E-02	0.02	-0.18	0.08	2.35E-02	-0.12	6.55E-03	0.01	0.21	0.39	Skin tanning
rs2092737	ZNF341	20	32.43	C	A	0.91	-0.06	0.03	2.59E-02	0.92	-0.07	0.04	1.19E-01	-0.06	6.58E-03	0.91	0.51	0.37	Skin tanning

Table S4. Continued

SNP	Gene	CHR	MB	EA	OA	JD (N = 5,034)				NSPT (N = 1,930)				META (N = 6,964)		EAF			Related Trait
						EAF	Beta	SE	P	EAF	Beta	SE	P	Beta	P	EAS	EUR	AFR	
rs12419811	GRM5	11	88.53	A	G	0.14	0.07	0.02	2.65E-03	0.13	0.01	0.03	6.76E-01	0.05	6.64E-03	0.10	0.03	0.05	Skin tanning
rs10756846	BNC2	9	16.95	G	C	0.08	0.05	0.03	8.00E-02	0.07	0.10	0.05	2.19E-02	0.07	6.70E-03	0.10	0.17	0.38	Skin tanning
rs11021556	GRM5	11	88.57	T	C	0.07	0.11	0.03	4.89E-04	0.07	-0.01	0.04	8.58E-01	0.07	6.89E-03	0.05	0.02	0.01	Skin tanning
rs1903841	GRM5	11	88.53	T	C	0.59	0.05	0.02	1.32E-03	0.60	0.00	0.02	9.23E-01	0.04	7.01E-03	0.62	0.28	0.77	Skin tanning
rs117941243	GRM5	11	88.60	A	G	0.07	0.11	0.03	5.21E-04	0.07	-0.01	0.04	8.69E-01	0.07	7.14E-03	0.05	0.02	0.01	Skin tanning
rs13006518	PRKCE	2	46.22	T	C	0.00	0.05	0.02	2.54E-02	0.13	0.05	0.04	1.41E-01	0.05	7.45E-03	0.14	0.23	0.30	Eye color
rs2804740	EXOC2	6	0.73	A	G	0.11	-0.07	0.03	1.23E-02	0.10	-0.04	0.04	2.76E-01	-0.06	7.47E-03	0.13	0.34	0.68	Skin tanning
rs1304320	NOX4	11	89.18	T	G	0.53	0.03	0.02	3.45E-02	0.52	0.04	0.02	1.02E-01	0.04	7.56E-03	0.53	0.43	0.27	Skin tanning
rs164741	SPG7	16	89.69	A	G	0.91	-0.10	0.03	5.45E-04	0.93	0.02	0.04	6.53E-01	-0.06	7.66E-03	0.93	0.34	0.40	Skin tanning
rs2747560	PXMP4	20	32.36	G	A	0.39	0.03	0.02	1.24E-01	0.37	0.06	0.02	1.32E-02	0.04	7.74E-03	0.34	0.34	0.74	Skin tanning
rs35732924	MANBAL	20	35.98	C	G	0.03	-0.08	0.05	8.93E-02	0.02	-0.18	0.08	2.19E-02	-0.11	7.77E-03	0.99	0.78	0.58	Skin tanning
rs2889785	PXMP4	20	32.37	C	T	0.39	0.02	0.02	1.32E-01	0.37	0.06	0.02	1.22E-02	0.04	7.96E-03	0.33	0.34	0.74	Skin tanning
rs11478671	ZNF341	20	32.41	T	TA	0.91	-0.07	0.03	1.64E-02	0.92	-0.05	0.04	2.45E-01	-0.06	8.04E-03	0.90	0.50	0.70	Skin tanning
rs4002398	GRM5	11	88.53	T	C	0.59	0.05	0.02	1.58E-03	0.60	0.00	0.02	9.31E-01	0.04	8.10E-03	0.62	0.28	0.77	Skin tanning
rs171307	ANKRD11	16	89.64	C	T	0.11	0.04	0.03	1.43E-01	0.11	0.10	0.04	1.09E-02	0.06	8.11E-03	0.11	0.08	0.01	Skin tanning
rs72643352	NOX4	11	89.39	C	T	0.22	0.06	0.02	1.20E-03	0.21	0.00	0.03	9.94E-01	0.04	8.14E-03	0.19	0.08	0.00	Skin tanning
rs1808431	ANKRD11	16	89.42	A	G	0.11	0.05	0.03	6.10E-02	0.10	0.07	0.04	5.16E-02	0.06	8.16E-03	0.12	0.07	0.00	Skin tanning
rs992702	GRM5	11	88.54	C	A	0.46	-0.05	0.02	1.50E-03	0.49	0.00	0.02	9.67E-01	-0.03	8.21E-03	0.52	0.25	0.40	Skin tanning
rs11021647	GRM5	11	88.61	T	C	0.07	0.11	0.03	6.91E-04	0.07	-0.01	0.04	8.78E-01	0.07	8.27E-03	0.05	0.02	0.01	Skin tanning
rs187794284	GRM5	11	88.62	C	T	0.07	0.11	0.03	6.17E-04	0.07	-0.01	0.04	8.55E-01	0.07	8.29E-03	0.05	0.02	0.02	Skin tanning
rs139861745	GRM5	11	88.62	C	T	0.07	0.11	0.03	6.17E-04	0.07	-0.01	0.04	8.55E-01	0.07	8.29E-03	0.05	0.02	0.02	Skin tanning
rs118099397	GRM5	11	88.62	A	C	0.07	0.11	0.03	6.17E-04	0.07	-0.01	0.04	8.55E-01	0.07	8.29E-03	0.05	0.02	0.02	Skin tanning
rs12363229	GRM5	11	88.62	T	C	0.07	0.11	0.03	6.17E-04	0.07	-0.01	0.04	8.55E-01	0.07	8.29E-03	0.05	0.02	0.02	Skin tanning
rs4911363	PXMP4	20	32.37	G	A	0.39	0.03	0.02	1.25E-01	0.37	0.06	0.02	1.49E-02	0.04	8.36E-03	0.33	0.34	0.47	Skin tanning
rs4911132	PXMP4	20	32.37	G	A	0.39	0.02	0.02	1.34E-01	0.37	0.06	0.02	1.28E-02	0.04	8.36E-03	0.33	0.34	0.73	Skin tanning
rs10810694	BNC2	9	16.95	C	G	0.08	0.05	0.03	8.63E-02	0.07	0.10	0.05	2.69E-02	0.06	8.40E-03	0.10	0.16	0.31	Skin tanning
rs10765809	GRM5	11	88.59	T	A	0.07	0.11	0.03	5.76E-04	0.07	-0.01	0.04	8.18E-01	0.07	8.41E-03	0.95	0.98	0.85	Skin tanning
rs1391954	GRM5	11	88.58	T	G	0.60	-0.05	0.02	3.35E-03	0.56	-0.01	0.02	7.13E-01	-0.04	8.49E-03	0.54	0.43	0.53	Skin tanning
rs4270425	PXMP4	20	32.37	A	G	0.39	0.02	0.02	1.45E-01	0.37	0.06	0.02	1.11E-02	0.04	8.51E-03	0.33	0.34	0.45	Skin tanning
rs6087519	PXMP4	20	32.36	C	G	0.39	0.03	0.02	1.24E-01	0.37	0.06	0.02	1.59E-02	0.04	8.59E-03	0.67	0.66	0.18	Skin tanning
rs7271022	PXMP4	20	32.37	C	T	0.39	0.03	0.02	1.24E-01	0.37	0.06	0.02	1.59E-02	0.04	8.59E-03	0.33	0.34	0.84	Skin tanning
rs2747562	PXMP4	20	32.38	T	C	0.37	0.03	0.02	9.21E-02	0.35	0.05	0.02	2.84E-02	0.04	8.65E-03	0.31	0.34	0.74	Skin tanning
rs79743671	OCA2	15	28.32	A	G	0.60	-0.02	0.02	1.42E-01	0.64	-0.06	0.02	1.28E-02	-0.04	8.65E-03	0.63	0.08	0.06	Skin tanning
rs2626522	ZNF341	20	32.40	G	C	0.90	-0.06	0.03	2.87E-02	0.92	-0.06	0.04	1.47E-01	-0.06	8.67E-03	0.10	0.49	0.65	Skin tanning
rs2243719	BNC2	9	16.81	T	A	0.09	-0.07	0.03	8.68E-03	0.15	-0.03	0.04	3.77E-01	-0.06	8.71E-03	0.84	0.94	0.84	Skin tanning
rs28469723	TRPC4AP	20	33.70	G	A	0.07	0.04	0.03	2.67E-01	0.09	0.13	0.04	3.37E-03	0.07	8.74E-03	0.09	0.09	0.17	Skin tanning
rs79341738	TRPC4AP	20	33.70	C	T	0.07	0.04	0.03	2.67E-01	0.09	0.13	0.04	3.37E-03	0.07	8.74E-03	0.09	0.09	0.16	Skin tanning
rs79438986	TRPC4AP	20	33.70	G	T	0.07	0.04	0.03	2.67E-01	0.09	0.13	0.04	3.37E-03	0.07	8.74E-03	0.09	0.09	0.05	Skin tanning
rs112318873	TRPC4AP	20	33.70	C	T	0.07	0.04	0.03	2.67E-01	0.09	0.13	0.04	3.37E-03	0.07	8.74E-03	0.09	0.09	0.17	Skin tanning
rs75888794	TRPC4AP	20	33.70	C	G	0.07	0.04	0.03	2.67E-01	0.09	0.13	0.04	3.37E-03	0.07	8.74E-03	0.91	0.91	0.83	Skin tanning
rs144862523	GRM5	11	88.62	A	G	0.07	0.11	0.03	6.76E-04	0.07	-0.01	0.04	8.55E-01	0.07	8.77E-03	0.05	0.02	0.02	Skin tanning

(continued)



Table S4. Continued

SNP	Gene	CHR	MB	EA	OA	JD (N = 5,034)				NSPT (N = 1,930)				META (N = 6,964)		EAF			Related Trait
						EAF	Beta	SE	P	EAF	Beta	SE	P	Beta	P	EAS	EUR	AFR	
rs13043800	PXMP4	20	32.37	C	T	0.39	0.02	0.02	1.30E-01	0.37	0.06	0.02	1.49E-02	0.04	8.80E-03	0.33	0.34	0.83	Skin tanning
rs112380351	OCA2	15	28.32	G	C	0.60	-0.02	0.02	1.46E-01	0.64	-0.06	0.02	1.28E-02	-0.04	8.94E-03	0.37	0.92	0.93	Skin tanning
rs10831459	GRM5	11	88.54	A	G	0.52	0.05	0.02	2.23E-03	0.53	0.00	0.02	8.71E-01	0.03	9.10E-03	0.55	0.28	0.63	Skin tanning
rs585423	GRM5	11	88.63	C	G	0.31	0.05	0.02	1.91E-03	0.30	0.00	0.03	9.37E-01	0.04	9.12E-03	0.71	0.62	0.71	Skin tanning
rs10765802	GRM5	11	88.57	T	C	0.07	0.11	0.03	6.49E-04	0.07	-0.01	0.04	8.06E-01	0.07	9.16E-03	0.05	0.02	0.00	Skin tanning
rs10765803	GRM5	11	88.57	T	C	0.07	0.11	0.03	6.49E-04	0.07	-0.01	0.04	8.06E-01	0.07	9.16E-03	0.05	0.02	0.00	Skin tanning
rs2626547	ZNF341	20	32.40	A	G	0.91	-0.06	0.03	2.21E-02	0.92	-0.05	0.04	2.11E-01	-0.06	9.22E-03	0.91	0.50	0.36	Skin tanning
rs6060246	TRPC4AP	20	33.70	G	A	0.07	0.03	0.03	2.77E-01	0.09	0.13	0.04	3.37E-03	0.07	9.28E-03	0.09	0.09	0.17	Skin tanning
rs2747561	PXMP4	20	32.37	T	C	0.37	0.03	0.02	9.03E-02	0.35	0.05	0.02	3.30E-02	0.04	9.31E-03	0.31	0.34	0.83	Skin tanning
rs6060245	TRPC4AP	20	33.70	G	A	0.07	0.03	0.03	2.80E-01	0.09	0.13	0.04	3.37E-03	0.07	9.40E-03	0.09	0.09	0.17	Skin tanning
rs6058185	TRPC4AP	20	33.70	G	A	0.07	0.03	0.03	2.80E-01	0.09	0.13	0.04	3.37E-03	0.07	9.40E-03	0.09	0.09	0.60	Skin tanning
rs1890364	EXOC2	6	0.71	T	G	0.08	-0.07	0.03	3.02E-02	0.08	-0.06	0.04	1.52E-01	-0.06	9.40E-03	0.10	0.27	0.49	Skin tanning
rs117002968	GRM5	11	88.60	C	T	0.07	0.11	0.03	6.91E-04	0.07	-0.01	0.04	8.18E-01	0.07	9.48E-03	0.05	0.02	0.01	Skin tanning
rs10831539	GRM5	11	88.60	C	T	0.07	0.11	0.03	6.91E-04	0.07	-0.01	0.04	8.18E-01	0.07	9.48E-03	0.05	0.02	0.01	Skin tanning
rs317137	NOX4	11	89.16	C	T	0.55	0.04	0.02	2.21E-02	0.56	0.03	0.02	2.13E-01	0.03	9.51E-03	0.58	0.36	0.53	Skin tanning
rs2788223	EXOC2	6	0.72	G	A	0.07	-0.08	0.03	1.37E-02	0.08	-0.04	0.04	3.05E-01	-0.07	9.53E-03	0.10	0.20	0.55	Skin tanning
rs10738470	BNC2	9	16.94	T	C	0.09	0.05	0.03	9.57E-02	0.07	0.10	0.05	2.71E-02	0.06	9.61E-03	0.10	0.17	0.32	Skin tanning
rs4961508	BNC2	9	16.94	T	C	0.09	0.05	0.03	9.57E-02	0.07	0.10	0.05	2.71E-02	0.06	9.61E-03	0.10	0.17	0.32	Skin tanning
rs7861272	BNC2	9	16.94	G	C	0.09	0.05	0.03	9.57E-02	0.07	0.10	0.05	2.71E-02	0.06	9.61E-03	0.10	0.17	0.32	Skin tanning
rs55999610	BNC2	9	16.94	TA	T	0.09	0.05	0.03	9.57E-02	0.07	0.10	0.05	2.71E-02	0.06	9.61E-03	0.90	0.83	0.68	Skin tanning
rs1538587	BNC2	9	16.94	C	G	0.09	0.05	0.03	9.64E-02	0.07	0.10	0.05	2.71E-02	0.06	9.69E-03	0.10	0.17	0.32	Skin tanning
rs2626562	ZNF341	20	32.41	A	G	0.91	-0.06	0.03	2.40E-02	0.92	-0.06	0.04	2.05E-01	-0.06	9.69E-03	0.91	0.52	0.37	Skin tanning
rs17092297	TRPC4AP	20	33.70	A	G	0.07	0.03	0.03	2.80E-01	0.09	0.13	0.04	3.66E-03	0.07	9.74E-03	0.09	0.09	0.59	Skin tanning
rs11021471	GRM5	11	88.56	C	T	0.16	0.07	0.02	1.29E-03	0.15	0.00	0.03	9.14E-01	0.05	9.87E-03	0.13	0.03	0.06	Skin tanning
rs2207355	PXMP4	20	32.37	T	C	0.39	0.02	0.02	1.40E-01	0.37	0.06	0.02	1.56E-02	0.04	9.87E-03	0.33	0.34	0.81	Skin tanning
rs62068676	SPG7	16	89.65	T	C	0.11	0.04	0.03	1.43E-01	0.11	0.09	0.04	1.51E-02	0.06	9.87E-03	0.11	0.08	0.01	Skin tanning
rs7875833	BNC2	9	16.94	G	T	0.09	0.05	0.03	1.01E-01	0.07	0.10	0.05	2.59E-02	0.06	9.93E-03	0.10	0.17	0.32	Skin tanning
rs10810689	BNC2	9	16.94	T	A	0.09	0.05	0.03	1.01E-01	0.07	0.10	0.05	2.59E-02	0.06	9.93E-03	0.10	0.17	0.32	Skin tanning
rs10810691	BNC2	9	16.94	T	C	0.09	0.05	0.03	1.01E-01	0.07	0.10	0.05	2.59E-02	0.06	9.93E-03	0.10	0.17	0.31	Skin tanning
rs598952	GRM5	11	88.59	A	T	0.69	0.06	0.02	1.27E-03	0.70	0.00	0.03	8.93E-01	0.04	9.95E-03	0.25	0.70	0.31	Skin tanning

All SNPs with  $P < 0.01$  are shown.

Abbreviations: AFR, African; CHR, chromosome; EA: effect allele; EAF: effect allele frequency; EAS, East Asian; EUR, European; JD, Jidong cohort; MB, megabase; META, meta analysis; NSPT, National Survey of Physical Traits cohort; OA: other allele.