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Evaluation of skin-related variants in African ancestry populations and their role in personal identification

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ABSTRACT

Pigment-related genetic variants point out their role in personal identification as they can be considered predictors suitable for Forensic DNA Phenotyping (FDP) and mounting evidence suggest also their bio-geographic inferential power for gaining information about the individual geographical origin. As they could be regarded as AIMs (Ancestry Informative Markers) they are powerful tools for inferring genetic composition of admixed population. Despite the huge range of skin tones across our species, little is known about genetic basis in global population and particularly our knowledge is less precise for those showing a complex historical and genomic background. The current research aims to explore the allelic status in several SNPs mapped in selected genes known to be involved in skin pigmentation: *OCA2, HERC2, SLC45A2, SLC24A5* and two intergenic regions between *BEND7/PRPF18* and *EIF2S2/ASIP*. The genetic evaluation has been performed on selected African and African derived populations: Fon, Dendi, Bariba and Berba communities from Benin, and Afroecuadorians. Data integration has been made up merging genotypic results with available information from major biological data warehouse as Phase 3–1000 Genomes Project or International HapMap Project in order to obtain a selected populations panel useful for their use as inferential model training set to test the likelihood of correct assignment to geographically differentiated human groups. The proposed variants panel seems to properly interpret the geographic variation and some new interesting evidence could be pointed out in African mixed populations, that seem to be differentially distributed if the total panel is considered. Understanding human pigmentation architecture can provide fundamental insight into genetic interaction of complex traits and the relationship between environmental adaptation and population history. In addition, the results support the use of phenotypic inference along with bio-geographical ancestry information as valid auxiliary tools in personal identification.

1. Introduction

Skin pigmentation is one of the most variable phenotypic traits in human populations that is synergically determined by the interaction of multiple factors such as environmental, cultural and genetic ones. Indeed human skin pigmentation is the final outcome of the complex interactions of genetic mechanisms prone to be adjusted by Natural Selection for tuning the pigmentation levels according to UV radiation (UVR).

Remarkably, molecular data about pigmentation-related variants point out a well-known utility in personal identification as they can be considered suitable phenotypic predictors [1]. Forensic DNA Phenotyping (FDP) allows the prediction of the External Visible Characteristics (EVCs) of an individual, starting from genetic markers: DNA would be a "key witness" for phenotypic information, and skin pigmentation should be considered one of the leading features to be accounted for. Despite the phenotypic identification being the ultimate goal of FDP, some authors suggest the bio-geographic inferential information should be mandatory for compiling reliable individual profile due to the close relationship between the environment and the pigmentary traits [2]. This connection is partly mirrored by peculiar geographic distribution of genetic markers related to constitutional skin tones. The noticeable differences for their allelic distribution in worldwide populations make them a valid toolkit to identify the individual geographic origin, making them able to be considered as reliable Ancestry Informative Markers (AIMs). The genetically based prediction of ancestry seems to have a great potential in forensic genetics since it could provide worthwhile bio-geographical information,

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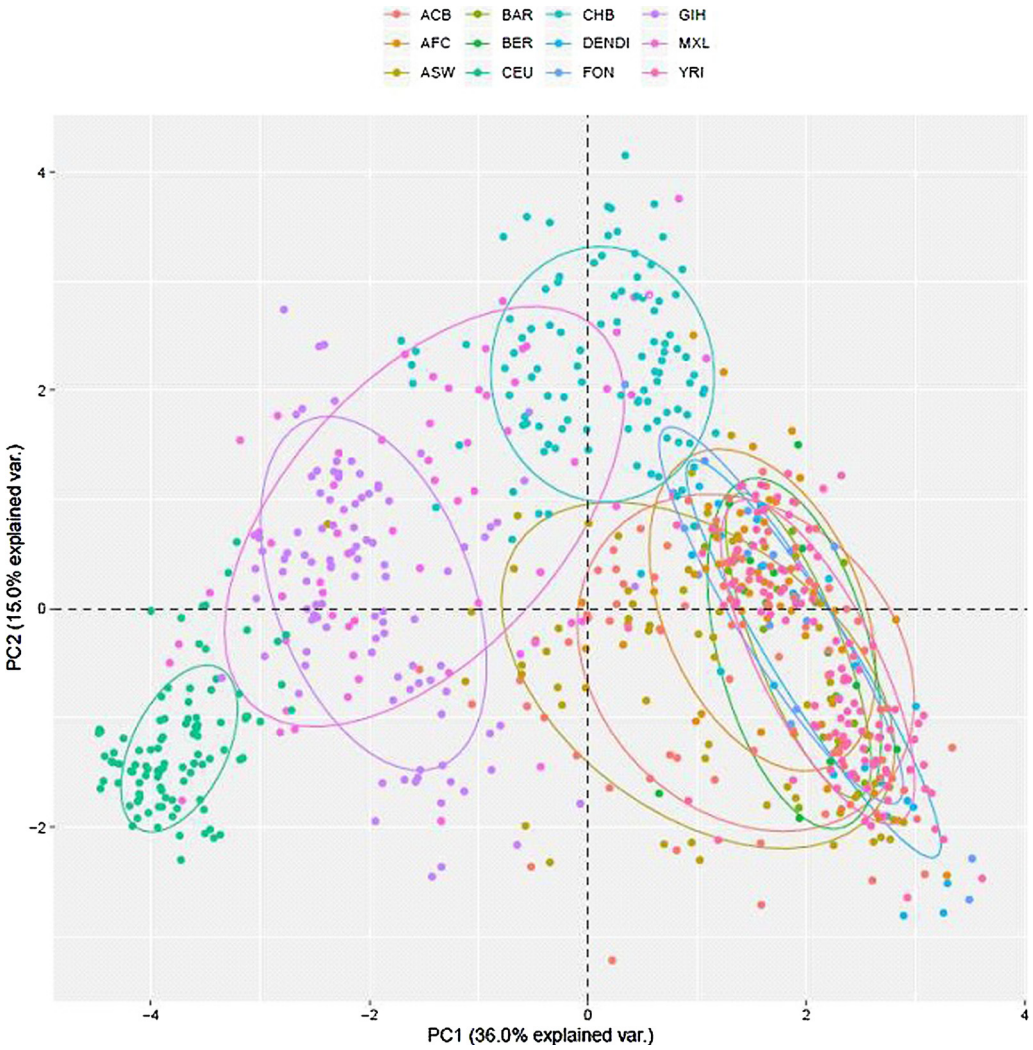

Fig. 1. PCA built on the whole mutational set for all sampled populations compared to the reference ones. ACB: African Caribbeans; AFC: Afroecuadorians; ASW: Americans of African Ancestry; BAR: Bariba; BER: Berba; CEU: Utah Residents (CEPH) with Northern and Western European Ancestry; CHB: Han Chinese; DENDI: Dendi; FON: Fon; GIH: Gujarati Indian from Houston; MXL: Mexican Ancestry from Los Angeles; YRI: Yoruba in Ibadan.

which ultimately should be a relevant auxiliary tool in personal identification. Accordingly, several projects are mounting to identify the variants that might be considered suitable AIMs able to support the FDP in gaining information about the individual geographical origin.

This paper aims to explore the allelic status in several SNPs mapped in genes known to be involved in skin pigmentation [3,4]: rs1448484 in *OCA2*; rs12913832 and rs7183877 in *HERC2*; rs16891982, rs2278007, rs78505258 and rs35398 in *SLC45A2*, rs2675345, rs1426654, rs2470102 in *SLC24A5*. Furthermore, rs6602665 and rs6602666 will be focused due to their mapping at an intergenic region between *BEND7/PRPF18* and rs6142102 in *EIF2S2/ASIP* area. They recently joined the skin-related variants short-list and appear to be significantly involved in eumelanic pigmentation [5]. Consequently, the availability of several African and African-derived population samples allows to deepen the knowledge about the genetic make-up at these candidate genes in dark skin people aiming to support their putative phenotypic predictability in order to confirm their proficient leverage as a suitable panel for personal identification purposes.

2. Materials and methods

The genetic evaluation by direct sequencing has been performed on 194 healthy people from selected African and African derived populations, whose biological samples were obtained after the acceptance of dedicated informed consent approved by the Ethics Committee of the University of Rome Tor Vergata (June 22nd 2011). The samples pertain to Fon (n = 35), Dendi (n = 31), Bariba (n = 30) and Berba (n = 20) communities from Benin, and 78 Afroecuadorians from Esmeralda district in the North of Ecuador. The individual genotypes were used to calculate the allele frequencies that were tested for the concordance with Hardy-Weinberg equilibrium. A data reduction method such as PCA (Principal Component Analysis) has been employed to validate the hypothesis that the identified variants could be considered an effective AIMs panel. The genotypic results for Beninese and Afroecuadorian communities have been integrated with the available data from Phase 3-1KGP release in order to obtain a reference panel. In addition, the genotype data for all the loci was integrated with data available for 30 random subjects of 4 HapMap project selected as representative of the four major continental groups: YRI (Yoruba for Africa) CHB (Han Chinese for East Asia), GIH (Gujarati Indians for South East Asia), CEU (Northern and Western European ancestry people for Europe), and MXL (Mexican ancestry individuals in Los Angeles for America). These populations were used as an inferential model training-set to test the likelihood of correct assignment to representative human groups for continental clusters.

3. Results

The multivariate evaluation of the whole variant panel allows to properly dissect the populations according to their geographical origin accounting for several area-specific clusters. Several iterations comparing eumelanic individuals from different geographic areas were performed to select the variants to be considered as significant determinants for the clusters: the synergic evaluation of rs1448484, rs16891982, rs2278007, rs78505258, rs35398, rs6602665, rs6602666 and rs6142102 returns the best clustering, explaining more than 50% of variance (Fig. 1). The first Component shows remarkable split among Europeans (CEU), Asians (GIH, CHB) and Americans (MXL); African (YRI, BER, BAR, FON, DENDI) and people with African origin (ACB, ASW, AFC). Specifically, Asian dark skin people (GIH) are apart from Chinese individuals (CHB) on the second Component (15.0% of variance). Vice-versa, the Afro-Americans lie in an intermediated position on the first Component (36.0% of variance): this evidence seems to confirm their heterogeneous genetic make-up despite their comparable pigmentary phenotype to that of South-Saharan populations. Those dark-skin people are roughly overlapping in the plot and the use of three variants known to be significantly linked to hyper-pigmentation (rs6602665, rs6602666 and rs6142102) does not seem enough for the reliably dissecting African or African-derived populations, even though they are apart from dark-skinned South-East Asian groups. This displacement is slightly enhanced when the variant located in *OCA2* (rs1448484) is added in the evaluation, supporting its specific variability pattern among South-East Asian groups [6].

4. Discussion and conclusion

The considered variants panel seems to significantly account for rough geographic variation even though the results do not appear clueless to what concerns populations with mixed origin and intermediate pigmentation. Thus, the results support the leverage of phenotypic inference by molecular information as a valuable auxiliary tool in the individual recognition even though these deductions should be complemented by bio-geographical data in order to enhance the outwardly visible characteristics power for genetic personal identification.

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Declaration of Competing Interest

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