Title: Genomic demography of world's ethnic groups and their genomic identity between two individuals

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Abstract: Categorizing extant humankinds based on common characteristics is a useful concept in many fields for correlating the category or demography to the variety of biological, societal, cultural, economic and other issues, but has many problems primarily because of the difficulties of defining the common characteristics *objectively and quantitatively*. All current categorizations, such as ethnicity, ancestry and race, are based on various selections and combinations of *subjectively*- and/or *qualitatively*-defined characteristics, such as ancestral lineage/location, cultural/societal norm, language, skin color and other phenotypes and traits perceived by the members within or from outside of the categorized group. Yet, such categorization has been broadly used in many fields, including the fields of human genetics, health sciences and medical practices (e.g., *1,2,3*), where the observed health characteristics are objectively- and quantitatively-definable, but the population categorization is not. Here we present a whole genome-based categorization that is objectively defined and quantitatively measurable. We observe that: (a) the world's ethnic populations form about 14 "genomic groups (GGs)"; (b) each GG consists of multiple ethnic groups (EGs); and (c) at an individual level, approximately 99.8%, on average, of the whole genome contents are identical between any *two individuals* regardless of their GGs or EGs.

Main Text (4,649 words--> 4,300)

Introduction

Background: Historically, classification or categorization of humankind, such as race, ethnicity, and ancestry has been attempted by using various sociological characteristics such as

physical appearance, subjectively presumed ancestry, language, cultural history, religions, socioeconomic status and others. Such categorizations and characteristics are, in general, difficult to define objectively and quantitatively. Therefore, they are, in general, unsuitable for correlating between the categories and the characteristics of whole genomic data gathered objectively and quantitatively in the fields of human genetics, health sciences and medical practices. Thus, there is an urgent need for a scientifically definable categorization of extant human population that can be used for correlating the scientifically gathered characteristics in these fields (*1, 2, 3*).

Several large-scale genomic studies have been published during the last decade to address the extent and types of genomic diversity of the extant human species, e.g., for 2,504 individuals from 26 large "population groups (PGs)" from diverse geographic locations in the 1000 Genomes Project (1KGP) (*4*), for 300 individuals from 142 ethnic groups (EGs) based on ancestry, linguistic, faith and cultural differences in the Simons Genome Diversity Project (SGDP) (*5*), and for 44 African ethnic populations in 4 linguistic groups (*6*). As a result of these studies as well as other similar or related studies (e.g., *7, 8*), a large body of whole genome Single Nucleotide Polymorphism (SNP) data became publicly available for a wide range of individuals representing different ethnic groups or "population" groups throughout the world.

We revisit these data for the purpose of (a) finding a whole genome-based categorization for all of the ethnic groups using a text-comparison method of Information Theory (*9*), which has not been applied in any of the earlier studies, and (b) quantifying the fraction of whole genome that enables such genome-based categorization.

Objectives: The itemized objectives of this study are: (a) using the concept of the "contextually-linked Single Nucleotide Variation (SNV) genotypes (c-SNVs)", identify genome-based groups (GGs) of world's EGs in the SGDP database (*5*), where c-SNVs are represented by overlapping short strings of ordered SNV genotypes, (b) correlate the relationship between GGs and EGs, (c) suggest the order of emergence of GGs; (d) quantify the magnitudes of genomic identity/difference between two individuals within each GG as well as between two different GGs to estimate the fraction of whole genome that contributes toward an individual's GG; and (e) perform a similar study as (d) above for the 1KGP samples, which has fewer EGs divided into 26 broadly defined "Population Groups(PGs)" with larger samples.

Approach: Our approach is to adapt a computational method of comparing and categorizing linear information such as texts or books in the field of Information Theory (*9*) by "word frequency profiles" (*10*). We generalized the method to be applicable to other linear informational "Features", such as genomic sequence, proteomic sequence, or SNV sequence. In this study we convert the whole-genome SNV genotypes of an individual into a "book" of "Feature Frequency Profile (FFP)" (*11*), where each "Feature" (which corresponds to a "word" in books) consist of a *unique* c-SNV as a "character" of the genomic feature, and its frequency in a genome, as the Feature's "character state", for a given length of c-SNVs (see **Feature Frequency Profile** in Materials and Methods of Supplementary Materials). Thus, an FFP of an individual's c-SNV genotypes and their frequencies contains all the information necessary to reconstruct the original sequence of the ordered SNV genotypes. Then, for a given length of the c-SNVs, all pair-wise divergence of the FFPs for all study population can be calculated to assemble a "genomic divergence matrix" for the given c-SNV length. This matrix is used both for Principal Component Analysis (PCA) (*12*) to discover the genome-based demographic

grouping pattern (as manifested by clustering) of the study population (see **FFP-based PCA** in Materials and Methods of Supplementary Materials) and for constructing a rooted neighbor-joining tree (*13*; see **FFP-based rooted NJ tree** and **Tree rooting** in Materials and Methods of Supplementary Materials). Among many such trees, each corresponding to a given length of the c-SNVs, one with the most topologically stable tree is selected as the final tree. From the final tree the order of the emergence of the founder nodes of GGs are predicted on an evolutionary progression scale, which corresponds to the normalized cumulative branch-lengths from the tree root to the founder nodes.

The uniqueness of our approach is two folds: (a) we compare the entirety of the individual's whole genomic variations *in context* and (b) each individual's whole genome variation is compared to that of each of all other individuals, not to that of one Eurocentric "human reference genome".

Results

Our results are divided into two parts: the first part focuses on, at the group level, the genome-based grouping pattern of the population of 164 ethnicities of the SGDP database, and on the emergence order of the founders of the groups. These provide the results for the first three specific objectives ((a) – (c)) listed under **Objectives** in the Introduction. The second part focuses, at the individual level, on the extent of genomic identity at all SNP loci between two individuals among: (a) all members of the SGDP population which has the largest number of ethnic groups, and (b) all members of the 1KGP population, which has the largest number of samples. Then, we extrapolate the percent identity for all SNP loci to that for the respective whole genome length to get an intuitively understandable quantity of the magnitude of the whole genomic identity between two human individuals within a given GG or PG and between two different GGs or PGs. These provide the results for the remaining two specific objectives ((d) and (e)) listed under **Objectives** in the Introduction.

I. Genomic demography: 14 "genomic groups (GGs)" and the order of their emergence

At a group level, we examined the genome-based grouping patterns and their relationships among all GGs by two different methods, both based on the individual's genomic variation expressed by the FFPs of c-SNVs: Principal Component Analysis (PCA) (*12*) and Neighbor-Joining (NJ) phylogeny methods (*13*).

Clustering by PCA: Figure 1 shows the grouping pattern, based on clustering, revealed by PCA for all members (345 individuals) of the study population from 164 EGs in the recent SGDP database (*5*), where the genomes were sequenced to an average coverage of 43-fold. In the PCA, the clustering is strictly based on the genomic divergence matrix calculated using FFPs of c-SNVs (see **FFP based PCA** in **Materials and Methods** of Supplementary Materials). The figure shows that:

(a) There are about 14 clusters in genomic variation space (i.e., c-SNV space) which we named "Genome-based Groups" or "Genomic Groups (GGs)" (one of which, GG3, consits of a collection of several not-well-resolved subclusters of various sizes);

(b) All GGs are divided into two interconnected super groups: one defined by a long linear arm in Fig. 1 containing all five African GGs (GG0 – GG4), most of which are linearly linked but not well clustered and account for all 45 African EGs in the SGDP. The other is a more

fanned-out arm containing all non-African GGs (GG5 – GG13), most of which are well clustered, accounting for all of the 119 non-African EGs;

(c) All African GGs are linearly connected, with GG0 (the EGs of Khomani_San and Jo_hoan) at one end, and GG4 (the EGs of Mozabite and Saharawi) at the other, but all non-African GGs appear to have originated from the Middle East GG (GG5). Most of non-African GGs are tightly-clustered and well-resolved, but, all un-clustered and isolated samples are found in this super group;

(d) Each GG consists of multiple EGs (see Supplementary Table S1), thus there is no one-to-one correspondence between any one GG and any one EG;

(e) Many of the 14 GGs can be assigned to various geographical or geological regions (see the upper inset of Fig. 1);

(f) The extant members of some large GGs (GG6, GG12 and GG13) are widely scattered in geographical space (see the upper inset of Fig. 1), but their genomes are closely clustered in genomic variation space (see the PCA plot of Fig. 1).

Some of the features described above (such as (b), (c) and (f) mentioned above) have been observed in the first SDGP publication (see Extended Data Fig. 4A of reference *5*). We also noticed a few unexpected observations in our PCA plot where some members of a given ethnic group are found in two geographic locations very far apart (see **Supplementary Note 1** in Supplementary Materials).

Clading in NJ tree: Figure 2 shows the clading pattern revealed in our rooted FFP-based tree with cumulative branch-lengths (see **FFP-based rooted NJ tree** of Materials and Methods in Supplementary Materials**)** by a neighbor-joining (NJ) method (*13, 14*) (for a corresponding topological tree with the names of EGs and clading details is shown in Supplementary Fig. S1, which can be expanded for an easier viewing). The genomic divergence matrix used as the input of the tree is the same as that used in the PCA clustering for Fig. 1 above, but, in the NJ tree building method, two additional constraints are imposed for the evolutionary model, which constrain the tree topology and clading: (a) two bifurcating branches emerging from each internal node and (b) maximum parsimony (minimal evolution) when choosing the neighbors to join as a sister pair. For comparison, all the GGs identified by the PCA clustering in Fig. 1 are also shown in the middle circular band of Fig. 2. Noticeable from the tree are:

(a) As was observed in Fig. 1, all African GGs (GG0 – GG4) emerged sequentially in multiple steps, but all non-African GGs (GG5 – GG13) emerged in a burst within one giant clade nested by 4 large clades and a few small clades plus isolated branches;

(b) We can identify 9 clades (inner circular bands), 8 of which are closely related to 8 out of the 14 GGs defined by the PCA clustering (middle circular band), and;

(c) Most of the 8 clades can be assigned to various geographical or geological regions; and

(d) Most or all of the EGs of GG6 in Europe and GG13 in East and Southeast Asia have emerged in a "burst", but the EGs of GG10 and GG12 appeared in multiple stages.

In the first SDGP publication (5) their NJ tree, when compared to ours, has many differences in clading pattern, relative branch lengths and branching order within each region (Extended Data Fig. 4B of reference *5*). These differences as well as those of clustering differences mentioned in previous section (**Clustering by PCA)** are primarily due to the difference of the descriptors of whole genome variation, i.e., SNVs vs. contextual SNVs.

Order of emergence of the founders of GGs on "Evolutionary Progression Scale (EPS)": The order of emergence of all the extant GGs can be inferred from Fig. 1 based on the nearest-neighbor relationship among the centers of each GGs (see Supplementary Fig. S2A and Table S3). The point on EPS at which the "founder(s)" of each GG emerged can be derived from Fig. 2 under the following processes: We start with two assumptions: (a) from the point of view of genomic information, the progression of evolution can be considered as the process of increasing divergence of genomic sequences; (b) the "founder(s)" of an extant GG can be considered as a selected subpopulation from the population of an internal node at a specific point on EPS (see the radial line scaled zero to 100 in Fig 2), and, then, the founder(s) diversifies and evolves to generate all the members of the extant (as well as extinct) GG. The genomic divergence, which corresponds to the cumulative branch-length, is set to EPS = 0 at the origin of our tree, and EPS = around 100 for the leaf-nodes of all extant individuals (see Fig. 2 and **Evolutionary Progression Scale** in Materials and Methods of Supplementary Materials). For example, the founder(s) of the first GG (GG0) emerges from the first internal node located at EPS = about 15.2 in Fig. 2.

Finally, we take the identification of GGs from Fig. 1 and their nearest-neighbor relationship from Supplementary Table S3, and combine with the EPS values for the founder(s) of each GG from our tree to estimate the order of the emergence of all the GGs and the point on the EPS of the emergence of the founder(s) of each GG in two spaces: (a) on PCA space (Supplementary Fig. S2A) and (b) on a world map (Supplementary Fig. S2B). Such combination suggests that:

(a). All extant African GGs (GG0 – GG4) emerged *sequentially*, and their founders emerged between EPS of 15.2 and 29.4, but any presumed earlier GGs emerged from the root of the tree during the period corresponding to EPS between 0.0 and 15.2 are not found among the study population;

(b). The first extant GG is GG0 consisting of two EGs of Khomani_San and Jo_hoan (see Fig. 1 for the numbering of the GGs and Supplementary Table S1 for the names of EGs in each GG) currently residing in the southern tip of Africa, and the last African GG (GG4) is composed of the EGs of Mozabite and Saharawi in Northern Africa at the end of the African supergroup in Fig. 1;

(c). The founders of the non-African GGs emerged in a *"burst"* into several lineages of the GGs during a period corresponding to a narrow range of EPS of 33.5 – 39.5 (see Fig. 2 and Supplementary Fig. S2). They all emerged from GG5 (the first non-African GG nearest from the last African GG (GG4) in Northern Africa), which consists of the EGs of Bedouin B, Druze, Iraqi Jew, Jordanian, Palestinian, Samaritan, and Yemenite Jew in the Middle East;

(d). The founders of two of the largest genomic groups, GG12 and GG13, emerged most recently at EPS of 39.5; and

II. Average genotype identity/difference between two individuals:

The genome-based grouping discussed above has been derived based on the "distance" between two FFPs of *contextually-linked* SNVs in each of all pairs of individuals. Although the distance is precisely defined from the Information-Theoretic view point it is not obvious what the distance between the two FFPs corresponds to physically in terms of two respective whole genome contents. Furthermore, although 1KGP study (4) showed that the average SNV

difference between the reference genome of European ancestry and each individual's genome of different population groups vary from 3.54 million (M) to 4.32M SNP loci, corresponding to 4.2% to 5.1% of total SNP loci, it is not certain whether similar variations will be observed between two individuals among *all* study populations (not comparing each to the one Eurocentric reference genome). To get a more intuitive understanding, we ask alternative questions: (a) What is the average percent identity/difference in terms of whole genome content between two individuals within one GG vs. from two different GGs?; (b) Are the percent identity/difference unique to each GG? ; and (c) What are the implications of the answers to the above questions?

For this portion of our study, genomic identity has been quantified in two steps: First, we quantify the genotype identity of all SNP loci within each pair of two individuals in each group as well as between two different groups, using the genomic data of the largest population size (the 1KGP data) and of the broadest diversity in ethnicity (the SGDP data). Then, we combine the results to generalize and extrapolate to estimate an approximate average magnitude for the genomic identity between two individuals as a percent of the most recent *whole* human genome sequence with no gaps (about 3.06 billion (B) base-pairs (*15*). These steps are taken under a few approximating and simplifying assumptions described below.

Quantifying genotype *differences* precisely is very challenging at present because of many types of differences. But we can quantify genotype *identity* precisely to make an estimate (at the level of order-of-magnitude) under a few reasonable approximations: There are many types of mutational events that result in individual genomic variations, such as single nucleotide substitutions, short Indels, large deletions/insertions, inversions and others. Of these, about 90% are due to SNPs, and the rest of variational events are an order-of-magnitude or rarer than SNPs (*4*). Therefore, under the first approximation that SNPs account for the overwhelming portion of all mutational events, we ignore all other mutational events, which are very rare and difficult to quantitate and compare. Thus, we estimate the extent of the individual SNV *identity* by counting identical genotypes between genomes of two individuals at all available SNP loci, then we extrapolate (re-scale) the SNV identity among all SNP loci to that for a whole genome length. This process was repeated for both data sets of the 1KGP (4) and the SGDP (5). We estimate the average percent-identity in four different ways, the results of which are summarized below and the detailed calculations are described in Supplementary Materials under **Four ways of estimating the average identity of whole genomes between two individuals among world's ethnic groups**.

(a). The average genomic identity between the human reference haploid genome, GRCh37 (*16*), were compared with each of all individual genomes from 26 "population groups (PGs)" of the 1KGP. Interestingly, the genotypes of 95.6%, on average, of all SNP loci (84.7M) between the reference genome and each individual is identical. Extrapolating or re-scaling this number to whole genome length, striking 99.86% of the whole genome of each individual have identical genotypes as those of the reference genome under the simplifying approximations mentioned above.

(b). Furthermore, the average genomic identity between two individuals (*excluding* the human reference genome) among *all* members of the 1KGP population is also found to be about 95.08% of the total SNP loci (Table 1A and Figs. 3A1 and 3A2), which corresponds to 99.87% of the whole genome of the recently updated human reference genome length (17, 18).

(c). Similar to the results with 1KGP population above, the average genotype identity between two individuals among all members of 164 ethnic groups of the SGDP is 90.39% of a

total of 34.4M SNP loci (Table 1B and Figs. 3B1 and 3B2), which corresponds to about 99.84%, on average, of whole genome length of SGDP.

(d). Extrapolating these consistently high estimates for genome identity between two individuals in the 1KGP and the SGDP samples to the latest values of 111M for the whole genome SNP loci (18) and of 3.1B base-pairs for whole complete human genome length (15), we arrive at a "generalized" and conservative estimation of 99.8% as the genotype identity between two individuals regardless of the types of categorization by the "population groups" in the 1KGP or GGs of the ethnic groups of the SGDP.

Summaries and Prospects:

At the level of the population of all 164 ethnic groups in the SGDP, we show the feasibility of objectively categorizing the ethnic population into approximately 14 exclusively genome-based groups (GGs) without any consideration of self-declared or subjectively perceived categorization, such as race, ancestry or ethnicity. Such genome-based categorization should provide a scientific footing for demographic studies of various areas such as:

a. Estimating or predicting the role of the inherited genomic components that contribute to certain phenotypes specific to a given GG in the health-related fields, such as epidemiology, disease diagnosis, disease susceptibility, and clinical practice in predicting, for example, drug or therapy responses;
b. Training and testing of various computational algorithms using Information Technology, e.g., Machine Learning and Artificial Intelligence in the fields mentioned above, where the development of such algorithms depend on having objectively definable demographic categorizations (called "labels" in this field) of the genomic input data.
c. Supplementing or replacing the current non-genome-based demographic categorization, such as race, ancestry, and ethnicity in estimating the genomic component of interpretation of social or cultural studies as well.

As for the public availability of the genomic diversity data, only sparse data are available for the ethnic groups in Northern Africa, Nordic Europe, and North and Central Asia.

At an individual level, taking all four estimates derived above together we make a simplified and conservative approximation that the genomic identity is, on average, about 99.8% of whole genome (ranges of the four estimates above: 99.82% - 99.87%) between two individuals regardless of the ethnicity in this study, i.e., the remaining 0.2% accounts for non-identical genotypes, which amount to about 6M genomic loci. This approximation is also under the final assumption that the degree of the genomic diversity of the ethnic groups in this study represents, approximately, the genomic diversity of the extant human species. The genomic identity of 99.8% between two individuals is more intuitively understandable than the genomic identity of 96.4% for the whole population of the extant human species. Possible implications derived from the observation of the uniformly very high genomic identity between two individuals regardless of categorization are discussed below in **Inherited "Passive" genomic information, Environmentally selected genomic variants** and **Environment-based vs. genome-based categorization** .

Implications and Discussions

The genome-based grouping pattern and individual genomic identity/difference described in Results are the *average* features of the grouping and quantifications for the *majority* of the extant ethnic and population groups at the time of this study, when the field continues moving toward obtaining higher quality (*18*) and completeness (*15*) of the reference human genome sequence. Not discussed in the Results are: (a) those features contributed by the "outliers" with rare degrees of genomic identity/difference between two individuals located in the long "tails" of the main bodies of the "violins" in Fig. 3, and (b) those contributed by other inherited but non-genomic elements, such as epigenomic chemical modifications of genome, non-genomic but inherited nucleic acids, microbiome, and others (*19*), for which no comprehensive data are available, at present, to make quantitative estimates of their contributions to a genome-based categorization. With these caveats we describe the implications of the Results with discussions below.

"Burst" of all extant non-African ethnic groups from the Middle Eastern GG. Our observations in part I of the Results above imply that**:** (a) the most recent ancestors of the extant ethnic groups in this study emerged sequentially from Southern Africa (GG0), and (b) all founders of the non-African ethnic groups emerged in a "burst" from the Middle Eastern genomic group (GG5), which emerged after the two Northern African ethnic groups of Mozabite and Saharawi (in GG4) in Northern Africa emerged. What event or events may have caused such burst is unknown.

About 99.8% genomic identity for individuals and 96.4% for all populations. Under the simplifying assumptions mentioned in part II of the Results above and at the level of order-of-magnitude, we find that the contents of the whole genomes of any two individuals in this study populations are strikingly similar (about 99.8 % identical on average (with a narrow range of 99.82% - 99.87%) between two individuals not only within a given GG or PG but also from two different GGs or PGs. On the other hand, the genomic identity at all SNP loci among *all* PGs in 1KGP is about 96.4% of the whole genome of 3.1B base-pairs (see section (d) of ***Four ways of estimating the average identity of whole genomes between two individuals among the world's ethnic groups*** in Supplementary Materials). This observation infers that the loci with different genotypes between two individuals in one pair is different, in general, from those in a different pair, although the magnitude of the difference is about the same for both pairs. Thus, the union of the loci with identical genotypes among *all* pairs is significantly lower than the number of loci with identical genotypes *between* two individuals, i.e., all members of the study population as a single group has 96.4% identical genome, but 99.8% identical genome between two individuals, in general. One more detail: the average % SNP identity between two individuals among African GGs or PGs is about 1% lower than that among non-African GGs or PGs, but when extrapolated to whole genome the 1% difference makes no significant difference. This is also true when we compare the SNP identity between one individual from African groups and the other from non-African groups (see Tables 1A and 1B). Thus, the genomic divergence among the members of African GGs or PGs are always slightly higher than those of non-African GGs or PGs.

Inherited "Passive" genomic information. Our observation of almost uniform degree of very high genomic identity (99.8%) indicates that any two extant individuals have inherited an *almost complete* set of identical genomic information, despite apparently complex phenotypic differences. This apparent "inconsistency" implies that the information in the inherited whole genome may be a near-complete set of *"passive" information (or potentials)* that are differentially activated by a combination of the diverse non-genomic (environmental) factors and a very small fraction (0.2% of whole genome) of an individual's inherited genome (see next paragraph, and **A molecular scenario for converting environmental diversity to genomic divergence** in Supplementary Note 2) for basic survival and reproduction of the individuals. For example, a frozen embryo does not have life, although it has the complete set of genomic information and essential proteins and other chemicals to start life, until certain environmental signals, such as heat and essential nutrients, are received to start its life. In this scenario the environmental signals, be they from the "biological environment" (in-utero, microbiome, ecology, food, family, society, culture, faith, ideology, lifestyles, etc.) or "non-biological environment" (heat, radiation, geology, climate, atmosphere, etc.), can be considered as critical "activating" agents of the "passive" genomic information.

Environmentally-selected genomic variants. Although most of each GG form tight genomic clusters, the members of each GG are found spread broadly within one of about 11 geological/geographical regions (S. Africa, Mid Africa, N. Africa, Middle East, Europe, Central Asia, S. Asia, Oceania, North Asia, the Americas plus NE Asia, and E. plus SE. Asia) as shown in Fig. 1 and Supplementary Table S2. Many of the regions are definable by various geological features such as high mountain ranges, large body of water or desert, etc. For example, the members in GG6 are widely spread in Europe, but segregated from those of other non-African GGs by the Ural mountain range and Caspian sea; GG7 and GG8 (both in S. Asia) are separated by a large geological barrier, Thar desert; most members of GG12 are in the North and South America; and the members of GG13 (in E. and South East Asia) are segregated from those of the rest of Asia by Himalaya mountains on the South, Tianshan mountains, Alta mountains and the Gobi desert on the North. Thus, interestingly, the categorization of GGs, which are exclusively genome-based, appears to correlate with non-biological environment bordered by geological barriers. This observation implies or suggests that even the genome-based categorization of a GG may have been strongly influenced by the environmental selection of a unique set of genomic sub-variants from a diverse genomic variant population accumulated during a long environmental exposure specific to the survival advantage of the GG, on an evolutionary time scale.

Environment-based vs. genome-based categorization. The fact that there is no one-to-one correspondence between the 14 *explicitly* genome-based GGs and the 164 EGs (as designated based on "ethnicity" in the SGDP) or the 5 "racial groups" (Black or African Americans, White, Asian, Native Hawaiian or Other Pacific Islander, and American Indian or Alaska Native, as defined in US 2020 census based on skin color and geographical regions) (see Supplementary Table S3) indicates that the biologically inherited genomic diversity does not play significant role in the categorization by the current ethnicity or race. the overwhelming portion of the inherited genomes, which is about 99.8% identical between two individuals, do not play a very influential role in the categorization of ancestry, ethnicity or race. Furthermore, even the genome-based categorization of GGs is not only derived from a very small fraction (0.2%) of

the whole genome, but also may have originated from the environmental selection of the genomic variations of the 0.2% (see previous paragraph). Thus, our results imply that both ethnicity and race are non-genomic, i.e. *environmental,* categorization, be they biological and/or non-biological environmental.

Figure and Table legends

Figure 1. Clustering pattern by genomic-variation based PCA plotted for the three major principal component axes. PCA was performed using the "distance matrix", where each "distance" is calculated by JS divergence between two FFPs of c-SNVs. Most of 345 individuals from 164 ethnic groups from the updated SGDP form about 14 clusters shown in different colors and labeled as genomic groups (GGs) GG0 – GG13, of which 13 are tight clusters, but GG3 consists of multiple un-resolved clusters of African ethnic groups. All un-clustered individuals are shown as gray circles and located outside of Africa. Although the members of each cluster are tightly clustered in genomic variation space, they are widely spread out within a given geological region as shown at the geographical locations of the sample collection sites (see the top right inset). Sorted eigenvalues and variance explained in % for the first 20 principal component axes are shown in the bottom inset.

Figure 2. Rooted c-SNV-based NJ tree in circular form (*21*) with the "evolutionary progression scale (EPS)". The same "distance matrix" as was used in Fig. 1 is used to construct the tree (see **Rooting of c-SNV-based tree** in Materials and Methods in Supplementary Materials). "Evolutionary progression scale" is the scaled cumulative branch-length bounded such that EPS = 0.0 at the root of the tree and EPS = around 100 at the leaf nodes. Nine clades in the tree are shown in the inner circular band. Fourteen clusters (with GG labels in red) from Fig. 1 are shown in the middle band for comparison with the 9 clades of the tree. The outer band shows the regional classification used in the SGDP. The blanks on the circular bands are for those individuals with SDGP regional assignment (outer bend), but not clustered among GG0-GG13 (middle band), or not in any of the 9 clades. A corresponding linear topological tree with the names of EGs is shown in Supplementary **Fig. S1.**

Figure 3. "Violin plots" of the genotype identity for all SNP loci. (A1) Violin plot of the % genotype identity of pair-wise SNVs among all SNP loci within each of 26 "population groups" of the 1KGP samples. The long streak for the distribution of % identity within each of 4 groups of the Americans reflect loose categorization by "population grouping" of the American continental group in the 1KGP samples. The extent of the "streaking" is correlated to the SDs of each average value, which, in turn, is related to the "looseness" of each cluster (see the blue column in Table 1A). The average % identities within African PGs (about 94.4%) is slightly lower, i.e., slightly more diverse genomes, than those of non-African PGs (about 95.9%), revealing that (a) African PGs and non-African PGs form two separate super groups, and (b) the African PGs have slightly lower % genotype identity, i.e., slightly more diverse genomes than those among the members of non-African PGs within each continent. **(A2)** Violin plot of the % genotype identity of pair-wise SNVs among all SNP loci between the European group (consisting of the PGs of CEU, FIN, GBR, IBS, and TSI) and the rest. The % identity between

two different PGs are slightly lower than those within the same PG. The plots for those between each of non-European groups and the rest look similar, and not shown.
(**B1**) "Violin plot" of the % identity of pair-wise SNVs among all SNP loci within each GG of the SGDP samples. The average of the averages of % identity within each of all GGs equals 91.6%, that within African GGs is 89.4%, and that within non-African GGs is 92.6%, revealing that (a) African GGs and non-African GGs form two separate super groups, and (b) the African GGs have slightly lower % genotype identity, i.e., slightly more diverse genomes than those among the members of non-African GGs within each GG. (**B2**) The % identity of pair-wise SNVs between GG6 and the other GGs. Plots for those between each of non-European GGs and the rest look similar, and not shown. The % identity between two different GGs are slightly lower than those within the same GG. The long streak for the distribution of % identity between GG6 and GG3 is because GG3 is not a tight cluster but a diffuse distribution of the individuals from several loose sub-clusters. The plots for those between each of non-European GGs and the rest look similar, and not shown.

Table 1. Average genotype identity in % of whole-genome SNP loci between two individuals. **(A).** Average % SNV genotype identity between two individuals within each "population group" (PG) of the 1KGP population in column 1 and each of four categories on row 1. The numbers of pairs compared, average % SNV genotype identity, and standard deviations (SDs) are listed. Also listed are the minima, maxima, means, medians, and sums of sample sizes. **(B).** Average % SNV genotype identity of the SGDP samples between two individuals within each GG in column 1 and each GG category on row 1. Also listed are the minima, maxima, means, medians, and sums of sample sizes.

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Author contributions

Conceptual design of the study and speculative interpretations and implications of the results by SHK; all computational work including algorithm design, programming and execution for the study was done mostly by BJK and NJ trees by JJC; discussion and interpretation of computational results by BJK, JJC and SHK; manuscript preparation by SHK with extensive discussions with BJK and JJC; figures designed by BJK, JJC and SHK.

Competing financial interests

Authors declare that there are no competing financial interests in connection with this paper.

Computer code availability

The codes to parse VCF files, determine/visualize PCA and display geological locations are available at https://github.com/UCB-KIMLAB/peopling, and the programs to generate JSD distance matrix are available at https://github.com/jaejinchoi/FFP, using the version 2v.3.1.

Fig. 1

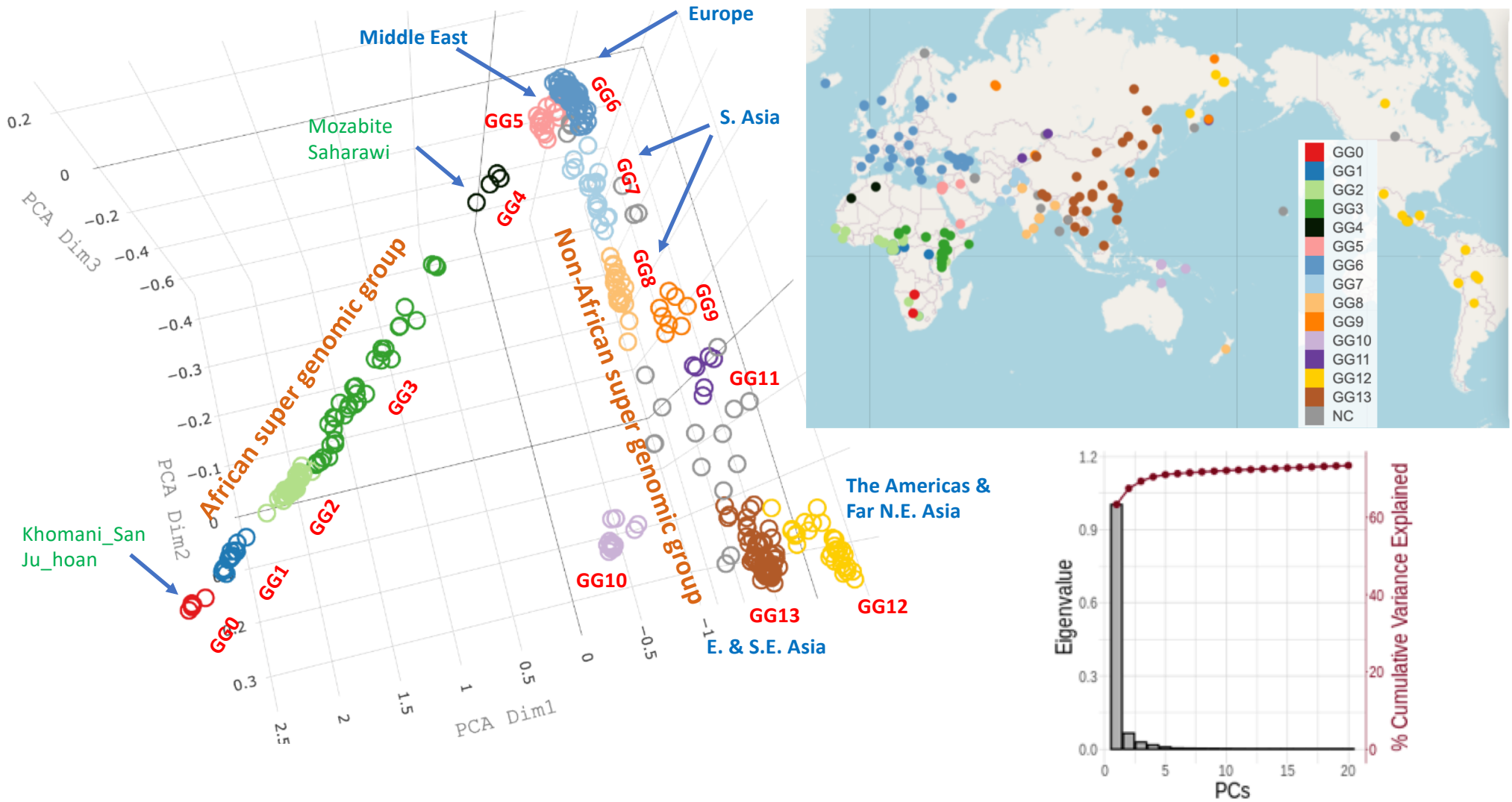

Europe
Middle East
Mozabite
Saharawi
S. Asia
GG5
GG6
GG4
GG7
GG8
GG9
GG11
GG3
GG2
GG1
GG0
GG10
GG13
GG12
African super genomic group
Non-African super genomic group
Khomani_San
Ju_hoan
The Americas &
Far N.E. Asia
E. & S.E. Asia
PCA Dim1
PCA Dim2
PCA Dim3
GG0
GG1
GG2
GG3
GG4
GG5
GG6
GG7
GG8
GG9
GG10
GG11
GG12
GG13
NC
Eigenvalue
% Cumulative Variance Explained
PCs

Fig. 2

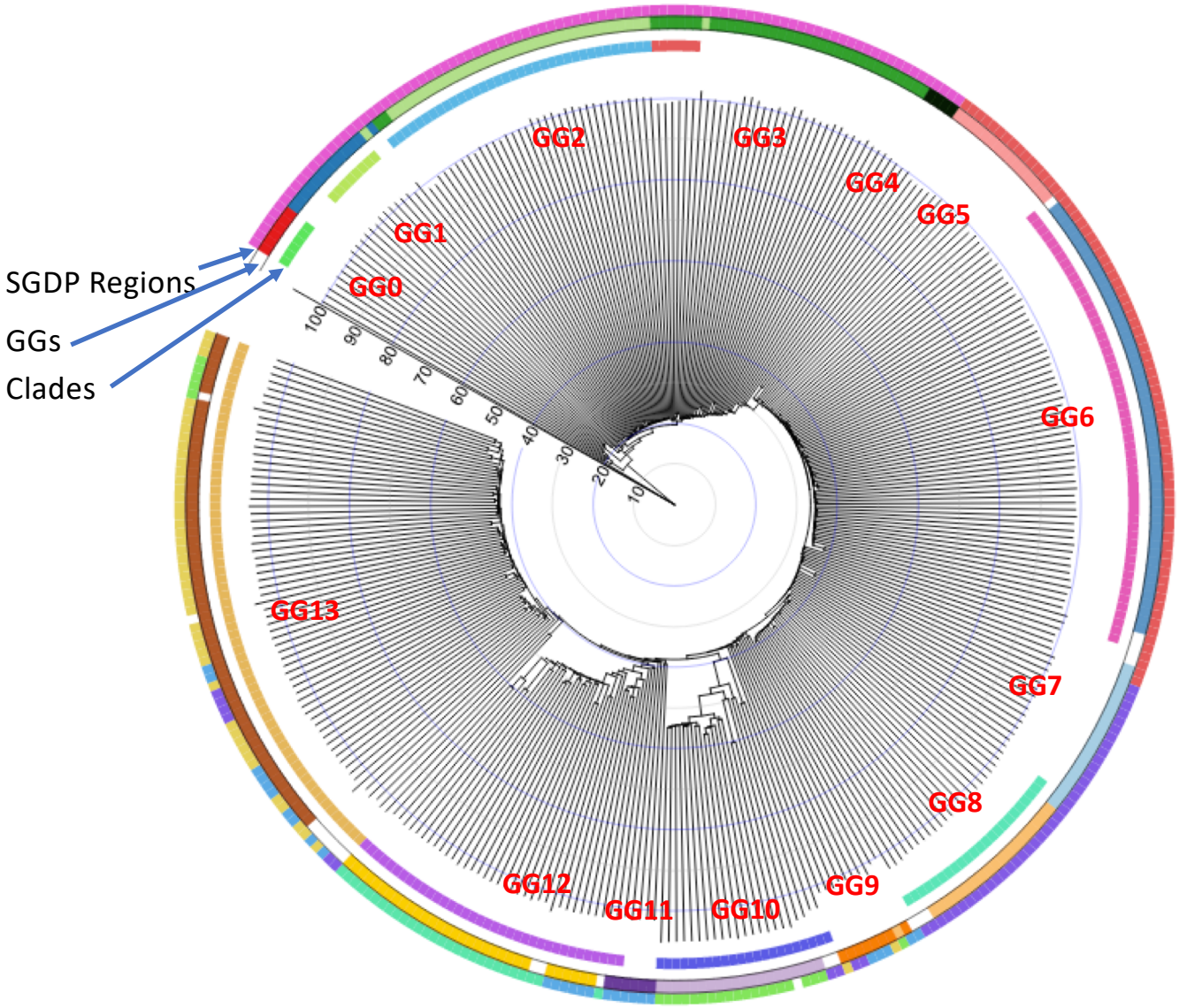
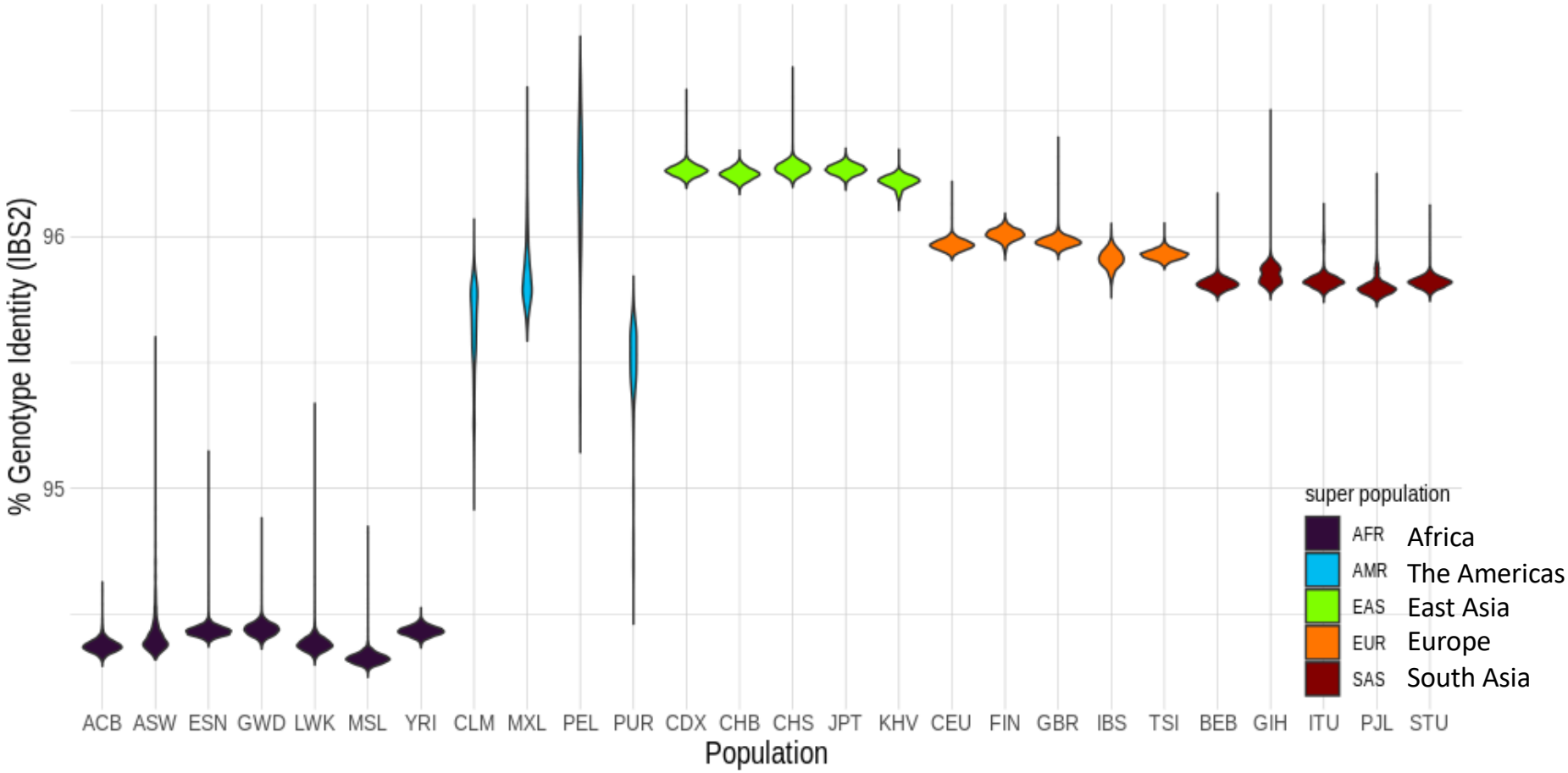
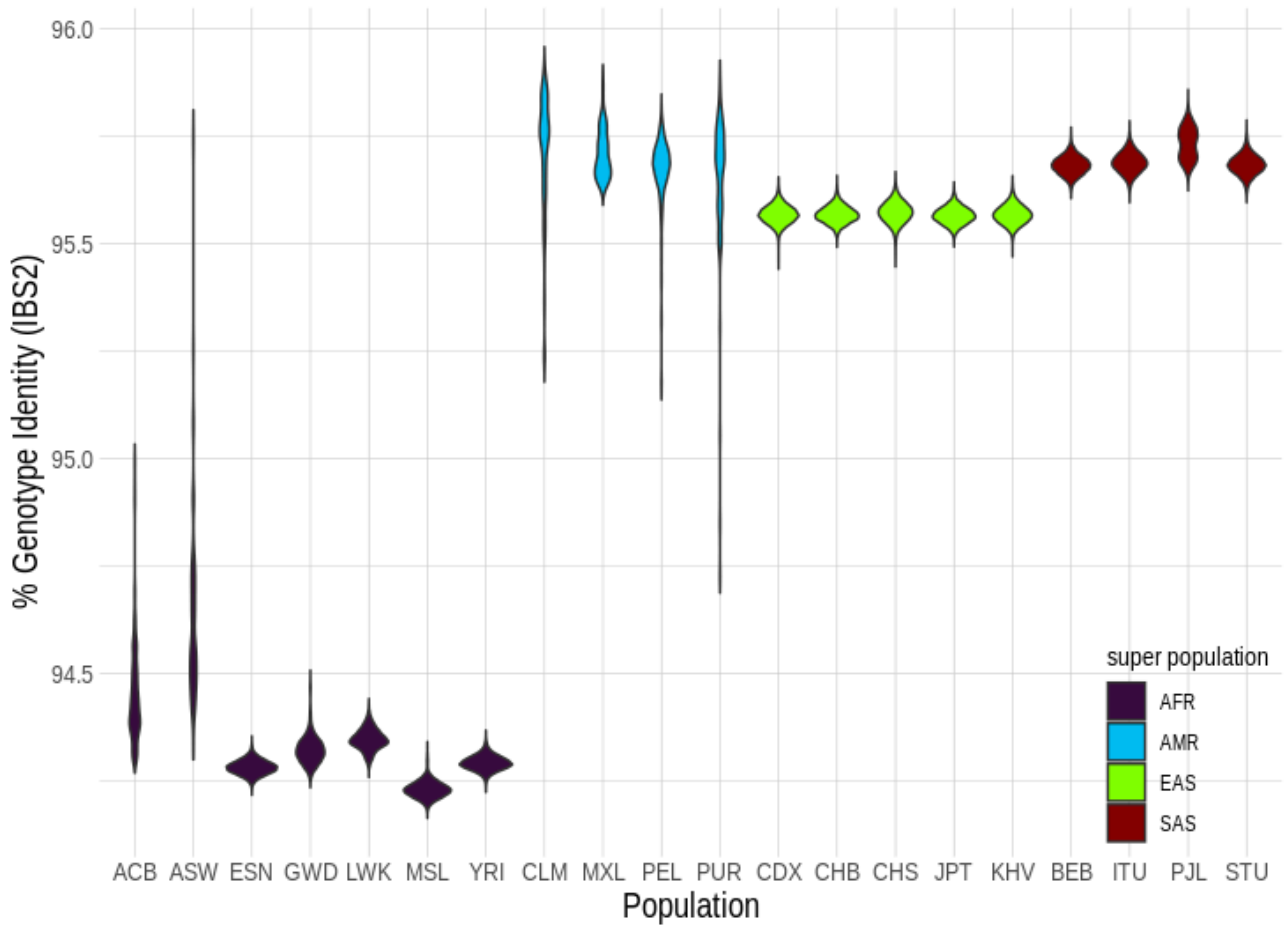

SGDP Regions
GGs
Clades
GG0
GG1
GG2
GG3
GG4
GG5
GG6
GG7
GG8
GG9
GG10
GG11
GG12
GG13
100
90
80
70
60
50
40
30
20
10

Fig. 3A1 (1KGP) Genotype identity in % of SNP loci between two individuals within each population group



For the three-alphabet names of “population” groups see Table 1A

Fig. 3A2 (1KGP) Genotype identity in % of SNP loci between Europe (EUR) and the rest of population groups

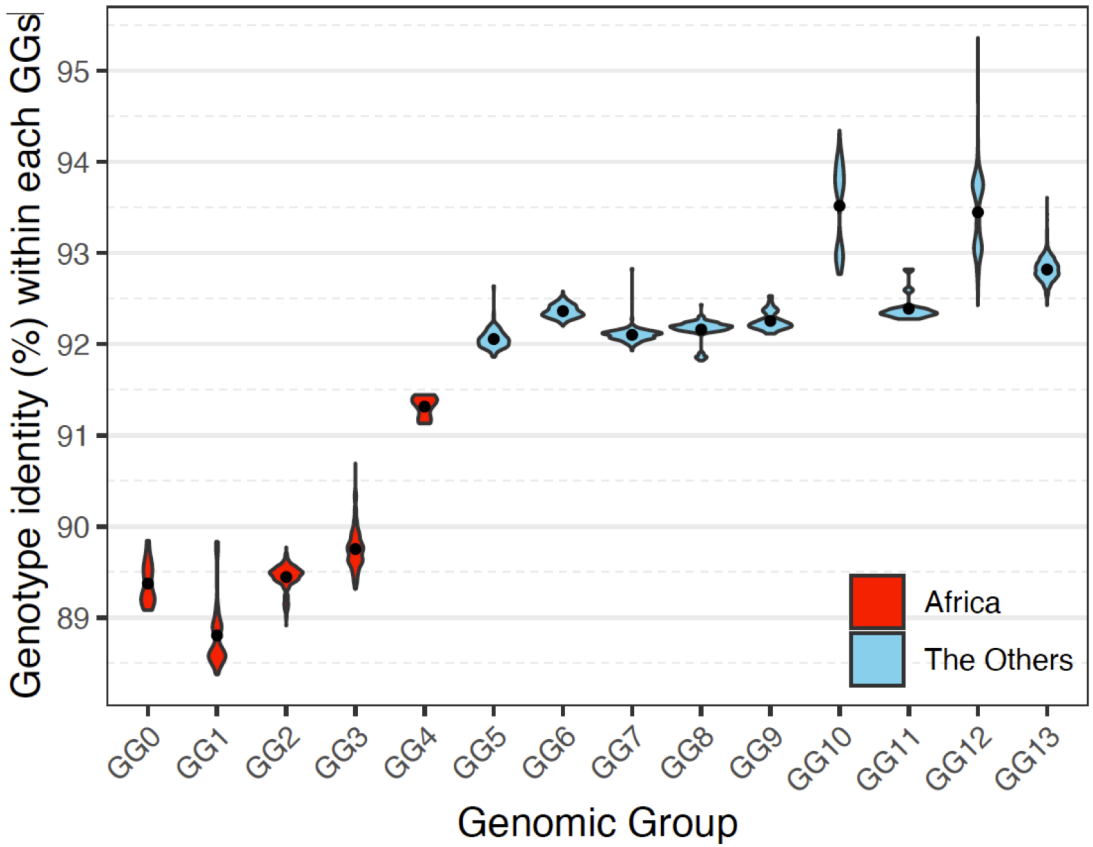


For the three-alphabet names of “population” groups see Table 1A

Genotype identity in % of SNP loci within each GG

Fig. 3B1 (SGDP)

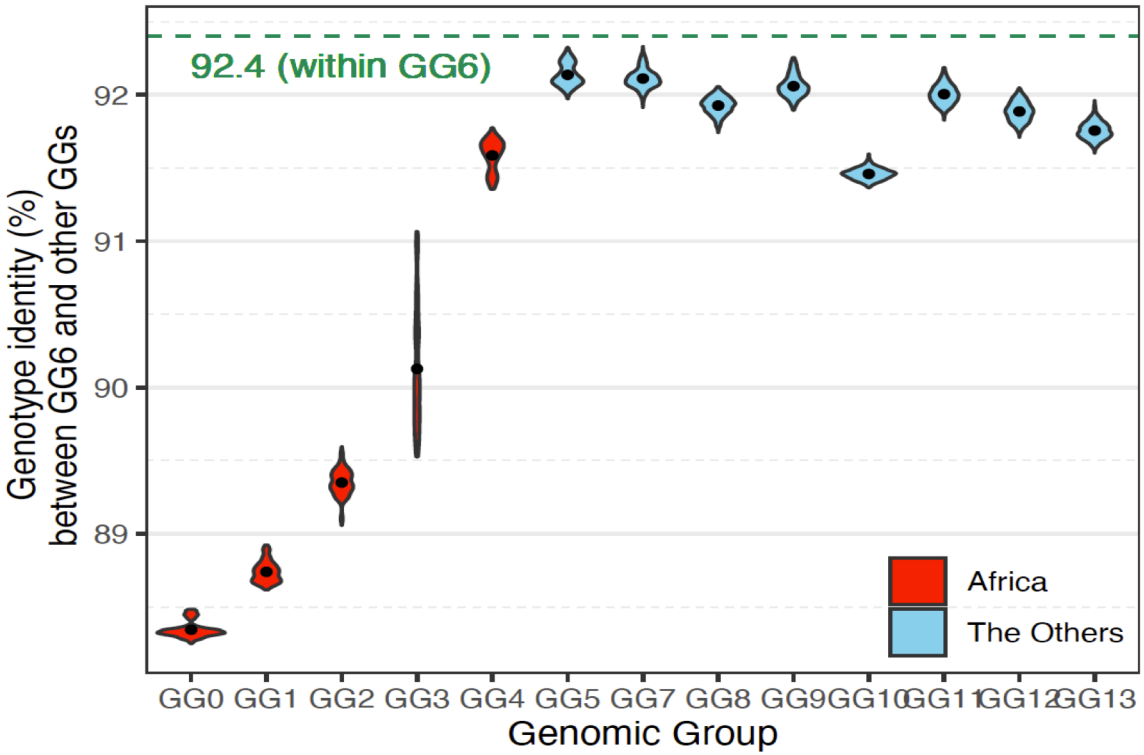
Average of the averages within each of all GGs = 91.6% (SD =1.6)
Average of the averages within each of African GGs = 89.4% (SD=0.4)
Average the averages of within each of non-African GGs = 92.6% (SD=0.6)



Genotype identity in % of SNP loci between GG6 and the other GGs

Fig. 3B2 (SGDP)

Reference GG6 (within-groups) is 92.4 ± 0.1 (total 1378 pairs) on average.



Average % identity between GG6 and each of all other GGs = 91.0% (14,363 pairs)
Average % identity between GG6 and each of all African GGs = 89.2% (4,929 pairs)
Average % identity between GG6 and each of other non-African GGs = 91.9% (9,434 pairs)

Table 1A (1KGP). Average genotype identity in percent of SNP loci between two individuals

Population information				Within Group			vs. African			vs. Non-African			vs. Rest		
Super-Population	Population	Description	Sample_Size[1]	# Pairs	% AVG	SD	# Pairs	% AVG	SD	# Pairs	% AVG	SD	# pair	% AVG	SD
AFR	ACB	African Caribbean	95	4,465	94.37	0.03	53,105	94.36	0.04	174,610	94.44	0.12	227,715	94.42	0.11
AFR	ASW	African Ancestry in Southwest US	56	1,540	94.42	0.09	33,488	94.35	0.04	102,928	94.61	0.24	136,416	94.55	0.24
AFR	ESN	Esan in Nigeria	99	4,851	94.43	0.03	54,945	94.37	0.04	181,962	94.29	0.02	236,907	94.31	0.04
AFR	GWD	Gambian in Western Division, The Gambia - Mandinka	113	6,328	94.44	0.03	61,133	94.36	0.03	207,694	94.32	0.03	268,827	94.33	0.03
AFR	LWK	Luhya in Webuye, Kenya	98	4,753	94.38	0.04	54,488	94.33	0.03	180,124	94.34	0.03	234,612	94.34	0.03
AFR	MSL	Mende in Sierra Leone	85	3,570	94.33	0.03	48,365	94.32	0.04	156,230	94.24	0.02	204,595	94.26	0.05
AFR	YRI	Yoruba in Ibadan, Nigeria	108	5,778	94.43	0.02	58,968	94.38	0.03	198,504	94.29	0.02	257,472	94.31	0.04
AMR	CLM	Colombian in Medellin, Colombia	94	4,371	95.64	0.17	61,476	94.35	0.13	163,936	95.63	0.15	225,412	95.28	0.59
AMR	MXL	Mexican Ancestry in Los Angeles, California	64	2,016	95.85	0.14	41,856	94.35	0.14	113,536	95.71	0.12	155,392	95.34	0.62
AMR	PEL	Peruvian in Lima, Peru	85	3,570	96.22	0.26	55,590	94.35	0.14	149,005	95.73	0.16	204,595	95.36	0.63
AMR	PUR	Puerto Rican in Puerto Rico	104	5,356	95.48	0.20	68,016	94.35	0.12	180,336	95.53	0.18	248,352	95.21	0.55
EAS	CDX	Chinese Dai in Xishuangbanna, China	93	4,278	96.26	0.02	60,822	94.35	0.12	162,285	95.77	0.27	223,107	95.38	0.68
EAS	CHB	Han Chinese in Beijing, China	103	5,253	96.25	0.02	67,362	94.34	0.13	178,705	95.78	0.27	246,067	95.39	0.68
EAS	CHS	Han Chinese South	105	5,460	96.27	0.03	68,670	94.35	0.13	181,965	95.78	0.27	250,635	95.39	0.68
EAS	JPT	Japanese in Tokyo, Japan	104	5,356	96.27	0.02	68,016	94.34	0.13	180,336	95.77	0.26	248,352	95.38	0.68
EAS	KHV	Kinh in Ho Chi Minh City, Vietnam	99	4,851	96.22	0.02	64,746	94.34	0.12	172,161	95.77	0.27	236,907	95.38	0.68
EUR	CEU	Utah residents (CEPH) with Northern and Western European ar	99	4,851	95.97	0.02	64,746	94.35	0.14	172,161	95.73	0.15	236,907	95.35	0.63
EUR	FIN	Finnish in Finland	99	4,851	96.01	0.02	64,746	94.35	0.14	172,161	95.75	0.13	236,907	95.37	0.63
EUR	GBR	British in England and Scotland	91	4,095	95.98	0.02	59,514	94.35	0.14	158,977	95.73	0.15	218,491	95.36	0.63
EUR	IBS	Iberian population in Spain	107	5,671	95.91	0.04	69,978	94.36	0.14	185,217	95.70	0.15	255,195	95.33	0.62
EUR	TSI	Toscani in Italy	107	5,671	95.93	0.02	69,978	94.35	0.14	185,217	95.71	0.14	255,195	95.33	0.62
SAS	BEB	Bengali in Bangladesh	86	3,655	95.81	0.02	56,244	94.34	0.13	150,672	95.71	0.10	206,916	95.34	0.62
SAS	GIH	Gujarati Indians in Houston, TX	101	5,050	95.85	0.04	66,054	94.34	0.13	175,437	95.71	0.09	241,491	95.34	0.62
SAS	ITU	Indian Telugu in the UK	101	5,050	95.82	0.03	66,054	94.34	0.13	175,437	95.70	0.10	241,491	95.33	0.61
SAS	PJL	Punjabi in Lahore, Pakistan	96	4,560	95.80	0.04	62,784	94.34	0.13	167,232	95.70	0.09	230,016	95.33	0.62
SAS	STU	Sri Lankan Tamil in the UK	100	4,950	95.82	0.02	65,400	94.34	0.13	173,800	95.70	0.10	239,200	95.33	0.61
		minimum	56.00	1540.00	94.33	0.02	33488.00	94.32	0.03	102928.00	94.24	0.02	136416.00	94.26	0.03
		maximum	113.00	6328.00	96.27	0.26	69978.00	94.38	0.14	207694.00	95.78	0.27	268827.00	95.39	0.68
		mean	95.85	4623.08	95.54	0.05	60251.69	94.35	0.11	169254.92	95.35	0.14	229506.62	95.08	0.48
		median	99.00	4851.00	95.84	0.03	62130.00	94.35	0.13	174205.00	95.71	0.13	236907.00	95.33	0.62
		sum	2492	120200			1566544			4400628			5967172		

1 some samples in family relationship (<= 2nd kinship) were filtered out in the analysis.

Table 1B (SGDP). Average genotype identity in % of SNP loci between each GG in column 2 and GGs on row 1 (continental groups)

Population Information			Within Group			vs. African		vs. Non-African		vs. rest	
Region	Genomic Grp	Sample Size	# pairs	mean	sd	mean	sd	mean	sd	mean	sd
Africa	GG0	6	15	89.37	0.22	88.18	0.09	88.36	0.04	88.31	0.11
Africa	GG1	13	78	88.80	0.36	88.59	0.33	88.75	0.03	88.70	0.18
Africa	GG2	35	595	89.45	0.13	88.91	0.62	89.34	0.04	89.21	0.37
Africa	GG3	35	595	89.80	0.22	89.10	0.79	90.04	0.09	89.75	0.60
Africa	GG4	4	6	91.32	0.12	89.13	0.77	91.28	0.21	90.62	1.12
WestEurasia	GG5	15	105	92.06	0.10	89.63	1.25	91.75	0.24	90.94	1.31
WestEurasia	GG6	53	1378	92.36	0.07	89.63	1.28	91.92	0.22	91.04	1.39
WestEurasia	GG7	2	171	92.10	0.08	89.58	1.20	91.93	0.17	91.02	1.38
SouthAsia	GG7	17									
SouthAsia	GG8	19	190	92.16	0.11	89.54	1.15	91.93	0.13	91.01	1.38
Oceania	GG8	1									
CentralAsiaSiberia	GG9	4	28	92.25	0.10	89.56	1.18	92.06	0.24	91.10	1.45
SouthAsia	GG9	2									
EastAsia	GG9	2									
Oceania	GG10	19	171	93.52	0.45	89.55	1.00	91.66	0.21	90.79	1.29
CentralAsiaSiberia	GG11	6	15	92.39	0.14	89.15	1.16	92.09	0.28	91.11	1.47
CentralAsiaSiberia	GG12	6	496	93.45	0.41	89.57	1.08	92.10	0.32	91.13	1.44
America	GG12	26									
Oceania	GG13	4	1711	92.82	0.12	89.52	1.08	92.04	0.33	91.07	1.44
SouthAsia	GG13	4									
CentralAsiaSiberia	GG13	8									
EastAsia	GG13	43									
	minimum	2	6	88.80	0.07	88.18	0.09	88.36	0.03	88.31	0.11
	maximum	53	1711	93.52	0.45	89.63	1.28	92.10	0.33	91.13	1.47
	mean	15.43	396.71	91.56	0.19	89.26	0.93	91.09	0.18	90.41	1.07
	median	8	171.00	92.13	0.13	89.53	1.08	91.83	0.21	90.97	1.34
	sum	324	5554								