Supplementary Materials

Latin Americans show wide-spread *Converso* ancestry and the imprint of local Native ancestry on physical appearance

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SUPPLEMENTARY NOTES

Supplementary Note 1. Assessing the performance of NNLS, SOURCEFIND and GLOBETROTTER through simulations.

Simulations were performed modelling the admixture in Latin America in order to assess the robustness and accuracy of sub-continental ancestry estimations (NNLS and SOURCEFIND) as well as the estimated dates of admixture (GLOBETROTTER). Since the precision of sub-continental ancestry estimates is affected by the relatedness of surrogate clusters, and their level of genetic drift, these simulations also allowed the exploration of which sub-continental ancestries cannot be reliably distinguished. Subsets of some of the 56 surrogate clusters were used to generate simulated admixed individuals following the procedures described in e.g. Hellenthal *et al*. 2014[1] and Price *et al*. 2009[2].

The SOURCEFIND approach described in "Methods" is computationally expensive, due in part to having to run 50 independent runs in order to sample the parameter space effectively (as assessed by the simulations). Therefore, for some analyses we used an alternative, more computationally efficient version of SOURCEFIND that uses the same likelihood function, but which removes Lambda and replaces the prior on the β^r values with a truncated Poisson (mean=3) prior on the number of contributing surrogates S'. At each MCMC iteration, this alternative SOURCEFIND allows only a maximum of S' surrogates to have $\beta_s^r > 0$ and for the β_s^r values of each of these S' surrogates to be 0.01,…,1 in increments of 0.01. The proposed move at each MCMC iteration is as follows. The β_s^r value of a randomly chosen surrogate group is either completely (with probability 0.1) or partially (with probability 0.9) distributed across the other currently included surrogates. (This set of other included surrogates contains up to S' members, with new randomly chosen surrogates added if the total number of surrogates is less than S'.) With probability 0.5, the β_s^r value is added to that of a single other surrogate; otherwise it is distributed randomly across the other surrogates. This proposal is then accepted or rejected using a Metropolis-Hastings step. Here we used S'=6 and performed 100,000 total MCMC iterations, sampling posterior values of β_1^r,…, β_S^r every 5000 iterations after discarding the initial 50,000 iterations as "burn-in". Results under this approach ran much more quickly and gave qualitatively similar conclusions in applications to simulated and non-simulated data, as described in this section and Supplementary Note 5.

Simulations to assess the accuracy of sub-continental ancestry estimates:

For each set of simulations in this section, we generated 100 simulated individuals as mixtures of three surrogate groups intermixing 15 generations ago. From the clusters selected for the simulations, we used less than half the individuals in a cluster to simulate admixed individuals. The remaining individuals in a cluster were used for the SOURCEFIND inference. Simulations were as described in Price *et al*. 2009[2] and assume a model of instantaneous admixture followed by random mating. Briefly, each simulated haploid genome consists of a mosaic of blocks, each block of size M (in Morgans) sampled from an exponential distribution (of rate=15). For each

block, the SNP data exactly matched that of a randomly sampled haplotype from one of the surrogate clusters, with the probabilities for selecting a haplotype from each of the three surrogate clusters specified by the admixture proportions being simulated as indicated below. This random selection process was repeated independently for each block. Two haploid genomes were randomly combined to generate eac simulated diploid individual.

SOURCEFIND analyses were performed with 20 independent runs using 200,000 iterations each run as described in methods. NNLS was performed using the procedure encoded in GLOBETROTTER described in Hellenthal *et al*. 2014[1], which uses the non-negative linear least squares function (nnls) in R. As with the real data analysis, for each run results with highest posterior probability values were chosen, averaging inferred ancestry proportions across the 20 runs using this probability as a weight. We note that accuracy of both NNLS and SOURCEFIND depends in part on the number of individuals used in each surrogate group, so that removing ~30% of the individuals from each simulating group when performing inference may decrease accuracy.

Four sets of simulations with different admixture percentages were performed and these are described below (in parenthesis is indicated the fraction of individuals from a cluster that were used to generate the admixed individuals in that simulation)

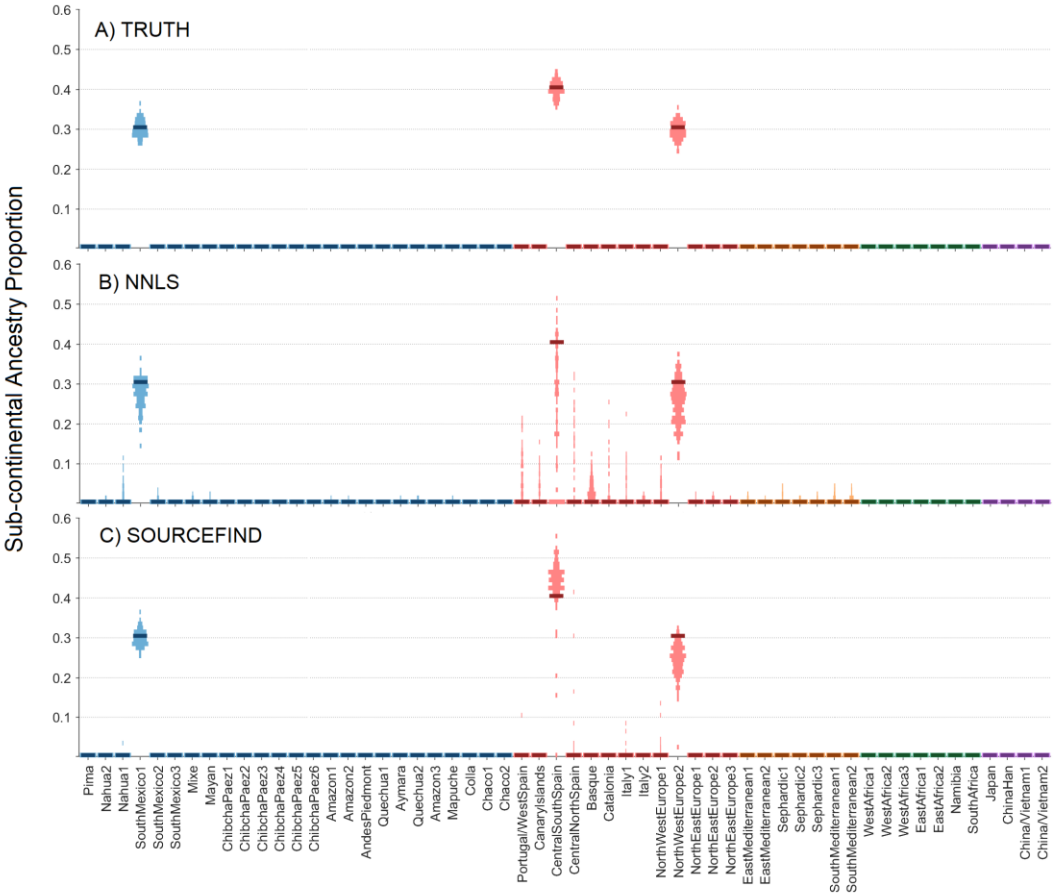
(i) 40% CentralSouthSpain (16/48), 30% NorthWestEurope2 (32/101), 30% SouthMexico1 (5/16).

When using NNLS as described in e.g. Leslie *et al*. 2015[3], ancestry from *SouthMexico1* is inferred with high accuracy, showing little marginal uncertainty and little misassignment even to *Nahua1,* a striking result considering that these two surrogate clusters are closely related as shown in the fineSTRUCTURE tree (Supplementary Fig. 3). The accuracy obtained with SOURCEFIND is even higher, having a nearly perfect match to the true simulated proportions and sources.

In the case of *CentralSouthSpain,* NNLS shows high levels of misassignment to other Iberian surrogates. The highest missassigned values are to *CentralNorthSpain,* which is the group genetically most similar to *CentralSouthSpain*. Additional contributions are inferred for East/South Mediterranean populations (up to ~5%). In contrast, SOURCEFIND estimations are highly accurate, with very minor inferred incorrect contributions related to *Italy1*. Importantly, there are no mis-inferred contributions from East/South Mediterranean populations when using SOURCEFIND.

The estimation of *NorthWestEurope2* ancestry is typically more accurate, with some incorrect assignment to *NorthWestEurope1* (max ~10%), that is considerably stronger under NNLS.

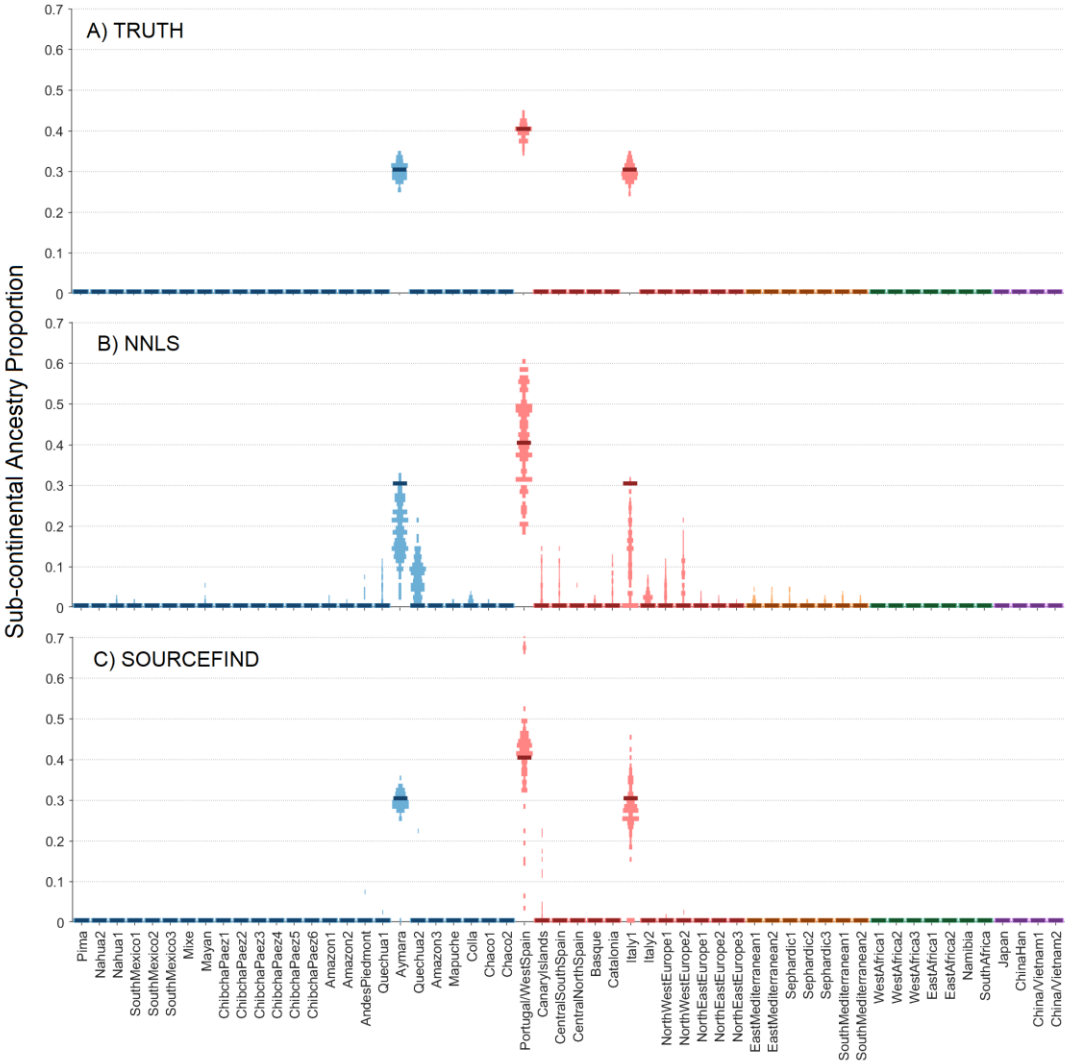
Overall, this simulation demonstrates the increased resolution of SOURCEFIND compared to NNLS for resolving ancestral origins among Iberian populations. SOURCEFIND also has reduced mis-specified contributions related to East/South Mediterranean groups.


A) TRUTH
B) NNLS
C) SOURCEFIND
Sub-continental Ancestry Proportion
0.6
0.5
0.4
0.3
0.2
0.1
Pima
Nahua2
Nahua1
SouthMexico1
SouthMexico2
SouthMexico3
Mixe
Mayan
ChibchaPaez1
ChibchaPaez2
ChibchaPaez3
ChibchaPaez4
ChibchaPaez5
ChibchaPaez6
Amazon1
Amazon2
AndesPiedmont
Quechua1
Aymara
Quechua2
Amazon3
Mapuche
Colla
Chaco1
Chaco2
Portugal/WestSpain
CanaryIslands
CentralSouthSpain
CentralNorthSpain
Basque
Catalonia
Italy1
Italy2
NorthWestEurope1
NorthWestEurope2
NorthEastEurope1
NorthEastEurope2
NorthEastEurope3
EastMediterranean1
EastMediterranean2
Sephardic1
Sephardic2
Sephardic3
SouthMediterranean1
SouthMediterranean2
WestAfrica1
WestAfrica2
WestAfrica3
EastAfrica1
EastAfrica2
Namibia
SouthAfrica
Japan
ChinaHan
China/Vietnam1
China/Vietnam2

(ii) 40% Portugal/WestSpain (16/53), 30% Italy1 (7/19), 30% Aymara (6 /16).

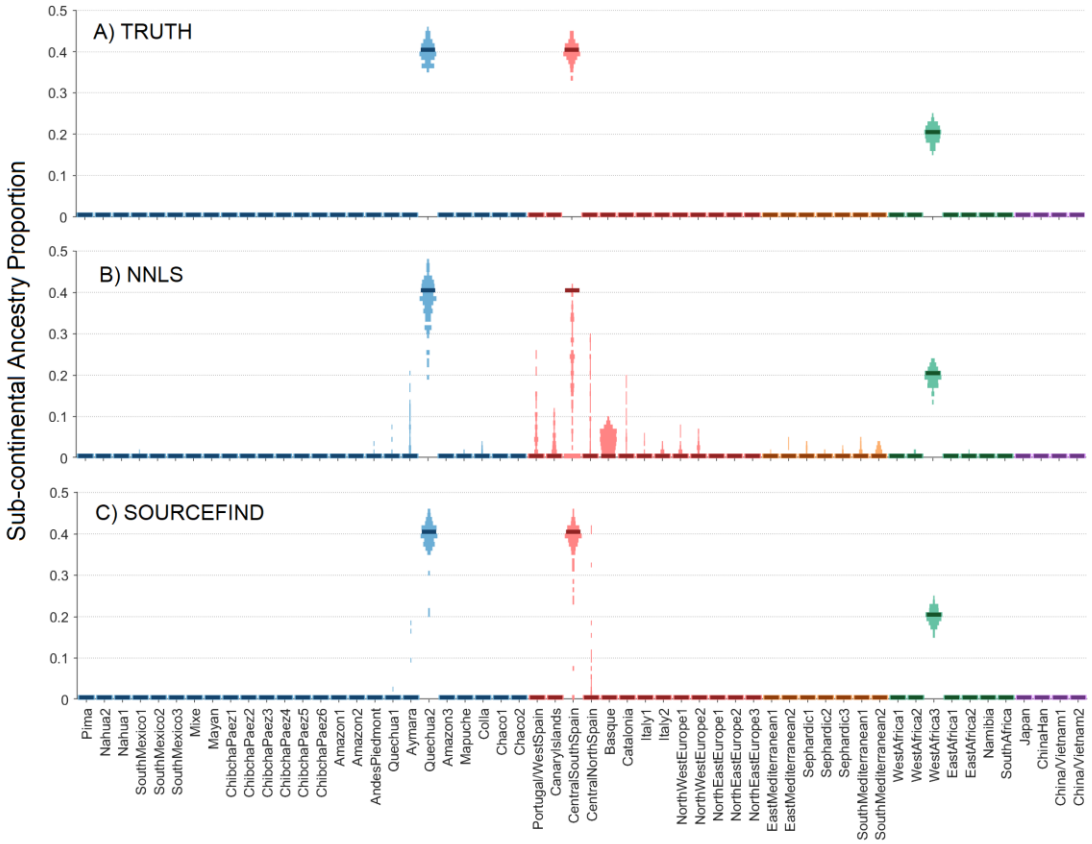
NNLS analysis results in a poor discrimination of *Aymara* from *Quechua2* ancestry, consistent with the high genetic similarity of these two groups and the small size for the *Aymara* cluster (n=16). We note that when *Quechua2* ancestry is included in the simulations instead of *Aymara* (simulation *iii* below) higher accuracy is obtained, showcasing the increased accuracy when using more surrogate individuals from the admixing group when performing inference. In the case of the SOURCEFIND analysis, both *Aymara* and *Quechua2* ancestries are accurately estimated under both simulation scenarios.

Both NNLS and SOURCEFIND slightly overestimate the *Portugal/WestSpain* contribution and slightly underestimate the ancestry from *Italy1*. However, SOURCEFIND inferences are closer to the simulated proportions than those of NNLS. Furthermore, as in the previous simulation, NNLS infers East/South Mediterranean contributions, as well as several other incorrect European contributions, which are not inferred in the SOURCEFIND analyses.



(iii) 40% Quechua2 (15/56), 40% CentralSouthSpain (16/48), 20% WestAfrica3 (22/99).

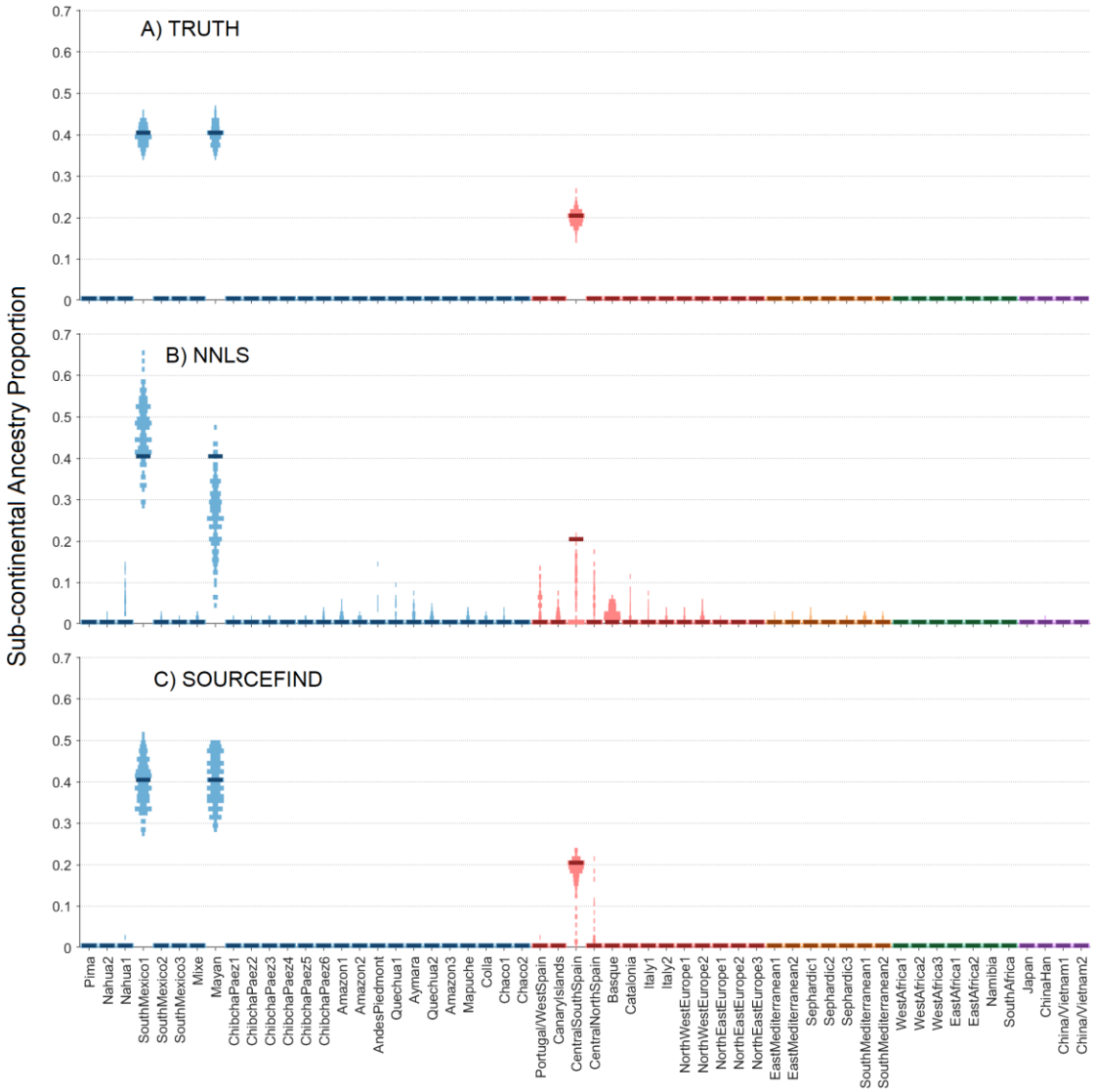
Estimated contributions from *WestAfrica3* and *Quechua2* are very accurate under both NNLS and SOURCEFIND, with the latter again showing more accurate estimates overall. We note that NNLS infers a notable spurious contribution from Basque, which suggests that inferred Basque-like contributions in the Americas using this approach should be treated with caution [4].



(iv) 40% SouthMexico1 (6 /16), 40% Mayan (3/7), 20% CentralSouthSpain (16/48).

These simulation results suggest that, for NNLS, the presence of different mis-specified signals of ancestry across the Iberian groups may be proportional to the amount of true ancestry from these sources, which could allow the establishment of noise thresholds in NNLS inference. For example, if the highest values of *Basque* ancestry in an individual with 20% *CentralSouthSpain* is around 2% for simulations here, and around 4% for an individual with 40% *CentralSouthSpain* (see simulation set (*iii*)), we could in theory predict that an individual in the real dataset with 80% *CentralSouthSpain*-like ancestry may have ~8% Basque ancestry attributable to noise. SOURCEFIND does not show this problem, instead showing only a slight mis-assignment of this Iberian component to the closest group (*CentralNorthSpain*).

The two Native American components, although closely related, are distinguishable by both approaches, although SOURCEFIND shows greater precision.

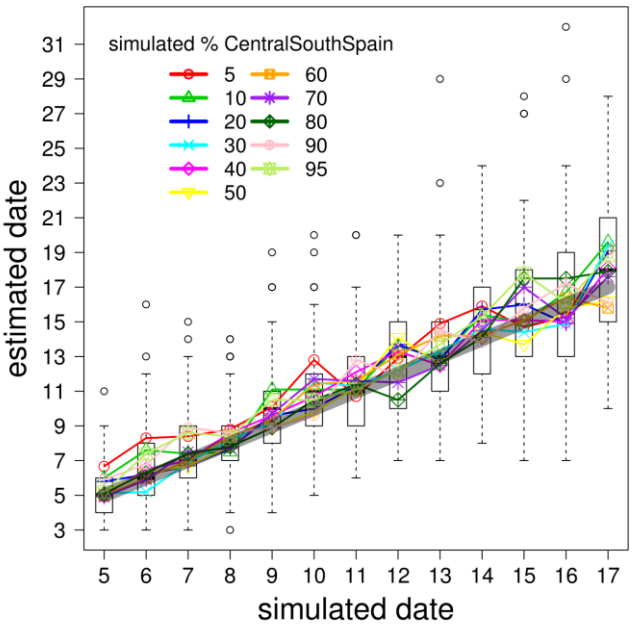


Simulations to assess the accuracy of per individual estimation of time since admixture and the effect of time since admixture on ancestry estimation

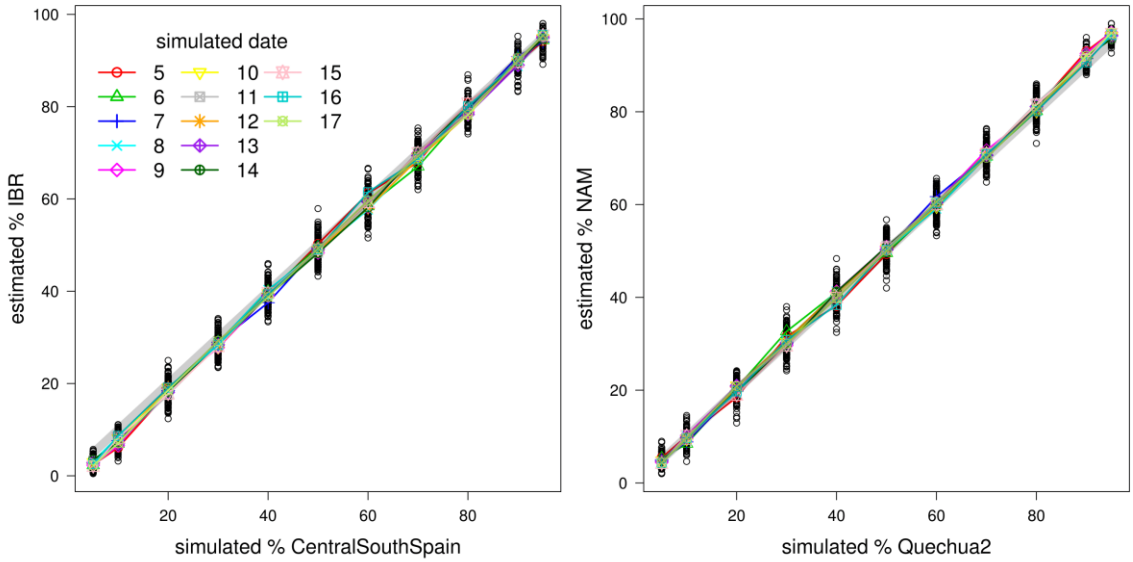
Simulations with a single admixture event

We simulated an additional 1,430 individuals with different proportions of admixture from two sources (*CentralSouthSpain* and *Quechua2*) and different times since admixture. Using the procedure described in the previous section, each individual was simulated as descending from an instantaneous admixture event that occurred *g* generations ago, with a proportion *p* of ancestry from *CentralSouthSpain*, and 1-*p* ancestry from *Quechua2*. We simulated *p* = 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 0.95 and *g* = 5-17 generations, with 10 simulated individuals for each combination of *p* and *g*, resulting in a total of 1,430 simulated individuals.

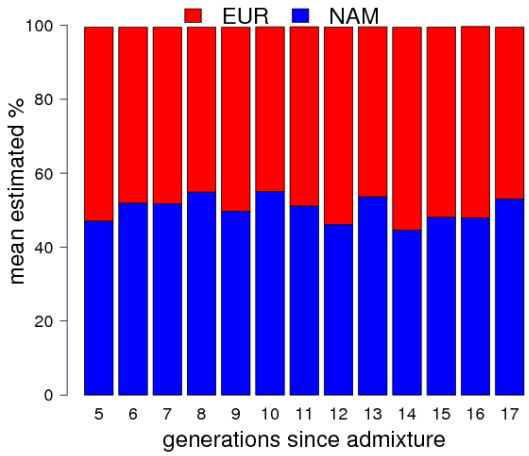
We used 16 *CentralSouthSpain* and 20 *Quechua2* individuals to generate the admixed individuals, using the remaining 32 *CentralSouthSpain* and 36 *Quechua2* individuals to infer ancestry using SOURCEFIND and GLOBETROTTER. SOURCEFIND and GLOBETROTTER were run separately on each simulated individual as described for the real data samples, with the slight modification that GLOBETROTTER was allowed to use all surrogates to describe the admixture (rather than only including surrogates inferred by SOURCEFIND to contribute >1%). In contrast to the simulations above, for these simulations we used the more computationally efficient version of SOURCEFIND, described at the start of this Supplementary Note, to infer proportions.



The figure above shows that on average, GLOBETROTTER's individual estimated dates accurately reflect the simulated dates (grey bar), and that this accuracy is not affected by variation in the admixture proportions. Similarly, the figure below shows that SOURCEFIND's accuracy in inferring ancestry proportions in the simulated individuals did not depend on the date of admixture (simulated proportions highlighted with a grey bar).



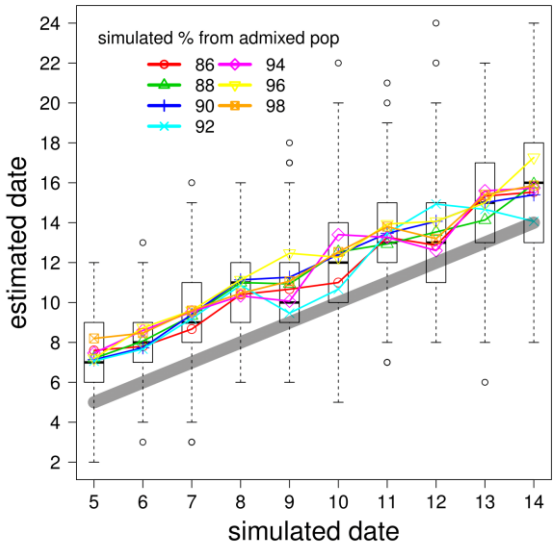
We also examined directly if in the 1,430 simulated individuals there is a pattern similar to that inferred in the CANDELA data (Fig. 3A), where Native American ancestry increases for more recent admixture events. To do so, we mimicked our real data analysis by first extracting the 1,297 simulated individuals for which GLOBETROTTER inferred to have a single date of admixture with one source "best-matching" a Native group and the other source "best-matching" a European group. We then binned individuals based on their inferred admixture date, and calculated the average inferred ancestry proportions in each bin. The figure below shows that no pattern is observed in the simulated data (Supplementary Table 4), suggesting that the pattern observed in the CANDELA data is not an artefact of the GLOBETROTTER estimation. We explore this trend relating inferred Native American ancestry to inferred admixture date with additional simulations below.



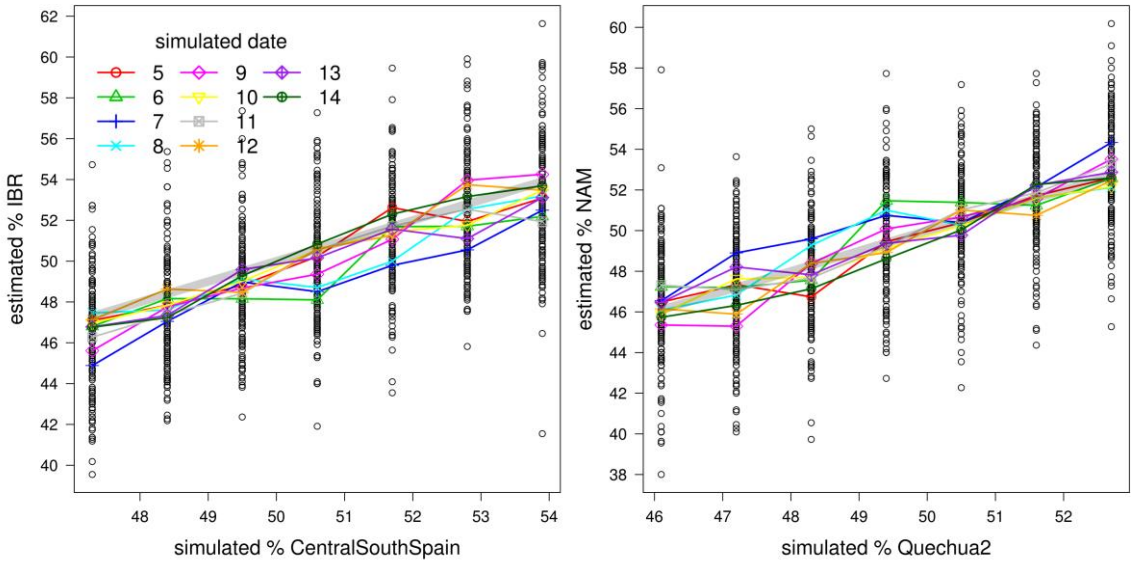
Simulations with two sequential admixture events

To further evaluate the trend of increasing Native ancestry at more recent dates of admixture seen in the CANDELA data, we simulated 1,050 additional individuals with two sequential admixture events. As before, we simulated different proportions of admixture from two sources (*CentralSouthSpain* and *Quechua2*), and varied the times for the two admixture events. Using the exponential sampling procedure described above, we first simulated individuals stemming from an instantaneous admixture event occurring 2 generations previously, with 55% *CentralSouthSpain* ancestry and 45% *Quechua2* ancestry. We then simulated a second instantaneous admixture event with *p* ancestry from the population generated in the first admixture event, and 1-*p* ancestry from *Quechua2* occurring *g* generations ago. We simulated *p* = 0.86-0.98 (at 0.02 intervals) and *g* = 5-14 generations, with 15 simulated individuals for each combination of *p* and *g* (1,050 simulated individuals in total). Note that, under this simulation procedure, the first admixture event occurred *g*+2 generations ago, the more recent event occurred *g* generations ago, and the final expected proportion of ancestry from *CentralSouthSpain* is 0.55**p*. SOURCEFIND and GLOBETROTTER were run separately on each simulated individual as before. As with the previous section, for these simulations we used the more computationally efficient version of SOURCEFIND, described at the start of this Supplementary Note, to infer proportions.

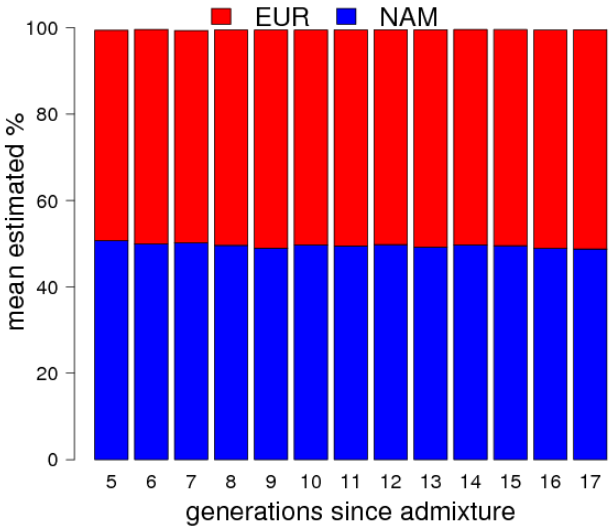
In 923 (~88%) of the 1,050 individuals, GLOBETROTTER concluded only a single date of admixture, which is not surprising given the inherent difficulty in distinguishing between two pulses of admixture separated by only 2 generations that involve the same source groups. The figure below shows results when assuming a single date of admixture, which infers dates that typically are 2 generations above *g* (simulated date given with the grey bar). Therefore, GLOBETROTTER most often concludes a single date of admixture, with the inferred date reflecting mainly the older event.



The figure below illustrates that SOURCEFIND accurately estimates the admixture proportions in the simulated individuals (grey bar gives simulated proportion).



In addition, as above, we extracted the 923 simulated individuals that GLOBETROTTER inferred to have a single admixture event between source groups that best-matched Native and European surrogate groups. We binned these individuals based on their inferred admixture date, and calculated the average ancestry inferred proportions in each bin. While not as striking as that observed in our real data (Fig. 3A of the main text), the figure below shows an analogous trend for decreasing Native American ancestry at increasing g that is significant ($p<0.001$) under the same simple linear regression model used for analysing this trend in the real data (Supplementary Table 4). While we did not simulate increasing Native ancestry over time, individuals here are simulated with different proportions of admixture from the earlier admixture event occurring g+2 generations ago. Individuals with more simulated ancestry from this earlier admixed group have (i) more European ancestry and (ii) inferred dates that may be biased to be slightly older by retaining more signal from this older admixture event. Indeed, a simple linear regression of the bias in date estimate for these 923 individuals on their expected proportion of Spanish ancestry shows a significantly positive association ($p<0.007$). In contrast, for the 1,297 simulated individuals described in the previous section with only a single simulated admixture date, there is no such significant trend ($p=0.33$). Overall these simulation results suggest that mixture between unadmixed and admixed Natives over time, such as that we simulated in this section, could lead to the trend we observe in Figure 3A.



Assessing the reliability of East/South Mediterranean ancestry estimation

The simulations above do not include East/South Mediterranean (ESM) ancestry. We can therefore use them to assess the amount of spurious ESM ancestry inferred in our analyses. For the 400 individuals described in "Simulations to assess the accuracy of sub-continental estimates", where the proportion of simulated Iberian ancestry ranges from 20-40%, SOURCEFIND estimates that none of these have >1% ESM ancestry. Across all simulations (2,880 individuals), only 2 (~0.07%) had >5% ESM ancestry (maximum = 6.2%, with both of these 2 simulated individuals having >90% Iberian ancestry, and 72 (2.5%) had inferred ESM ancestry >2%. In the main text, we note that ~23% of CANDELA individuals are inferred by SOURCEFIND to have >5% ESM ancestry (Fig. 1E). Furthermore, in the CANDELA data, 878 (~14.6%) individuals are inferred to have >10% ESM ancestry, an amount never inferred in any of the simulations performed (even in individuals with 90% simulated Iberian ancestry). The simulation results are therefore consistent with ancestors of these Latin American individuals having substantially greater ESM ancestry than the present Iberian groups sampled.

Supplementary Note 2. Definition of the phenotypes examined in Figure 4.

Detailed information on these phenotypes found in previous CANDELA papers[5-8]. Briefly:

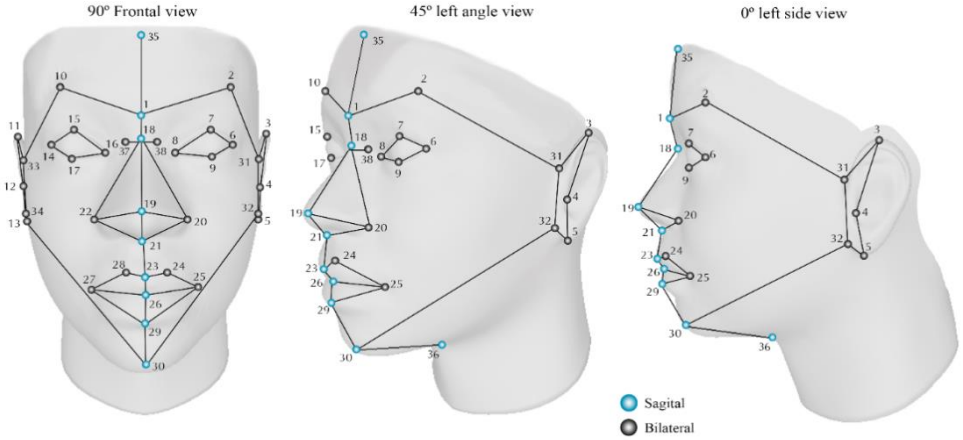
- *Height*. Quantitative measurement (in cm).

Scalp and face hair:
- *Monobrow and Eyebrow density (in men).* 1: low, 2: medium or 3: high (thinner to thicker).
- *Beard density (in men).* 1: low, 2: medium or 3: high.
- *Scalp hair shape.* 1: straight, 2: wavy, 3: curly or 4: frizzy.
- *Scalp hair greying*. 1: no greying, 2: predominant no greying, 3: 50% greying, 4: predominant greying or 5: totally white hair.
- *Balding (Measured in men and women).* 1: low, 2: medium or 3: high.

Pigmentation:
- *Natural hair colour*. 1: blond, 2: dark blond/light brown or 3: brown/black.
- *Skin colour (Melanin index).* Quantitative measurement using DermaSpectrometer DSMEII reflectometer (Cortex Technology, Hadsund, Denmark). The value used for each individual corresponds to the mean index for both inner arms.
- *Eye color*. 1: blue/grey, 2: Honey, 3: Green, 4: light brown, 5: dark brown/black.

Categorical face traits:
- *Brow ridge protrusion***.** The presence and degree of a ridge in lateral view. 0: none, 1: slightly pronounced or 2: strongly pronounced.
- *Eye fold***.** Skin fold of the upper eyelid, covering the inner corner (medial canthus) of the eye. 0: no fold, 1: partial, 2: completely.
- *Chin shape.* Chin contour in frontal view. 0: pointed, 1: rounded or 2: square.

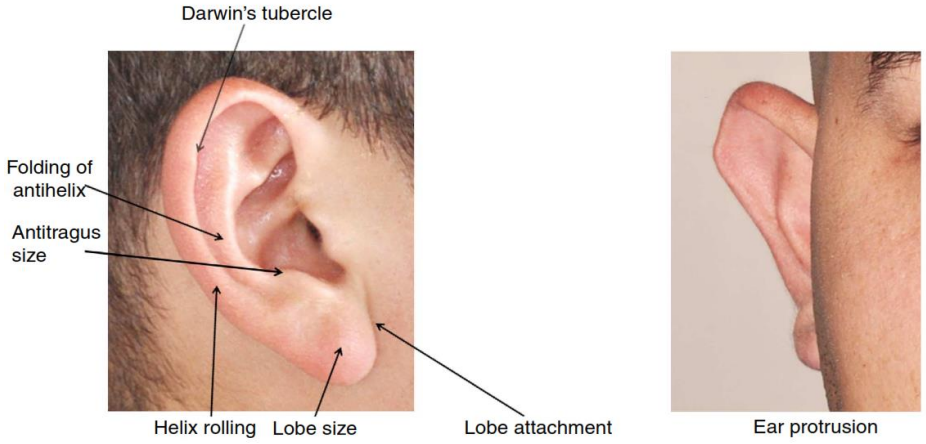
Quantitative face traits:
These were defined based on landmarks placed on facial photographs as detailed in the figure below:



This figure is modified from Quinto-Sanchez *et al*. 2015[9].

- *Forehead profile.* Slope of line joining 35-1.
- *Nasion position***.** Distance from landmark 18 to the mid-point of a line joining landmarks 8 and 16.
- *Nose bridge breadth*. Distance between landmarks 37 and 38.
- *Nose wing breadth.* Distance between landmarks 20 and 22.
- *Columella Inclination***.** Angle between landmarks 19-21-23
- *Nose protrusion*. Distance of landmark 19 to a line joining landmarks 18 and 21
- *Nose tip angle.* Angle between landmarks 18-19-21.
- *Chin protrusion.* Distance of point 30 from line joining 35-36.
- *Facial flatness*. Distance 30-32/ distance 32-18.

Ear traits:
The location of these features is shown in the photographs below. All traits were ordinal and scored on a 3-point scale (low, medium, high).



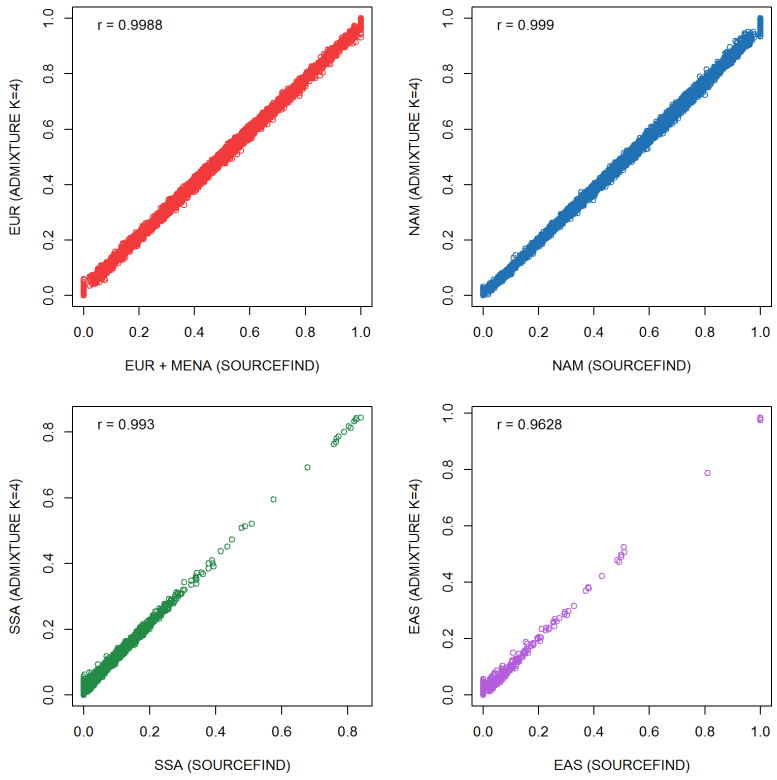
- *Ear protrusion*. Degree of protrusion of the ear in relation to the frontal face view (less to more protruded).
- *Lobe attachment*. Degree of attachment of the inferior part of the pinna to the anteroinferior part of the face (no attached to completely attached).
- *Lobe size.* Small to bigger size.
- *Helix rolling.* The outer rim of the ear that extends from the superior insertion of the ear on the scalp (root) to the termination of the cartilage at the earlobe (less to more pronounced helix rolling).
- *Fold of antihelix.* Less to more pronounced fold of antihelix.
- *Antitragus size.* Small to bigger size. The anterosuperior cartilaginous protrusion lying between the incisura and the origin of the antihelix. The anterosuperior margin of the antitragus forms the posterior wall of the incisura.

Supplementary Note 3. ADMIXTURE and Principal Components Analysis (PCA)

The merged dataset was pruned to select SNPs not in Linkage Disequilibrium (LD) using PLINKv1.9 with the option *--indep 50 5 2*, resulting in 150,858 SNPs being retained. Supervised ADMIXTURE analysis (not shown) was carried out in order to obtain continental ancestry estimates independent from those obtained with SOURCEFIND. For this, the same reference individuals included in the SOURCEFIND analyses were grouped into continental groups, considering three scenarios:

(i) 5 groups– Native American, East Asian, Sub-Saharan African, European and East/South Mediterranean
(ii) 4 groups – Native American, East Asian, Sub-Saharan African, Caucasian (European + East/South Mediterranean)
(iii) 4 groups – Native American, East Asian, Sub-Saharan African, European.

The figures below compare SOURCEFIND or ADMIXTURE ancestry estimates for scenario (ii).



To contrast the components of ancestry inferred in the CANDELA dataset using the haplotype-based approach used here with those inferred by allele-based approaches, the same dataset was subjected to unsupervised ADMIXTURE analysis (up to K = 10, Supplementary Fig. 7) and

to PCA (up to PC 10, Supplementary Fig. 8). Below we describe some major features from these analyses, which are relevant for the discussion of the SOURCEFIND results.

ADMIXTURE analysis (Supplementary Fig. 7) at K = 3 detects three major continental ancestry components, reaching 100% frequency in certain European, Native American and Sub-Saharan African reference populations. CANDELA individuals show highly variable proportions of these three components.

At K = 4, another major continental ancestry component is inferred, reaching 100% frequency in certain East Asians. This Asian component is found at low frequency in Native Mexicans and in CANDELA samples from Mexico, possibly reflecting a closer genetic affinity of Natives from Mexico to East Asians, compared to Native Americans further South, as has been inferred from other analyses[10].

At K = 5 two sub-continental components are detected in Native Americans, one reaching frequencies of up to 100% in Mesoamericans, the other reaching 100% frequency in Andeans, with Native populations from Central America and Northern South America showing intermediate frequencies. The MesoAmerican component reaches high frequency in the Mexican CANDELA samples and is also the predominant Native component in Colombians. By contrast the Andean component reaches high frequency in Peruvians and Chileans.

At K=6 a component is seen at high frequency in the Colombian CANDELA data. Comparing this profile with results for the same CANDELA samples at K=5 it is apparent that this component corresponds mainly to the inferred European ancestry and possibly represents a case of drift in the Americas (the PCA results described below also provide suggestive evidence of this interpretation).

At K=7 a third Native American component is observed, reaching 100% frequency in the Chilean Mapuche Natives. This component reaches high frequency in Chilean CANDELA samples.

At K = 8 a minor component specific to Sub-Saharan Africans is detected, which reaches highest frequency in East African samples.

At K = 9 a component reaching frequencies close to 100% in North East Europe is observed. This component shows a gradient of decreasing frequency from North West Europe to Iberia. It is also observed in the CANDELA samples, reaching highest frequency in Brazilians.

At K = 10 a component reaching maximum frequencies in Western Europeans is detected, distinct from a component seen mostly in Southern Europe but which reaches maximum frequencies in East/South Mediterraneans. These two components are detected at variable frequencies in the CANDELA samples.

Altogether, these ADMIXTURE analyses inferred nine ancestry components in the reference population data. Of these, six reach frequencies close to 100% in certain reference population groups (from East Asia, Sub-Saharan Africa, North East Europe, the Andes, Meso America and the Mapuche). Of these, two have a close correspondence with components defined by the SOURCEFIND analyses (the Mapuche and North East European components). The other three components detected by ADMIXTURE in the reference data are further sub-divided by the fineSTRUCTURE analyses. In addition, most ADMIXTURE components show gradients in frequency across many reference samples, which are recognized as distinct population clusters in the SOURCEFIND analyses (Fig. 1).

Some basic observations from the PCA analyses (Supplementary Fig. 8) are as follows:

PC1-PC3 represent axis of differentiation between continental populations (PC1 distinguishing Africans from Non-Africans, PC2 Europeans from Native Americans and PC3 East Asians from Native Americans). The CANDELA individuals are spread out mostly along the European-Native American axis, consistent with their mostly Native American-European admixture. Certain CANDELA individuals also show evidence of some African or East Asian ancestry.

PCs from PC4 onwards detect sub-continental axis of genetic differentiation:

PC4 detecting genetic variation within Africa and distinguishing West Africans from South Africans.

PC5-PC7 represent axis of differentiation between Native Americans (PC5 corresponding to a Mexican-Southern Chilean Natives axis;

PC6 to a Mapuche-Chibchan axis and PC7 to a Mapuche-Central Andean axis).

The CANDELA samples place themselves along these axes of Native American variation in accordance with the Natives from the corresponding geographic region. These observations illustrate how Native American population structure is being reflected in the CANDELA samples, a pattern standing out even more clearly in the SOURCEFIND results shown in Figure 1.

Interestingly, the Colombian samples are placed somewhat at an offset along the Chibchan (i.e. Native Colombians) axis, consistent with the component detected by ADMIXTURE at K = 6 representing a case of drift specific to the Colombian sample.

PC8 corresponds to an axis of South/East Mediterranean-NorthEast European differentiation,

PC9 to an axis of West African-East African differentiation,

and PC10 to an axis of Japan-China/Vietnam differentiation.

Altogether, PCA revealed four axis of continental and six axis of sub-continental genetic differentiation, placing CANDELA individuals along some of these axes.

Supplementary Note 4. Correlation of regression P-values from different approaches to the *CentralAndes-Mapuche* ancestry contrast.

Regression analyses for testing the phenotypic effect of the contrast between CentralAndes and Mapuche ancestry were performed using three different approaches to the definition of these ancestry components, based on the SOURCEFIND, ADMIXTURE, or PCA (Supplementary Figures 7 and 8).

- SOURCEFIND: estimates of the *Aymara*, *Quechua1*, *Quechua2*, and *Colla* components were added and the sum (taken as the CentralAndes component) contrasted to the Mapuche component. Regressions were performed in three ways: (i) including individuals from all countries, (ii) including only Peruvians and Chileans (both the CentralAndes and Mapuche components are only present in these two countries, Fig. 1), (iii) including only Chileans (as only this country has both the CentralAndes and the Mapuche components at high frequency, Figure 1).
- ADMIXTURE: the unsupervised run at K=7 distinguishes three components in Native Americans (Supplementary Fig. 7). A light-blue colored component reaches 100% frequency in the Central Andean groups while a grey colored component reaches 100% frequency in the Mapuche. The difference in the proportions of these two ancestry components was taken as the CentralAndes-Mapuche contrast. Regression analysis was performed including individuals from all countries.
- PCA: PC7 places Central Andean and Mapuche clusters at opposite ends (Supplementary Fig. 8). Individual values on this PC were taken directly as an approximation to the contrast between these two components. However, since this PC shows some confounding with other ancestry differences, the regression included only Chileans (as these individuals have a relatively low frequency of other Native American ancestry components, Fig. 1, Supplementary Fig. 7).

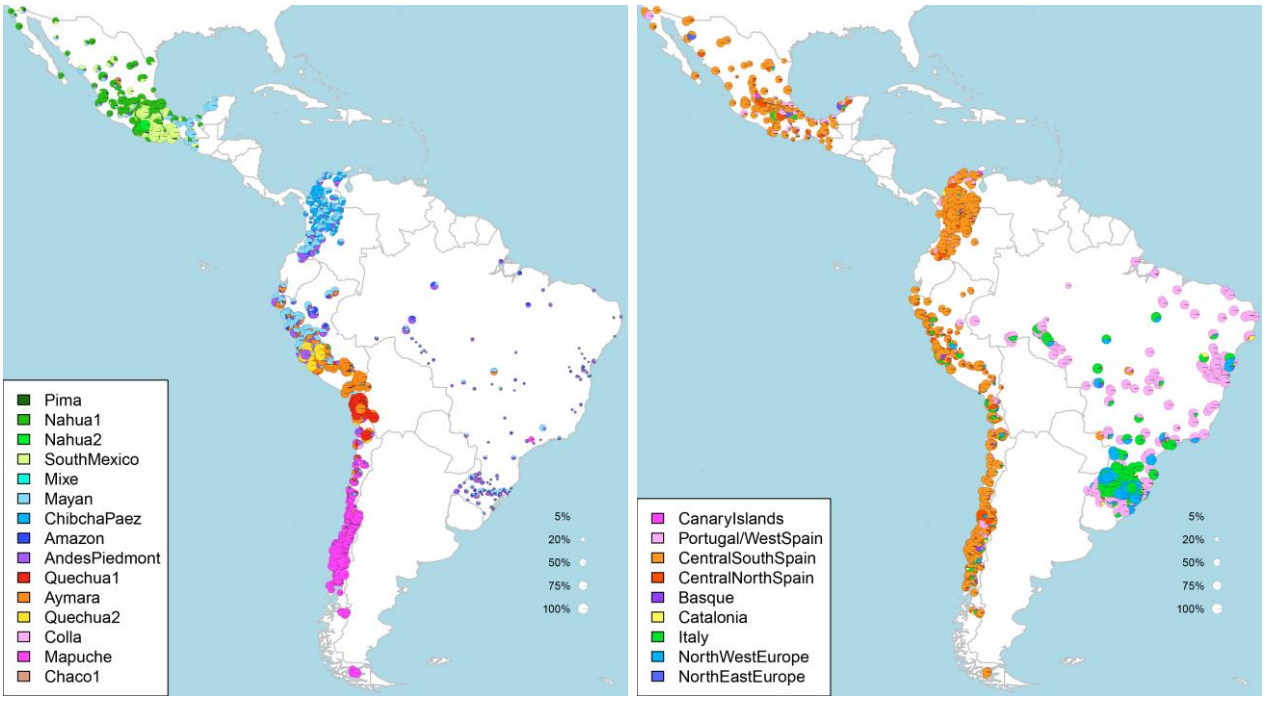
Below are Spearman's rank correlations calculated between the -log P-values obtained in the regressions described above (Sample sizes: all individuals N = 5794, Peruvians and Chileans N = 2594, Chileans N = 1542).

	ADMIXTURE	SOURCEFIND (all individuals)	SOURCEFIND (Peruvians and Chileans)	SOURCEFIND (Chileans)	PCA
ADMIXTURE	1.00	0.94	0.83	0.92	0.90
SOURCEFIND (all individuals)	0.94	1.00	0.83	0.91	0.88
SOURCEFIND (Peruvians and Chileans)	0.83	0.83	1.00	0.92	0.84
SOURCEFIND (Chileans)	0.92	0.91	0.92	1.00	0.92
PCA	0.90	0.88	0.84	0.92	1.00

Supplementary Note 5. Robustness of SOURCEFIND ancestry inference to the exclusion CANDELA individuals used as reference samples

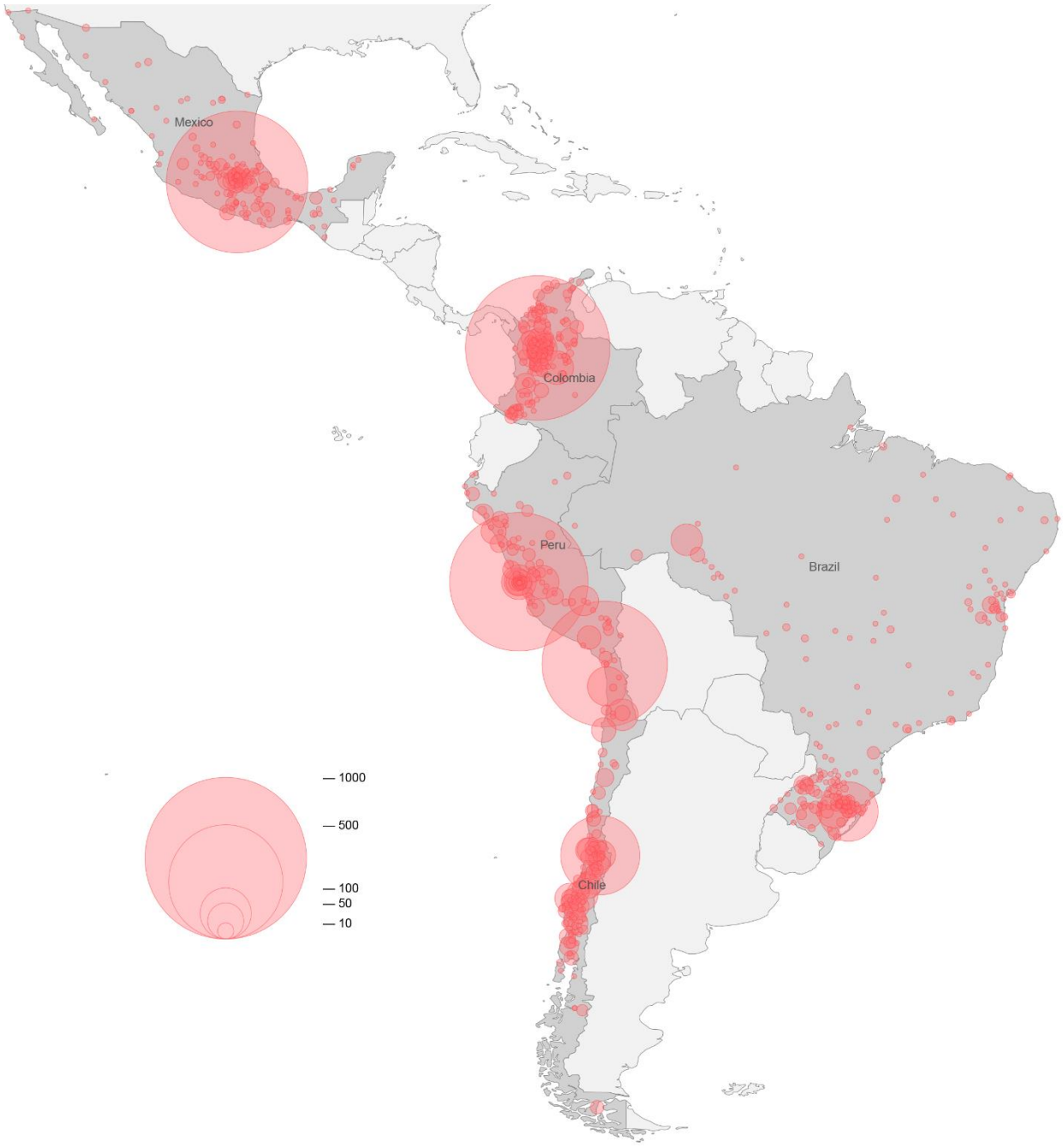
To assess the impact of having included some CANDELA individuals as reference samples in the SOURCEFIND analyses, we repeated our analyses after excluding CANDELA individuals from the reference samples. We also removed individuals that were excluded from the surrogate groups as described in "Definition of homogeneous clusters of reference population individuals" above, resulting in this analysis including only 55 surrogate clusters. The loss of one surrogate cluster relative to the initial analyses was due to the "Germany" surrogate cluster consisting entirely of CANDELA individuals. As described at the start of Supplementary Note 1, for this analysis we used an alternative, more efficient version of SOURCEFIND that used a truncated Poisson prior on the number of contributing surrogates and allowed a maximum of 6 surrogates to contribute at each MCMC iteration.

Maps with the distribution of the new estimated individual ancestry proportions are shown below. Ancestry matching to European, East/South Mediterranean, Sub-Saharan African, and East Asian groups are largely consistent with the results shown in Figure 2. For Native American ancestry, results are similar across most of the CANDELA sample. However there is a marked decrease in inferred ancestry related to the *AndesPiedmont* and *Quechua1* surrogate groups. This is probably due to these groups being made up of only one individual, after removal of CANDELA samples, thus decreasing the power of ancestry inference from these groups. The inferred ancestry contributions of these groups are, for the most part, substituted by ancestries from related, geographically proximate, surrogate groups.



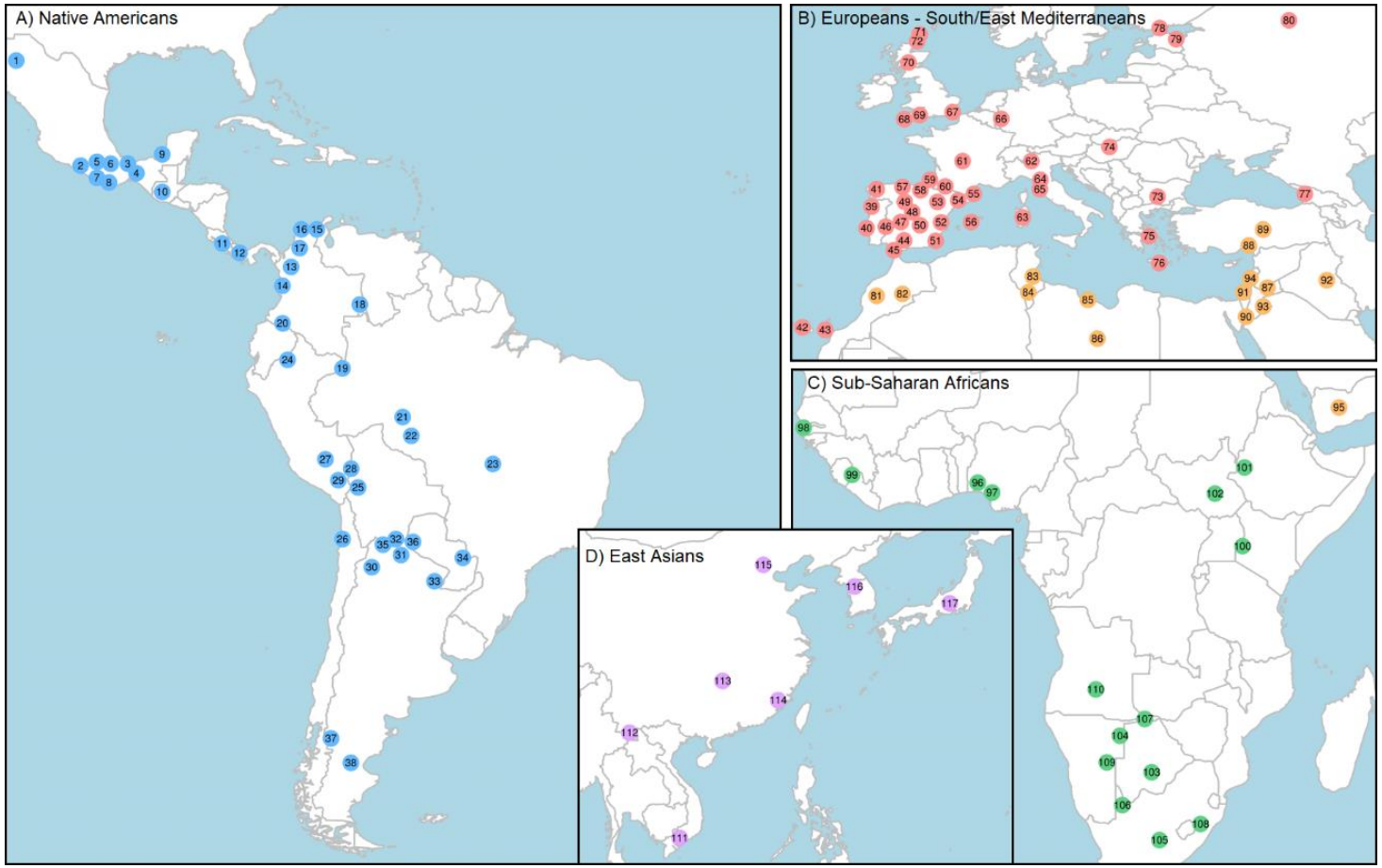
SUPPLEMENTARY FIGURES

Supplementary Figure 1. Birthplace of the 6,589 individuals included in this study.



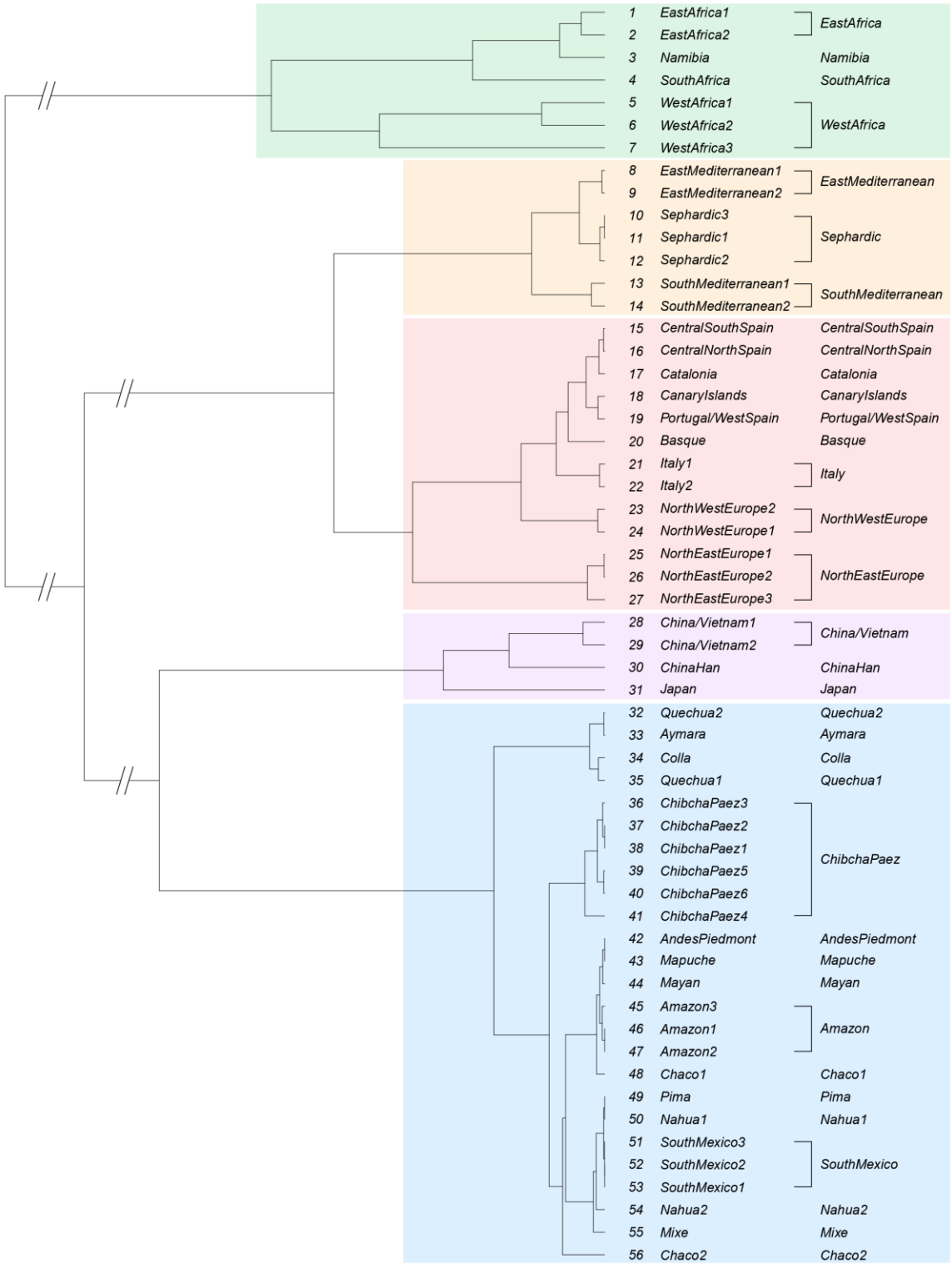
Circles are centered on birthplace with size proportional to the number of individuals born at that location.

Supplementary Figure 2. Approximate geographic location of the 117 reference population samples included in this study.



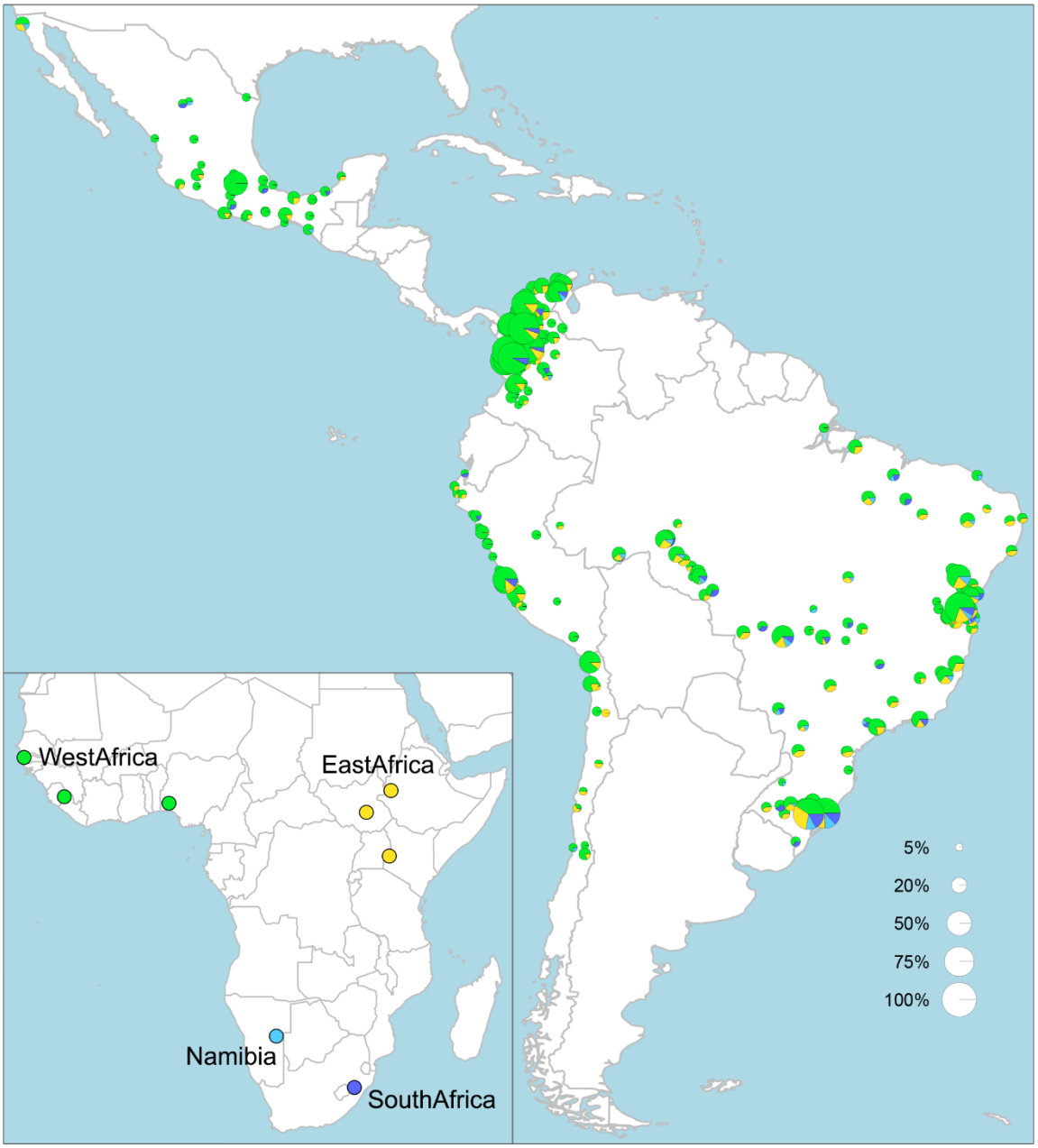
Populations have been color-coded as: blue (38 Native American), red (42 European), yellow (15 East/South Mediterranean), green (15 Sub-Saharan African) and purple (7 East Asians). Numbers inside the dots correspond to those used in Supplementary Table 1 with additional information on these samples.

Supplementary Figure 3. Tree relating the 56 clusters defined by fineSTRUCTURE and retained for ancestry inference.



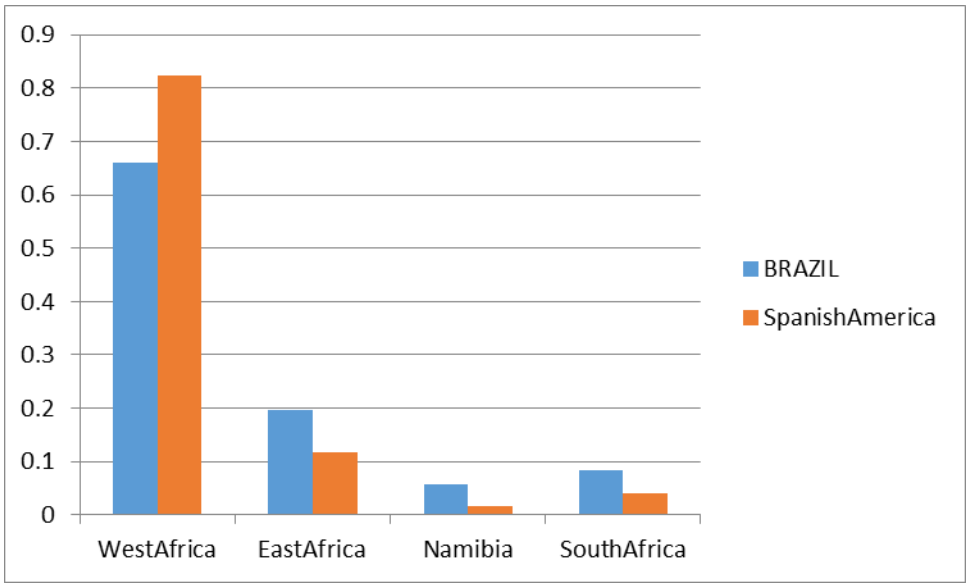
Brackets on the right indicate the 35 groups of clusters displayed in Figure 1.

Supplementary Figure 4. Geographic distribution of Sub-Saharan African ancestry sub-components in CANDELA individuals.



*Details about the maps in Figure 2.

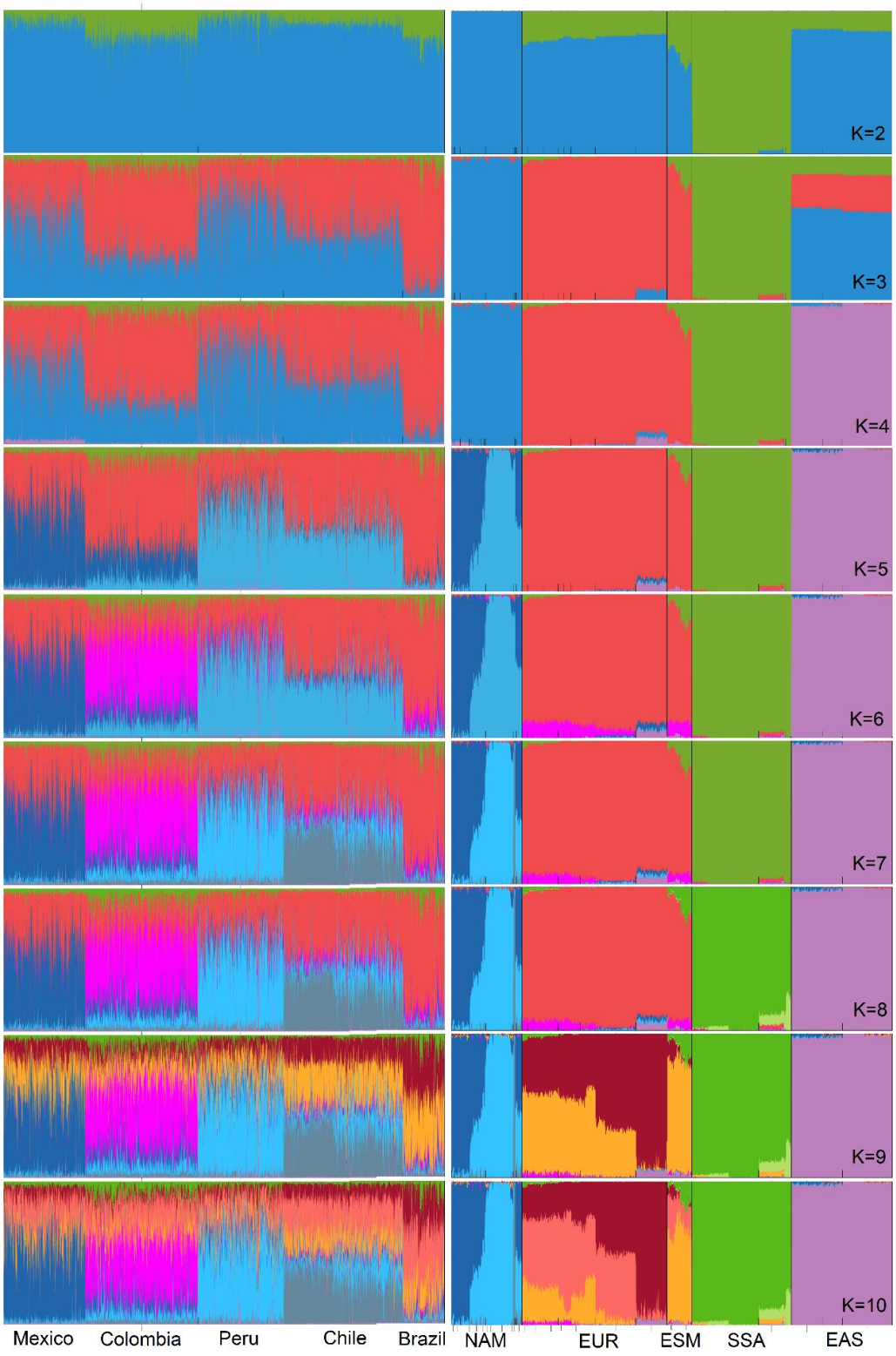
Supplementary Figure 5. Average sub-continental ancestry proportion for the 1,472 individuals with >5% Sub-Saharan African ancestry in Brazil and the four Spanish American countries sampled (Chile, Colombia, Mexico and Peru).



Supplementary Figure 6. Geographic distribution of East Asian ancestry sub-components in CANDELA individuals.

*Details about the maps in Figure 2.

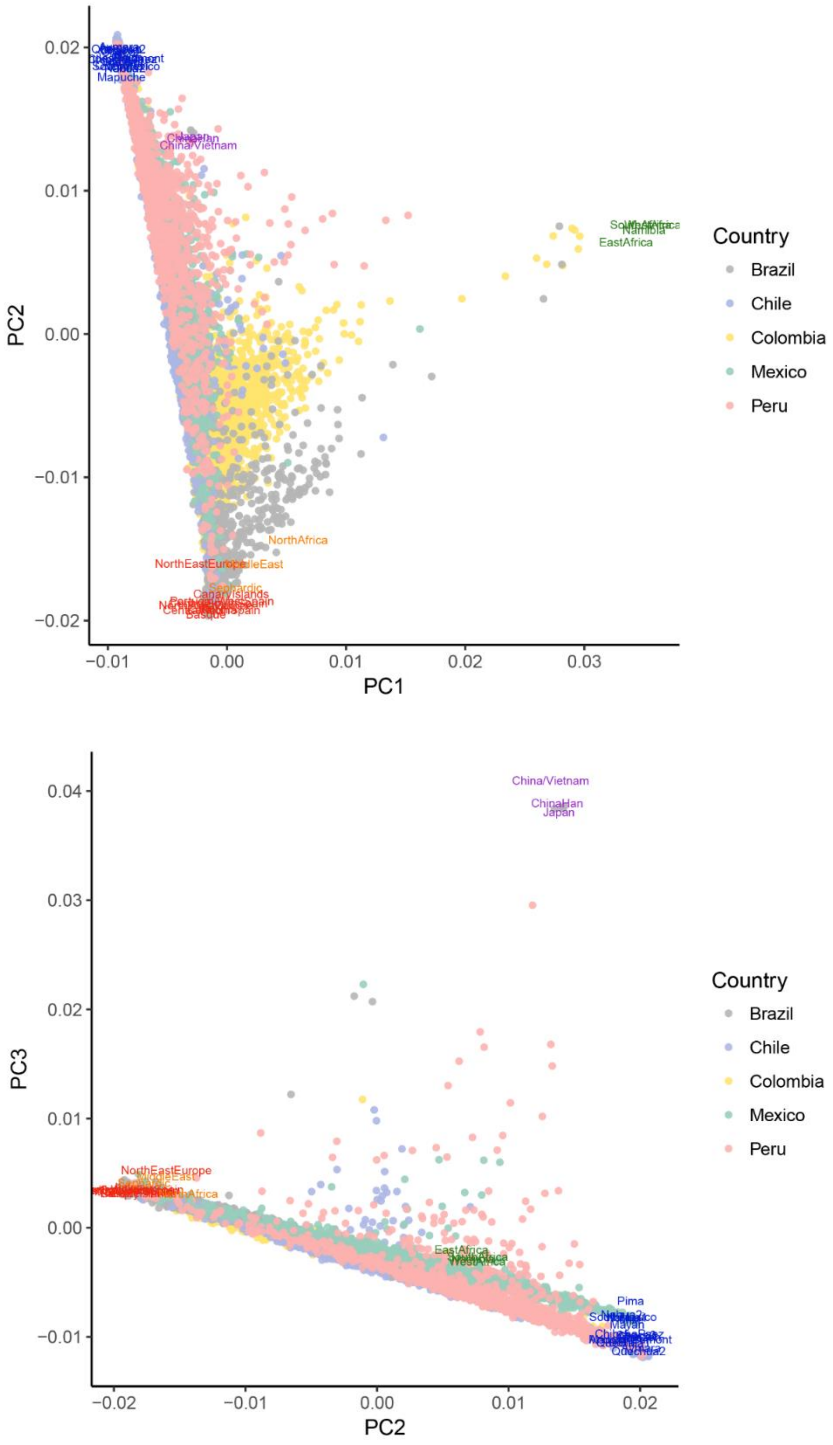
Supplementary Figure 7. Unsupervised ADMIXTURE analysis at K=2 to K=10 for the 6,561 CANDELA individuals included in the SOURCEFIND analyses and the 1,444 reference samples included in the 35 surrogate groups.

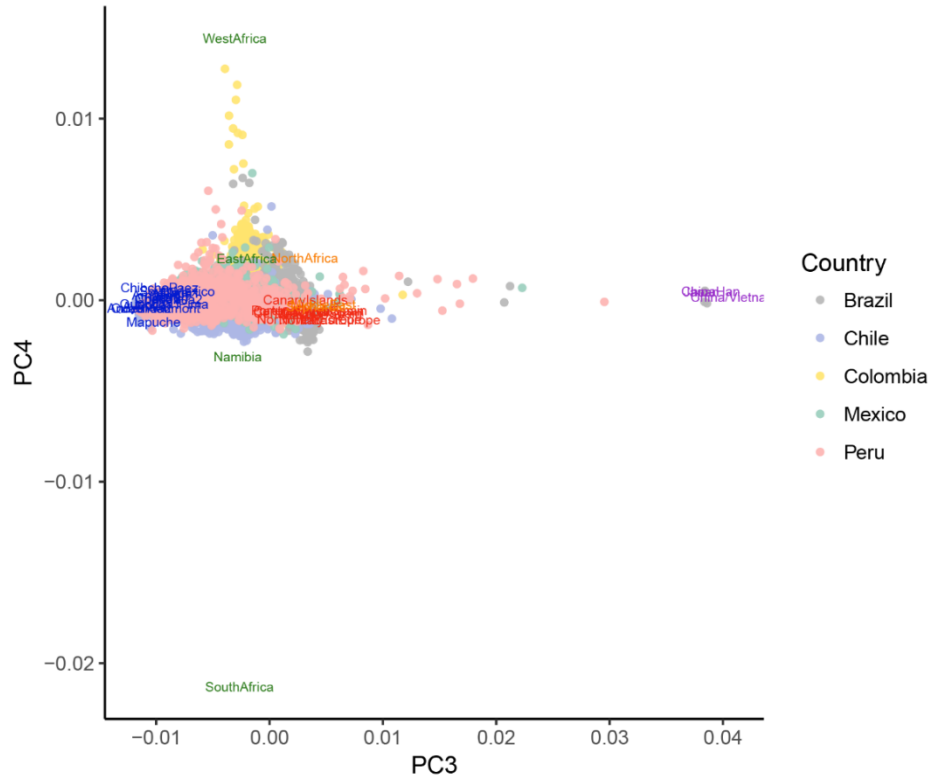


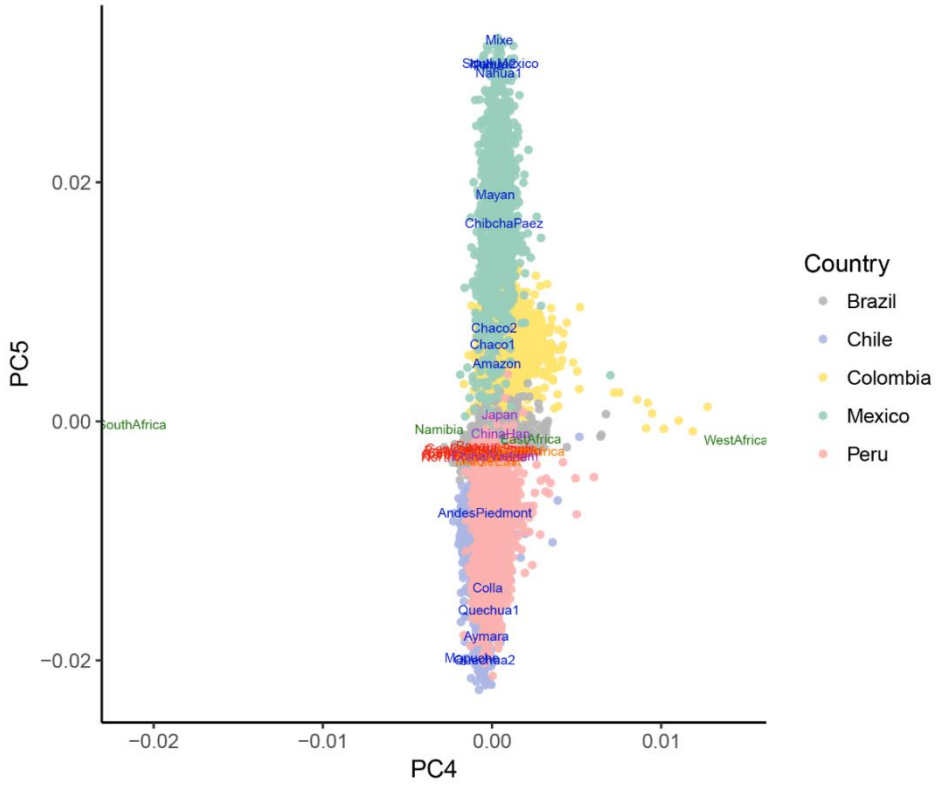
CANDELA individuals are shown on the left, grouped by country of birthplace. On the right are reference individuals grouped by major geographic region (NAM = Native American, EUR = European, ESM = East/South Mediterranean, SSA = Sub-Saharan African, EAS = East Asian), sub-grouped according to the 35 surrogate groups defined by fineSTRUCTURE (Supplementary Fig. 3).

Supplementary Figure 8. Principal Components Analysis for 6,561 CANDELA individuals and the 1,444 individuals included in the 35 groups of surrogate clusters.

Dots represent individuals in the Candela sample (color-coded by country). For reference samples, a label has been placed at the median PC score for individuals in each of the 35 groups (as defined in the fineSTRUCTURE analyses, Supplementary Fig. 2).




WestAfrica
EastAfrica
NorthAfrica
Mapuche
Namibia
SouthAfrica
0.01
0.00
−0.01
−0.02
PC4
−0.01
0.00
0.01
0.02
0.03
0.04
PC3
Country
Brazil
Chile
Colombia
Mexico
Peru


Mixe
Nahua1
Mayan
ChibchaPaez
Chaco2
Chaco1
Amazon
Japan
Namibia
EastAfrica
WestAfrica
AndesPiedmont
Colla
Quechua1
Aymara
0.02
0.00
−0.02
PC5
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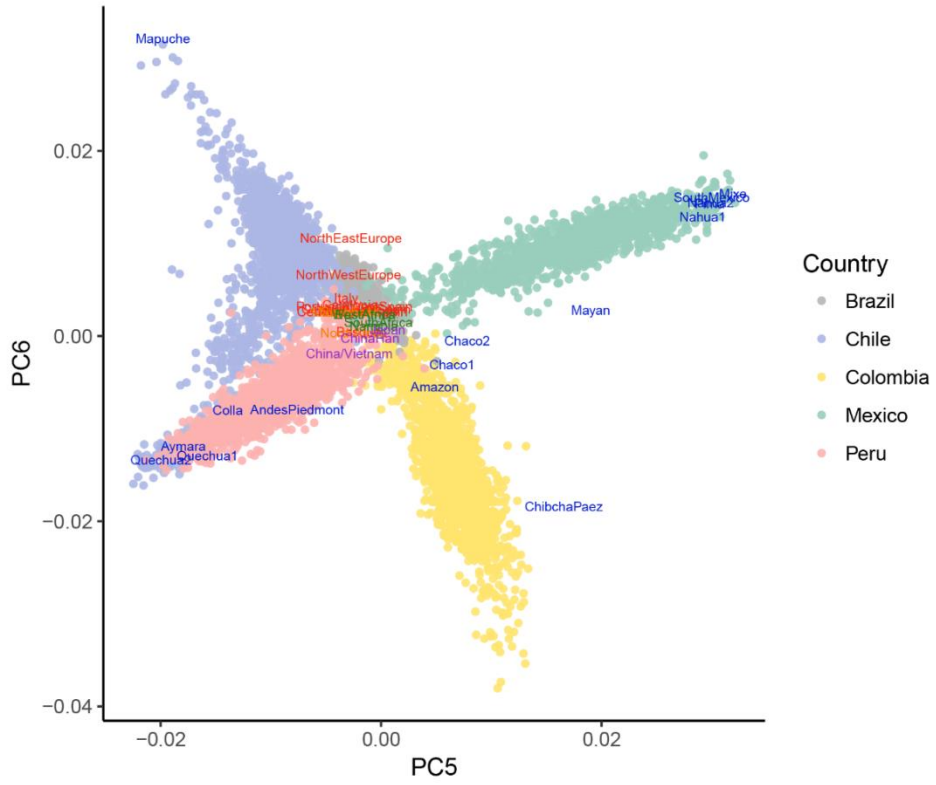
−0.01
0.00
0.01
PC4
Country
Brazil
Chile
Colombia
Mexico
Peru


Mapuche
NorthEastEurope
NorthWestEurope
Mayan
Nahua1
Chaco2
Chaco1
China/Vietnam
Amazon
Colla
AndesPiedmont
Aymara
Quechua1
ChibchaPaez
0.02
0.00
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PC6
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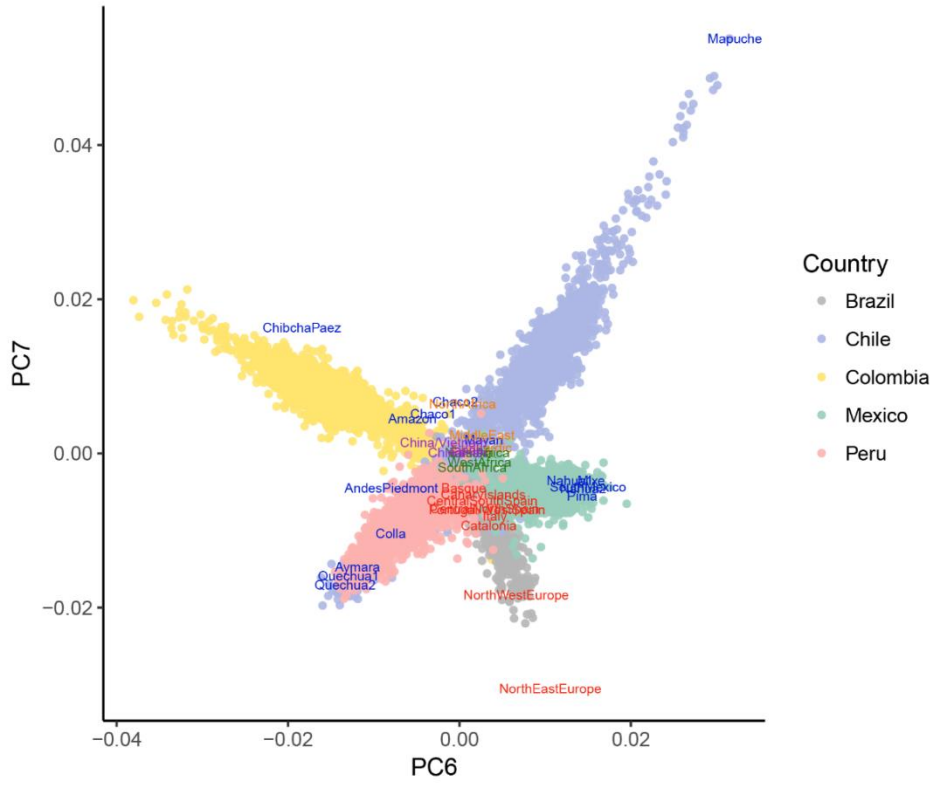
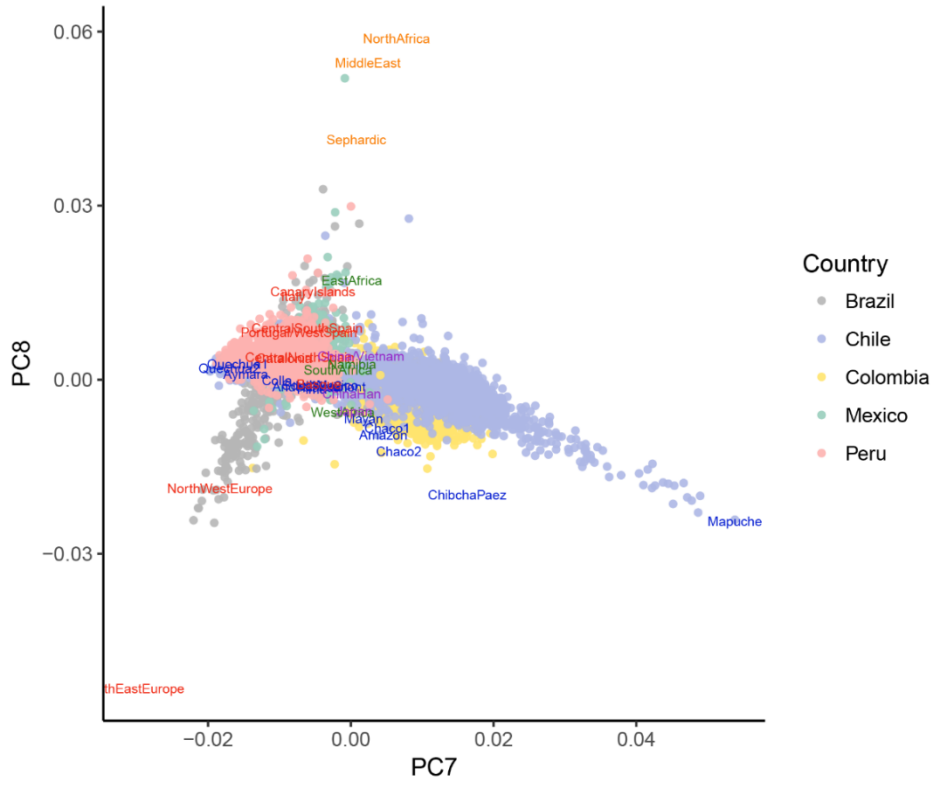
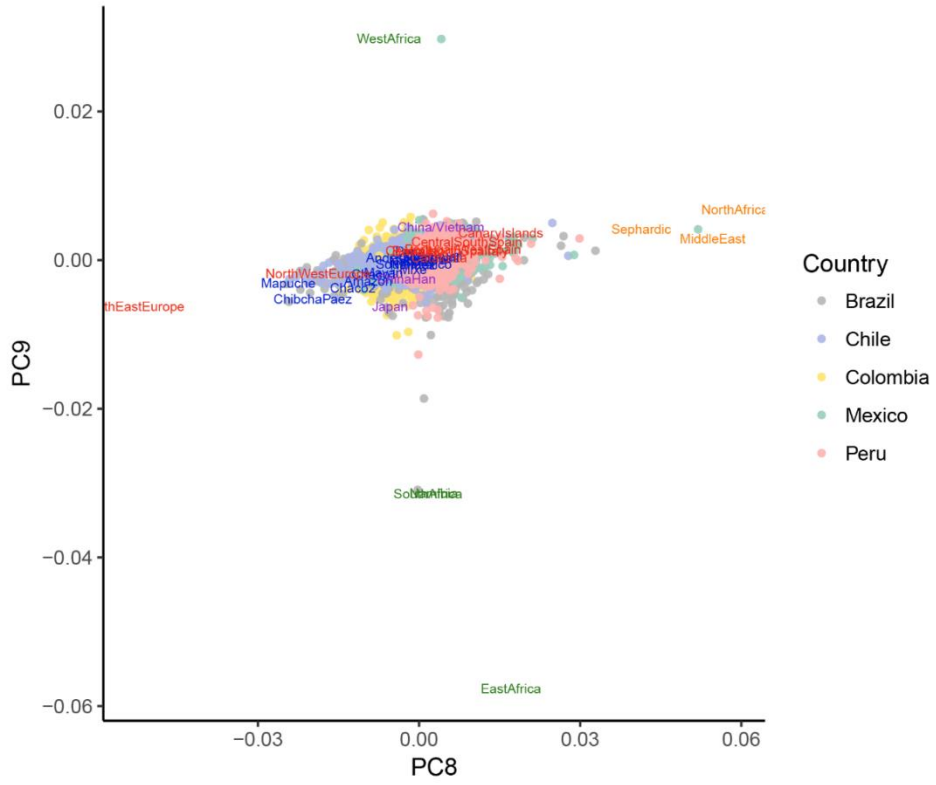
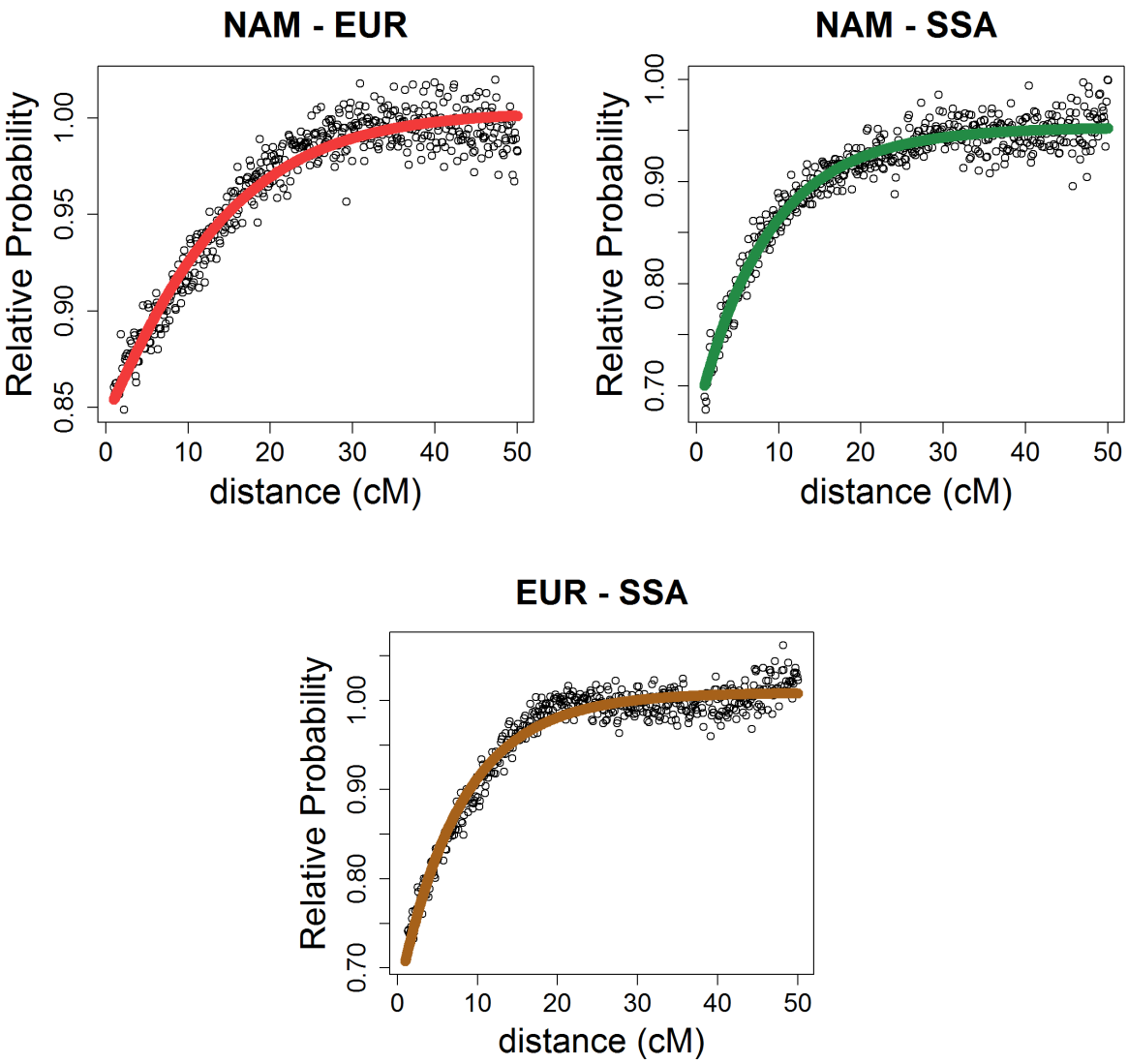
PC5
Country
Brazil
Chile
Colombia
Mexico
Peru


Mapuche
ChibchaPaez
Chaco2
Chaco1
Amazon
Mayan
AndesPiedmont
Colla
Aymara
Quechua1
Quechua2
Pima
Catalonia
NorthWestEurope
NorthEastEurope
0.04
0.02
0.00
−0.02
PC7
−0.04
−0.02
0.00
0.02
PC6
Country
Brazil
Chile
Colombia
Mexico
Peru


NorthAfrica
MiddleEast
Sephardic
EastAfrica
CanaryIslands
Italy
Portugal/WestSpain
CentralSouthSpain
China/Vietnam
Namibia
SouthAfrica
Quechua1
Aymara
Colla
Han
WestAfrica
Maya
Chaco1
Amazon
Chaco2
NorthWestEurope
ChibchaPaez
Mapuche
thEastEurope
0.06
0.03
0.00
−0.03
−0.02
0.00
0.02
0.04
PC7
PC8
Country
Brazil
Chile
Colombia
Mexico
Peru


WestAfrica
NorthAfrica
Sephardic
MiddleEast
China/Vietnam
CanaryIslands
CentralSouthSpain
NorthWestEurope
Mapuche
Chaco2
ChibchaPaez
Japan
thEastEurope
EastAfrica
0.02
0.00
−0.02
−0.04
−0.06
−0.03
0.00
0.03
0.06
PC8
PC9
Country
Brazil
Chile
Colombia
Mexico
Peru

Supplementary Figure 9. Example CANDELA individual for which GLOBETROTTER infers admixture involving three sources at about the same time.



Dots are the inferred relative probabilities that a pair of DNA segments in this individual are inherited from: (top left) Native American (NAM) and European (EUR) sources, (top right) NAM and Sub-Saharan African (SSA) sources, (bottom) EUR and SSA sources, as a function of the genetic distance between the DNA segments. The fitted exponential curves result in an estimated admixture date of 11 generations ago.

SUPPLEMENTARY TABLES

Supplementary Table 1. 117 Reference population samples.

n	Sample label	Group*	N (Pre-QC)	N (Post-QC)	Country of origin (.sample)	Data source (reference)
1	Pima	NAM	2	2	Mexico.1	1
2	Nahua	NAM	25	25	Mexico.2	This study
3	Mixe	NAM	2	2	Mexico.3	1
4	Mixe.B	NAM	16	16	Mexico.4	This study
5	Mixtec	NAM	2	2	Mexico.5	1
6	Mixtec.B	NAM	10	10	Mexico.6	This study
7	Zapotec	NAM	2	2	Mexico.7	1
8	Zapotec.B	NAM	12	12	Mexico.8	This study
9	Mayan	NAM	2	2	Mexico.9	1
10	Kaqchikel	NAM	8	8	Guatemala	This study
11	Cabecar	NAM	5	5	Costa.Rica.1	This study
12	Guaymi	NAM	4	4	Costa.Rica.2	This study
13	Embera	NAM	21	21	Colombia.1	This study
14	Waunana	NAM	5	5	Colombia.2	This study
15	Wayuu	NAM	3	3	Colombia.3	This study
16	Kogi	NAM	6	6	Colombia.4	This study
17	Zenu	NAM	7	7	Colombia.5	This study
18	Piapoco	NAM	2	2	Colombia.6	1
19	Ticuna	NAM	4	4	Colombia.7	This study
20	Inga	NAM	3	3	Colombia.8	This study
21	Karitiana	NAM	3	3	Brazil.1	1
22	Surui	NAM	2	2	Brazil.2	1
23	Xavante	NAM	4	4	Brazil.3	This study
24	Andoa	NAM	20	20	Peru.1	This study
25	Aymara.A	NAM	13	13	Bolivia.1	This study
26	Aymara.B	NAM	4	4	Chile.1	This study
27	Quechua	NAM	3	3	Peru.2	1
28	Quechua.B	NAM	14	14	Bolivia.2	This study
29	Uros	NAM	8	8	Peru.3	This study
30	Colla	NAM	25	23	Argentina.1	2
31	Wichi	NAM	25	19	Argentina.3	2
32	Wichi.B	NAM	4	4	Argentina.4	This study
33	Toba	NAM	4	4	Argentina.5	This study
34	Ache	NAM	5	5	Paraguay	This study
35	Guarani	NAM	5	5	Argentina.6	This study

36	Chane	NAM	2	2	Argentina.7	This study
37	Mapuche	NAM	9	9	Argentina.2	This study
38	Huilliche	NAM	10	10	Chile.2	This study
39	PRT.A	EUR	18	18	Portugal.1	This study
40	PRT.B	EUR	31	31	Portugal.2	This study
41	IBS-Galicia	EUR	12	8	Spain.1	3
42	SP-CAN	EUR	14	14	Spain.2	This study
43	IBS-Canarias	EUR	3	2	Spain.3	3
44	SP-AND	EUR	15	15	Spain.4	This study
45	IBS-Andalucia	EUR	4	4	Spain.5	3
46	IBS-Extremadura	EUR	12	8	Spain.6	3
47	IBS	EUR	7	7	Spain.7	3
48	SP-CSP	EUR	15	15	Spain.8	This study
49	IBS-Cast.Leon	EUR	18	12	Spain.9	3
50	IBS-Cast.Mancha	EUR	9	6	Spain.10	3
51	IBS-Murcia	EUR	12	8	Spain.11	3
52	IBS-Valencia	EUR	21	14	Spain.12	3
53	IBS-Aragon	EUR	6	6	Spain.13	3
54	SP-CTL	EUR	7	7	Spain.14	This study
55	IBS-Cataluna	EUR	15	10	Spain.15	3
56	IBS-Baleares	EUR	12	8	Spain.16	3
57	IBS-Cantabria	EUR	9	6	Spain.17	3
58	SP-BAS	EUR	14	14	Spain.18	This study
59	IBS-Pais.Vasco	EUR	12	8	Spain.19	3
60	Basque	EUR	2	2	France.1	1
61	French	EUR	3	3	France.2	1
62	Bergamo	EUR	2	2	Italy.1	1
63	Sardinian	EUR	3	3	Italy.2	1
64	TSI	EUR	107	106	Italy.3	3
65	Tuscan	EUR	2	2	Italy.4	1
66	CEU	EUR	99	91	NW.Europe	3
67	GBR-Kent	EUR	38	31	UK.1	3
68	GBR-Cornwall	EUR	32	29	UK.2	3
69	GBR-Corn-Devon	EUR	1	1	UK.3	3
70	GBR-Scotland	EUR	4	3	UK.4	3
71	Orcadian	EUR	2	2	UK.5	1
72	GBR-Orkney	EUR	26	21	UK.6	3
73	Bulgarian	EUR	2	2	Bulgaria	1
74	Hungarian	EUR	2	2	Hungary	1
75	Greek	EUR	2	2	Greece.1	1
76	Crete	EUR	2	2	Greece.2	1

77	Georgian	EUR	2	2	Georgia	1
78	FIN	EUR	99	99	Finland	3
79	Estonian	EUR	2	2	Estonia	1
80	Russian	EUR	2	2	Russia	1
81	MRC	ESM	14	11	Morocco.1	This study
82	Moroccan_Jew[#]	ESM	7	7	Morocco.2	This study
83	TUN	ESM	14	14	Tunisia.1	This study
84	Tunisian_Jew[#]	ESM	6	6	Tunisia.2	This study
85	LIB	ESM	15	14	Libya.1	This study
86	Libyan_Jew[#]	ESM	7	7	Libya.2	This study
87	JRD	ESM	15	15	Jordan.1	This study
88	Sephardi_Jew[#]	ESM	7	7	Turkey.1	This study
89	Turkish	ESM	2	2	Turkey.2	1
90	BedouinB	ESM	2	2	Israel.1	1
91	Druze	ESM	2	2	Israel.2	1
92	Iraqi_Jew	ESM	2	2	Iraq	1
93	Jordanian	ESM	3	3	Jordan.2	1
94	Palestinian	ESM	3	3	Palestine	1
95	Yemenite_Jew	ESM	2	2	Yemen	1
96	YRI	SSA	108	101	Nigeria.1	3
97	ESN	SSA	99	95	Nigeria.2	3
98	GWD	SSA	113	111	Gambia	3
99	MSL	SSA	85	69	Sierra.Leone	3
100	LWK	SSA	99	73	Kenya	3
101	Anuak	SSA	21	3	Ethiopia	4
102	South_Sudanese	SSA	21	8	South.Sudan	4
103	GuiGhanaKgal	SSA	15	14	Botswana	5
104	Juhoansi	SSA	18	15	Namibia.1	5
105	Karretjie	SSA	20	3	South.Africa.1	5
106	Khomani	SSA	39	4	South.Africa.2	5
107	Khwe	SSA	17	14	Namibia.2	5
108	SEBantu	SSA	20	19	South.Africa.3	5
109	SWBantu	SSA	12	9	Namibia.3	5
110	Xun	SSA	19	19	Angola	5
111	KHV	EAS	99	95	Vietnam	3
112	CDX	EAS	93	82	China.1	3
113	CHS-Hu_Nan	EAS	102	66	China.2	3
114	CHS-Fu_Jian	EAS	48	31	China.3	3
115	CHB	EAS	103	101	China.4	3
116	Korean	EAS	2	2	Korea	1
117	JPT	EAS	104	104	Japan	3

	Total		2359	2058		

Note: Genotypes at SNPs shared between published datasets were reported to have been obtained by full genome sequencing (1) or genotyping on the following platforms: (2) Illumina OmniExpress, (3) Illumina Omni2.5M, (4) Illumina Omni1M, (5) Illumina Omni2.5M.

References: (1) Mallick S et al 2016. The Simons Genome Diversity Project: 300 genomes from 142 diverse populations. Nature. 538. pp 201 - 206. (2) Eichstaedt CA et al. 2014. The Andean Adaptive Toolkit to Counteract High Altitude Maladaptation: Genome-Wide and Phenotypic Analysis of the Collas. PLoS One. 9(3): e93314. (3)The 1000 genomes project Consortium. A global reference for human genetic variation. Nature. 526. pp 68 - 74. (4) Pagani L et al. 2012. Ethiopian Genetic Diversity Reveals Linguistic Stratification and Complex Influences on the Ethiopian Gene Pool. American Journal of Human Genetics. 91(1). Pp 83 - 96. (5) Schlebusch CM et al. 2012. Genomic Variation in Seven Khoe-San Groups Reveals Adaptation and Complex African History. Science. 338(6105). Pp. 374 - 379.

* NAM: Native American, EUR: European, ESM: East/South Mediterranean, SSA: Sub-Saharan African, EAS: East Asian.

Samples obtained from The National Laboratory for the Genetics of Israeli Populations (http://yoran.tau.ac.il/nlgip/).

Supplementary Table 2. Description of the decisions made on the clusters based on the 129 clusters generated by fineSTRUCTURE.

fS Clust	**Contains**	**N**	**Decision**	**Explanation of decision**	**Donor/*Surrogate***	**Surrog**	**Additional notes**
1	South.Sudan(1/8)	1	Donor	Single sample cluster	Out.SouthSudan		
2	Ethiopia(3/3)+South.Sudan(7/8)	10	Surrogate		*EastAfrica1*	*1*	
3	Kenya(35/73)	35	Surrogate (Merged)	Similar according to TVD and tree distance	*EastAfrica2*	*2*	No clear assignment
4	Kenya(38/73)	38					
5	Namibia.3(1/9)	1	Donor	Single sample cluster	Out.Namibia.3		
6	Namibia.3(1/9)*	1	Donor	Single sample cluster	Out.Namibia.3		
7	Namibia.3(6/9)	6	Surrogate		*Namibia*	*3*	
8	Namibia.2(1/14)+Namibia.3(1/9)	2	Donor	Similar to **7**, no contribution	Out.Namibia.2 Out.Namibia.3		
9	South.Africa.3(1/19)	1	Donor	Single sample cluster	Out.South.Africa.3		
10	Namibia.2(1/14)	1	Donor	Single sample cluster	Out.Namibia.2		
11	Namibia.2(6/14)	6	Donor	No contribution	Out.Namibia.2		
12	Namibia.2(5/14)	5	Donor	No contribution	Out.Namibia.2		
13	South.Africa.3(10/19)	10	Surrogate (Merged)	Similar according to TVD and tree distance	*SouthAfrica*	*4*	
14	South.Africa.3(8/19)	8					
15	Gambia(3/111)+Sierra.Leone(1/69)	4	Donor	Similar to 18, small	Out.Gambia Out.SierraLeone		
16	Gambia(10/111)	10	Donor	Similar to 18, small	Out.Gambia		
17	Gambia(18/111)	18	Donor	Similar to 18, small	Out.Gambia		
18	Gambia(29/111)	29	Surrogate (Merged)	Similar according to TVD and tree distance	*WestAfrica1*	*5*	
19	Gambia(22/111)	22					
20	Gambia(29/111)*	29	Donor	Similar to 18, small	Out.Gambia		
21	Sierra.Leone(68/69)	68	Surrogate		*WestAfrica2*	*6*	

22	Nige-ria.1(31/101)+Nigeria.2(1/95)	32	Surrogate (Merged)	Similar according to TVD and tree distance	*WestAfrica3* Out.Nigeria.1 Out.Nigeria.2	*7*	2 Nigeria.2 and 1 inconsistent ind excluded
23	Nige-ria.1(69/101)+Nigeria.2(1/95)	70					
24	Nige-ria.1(1/101)+Nigeria.2(93/95)	94	Donor	Similar to **23**	Out.Nigeria.1 Out.Nigeria.2		
25	Botswana(1/14)	1	Donor	Single sample cluster	Out.Botswana		
26	Botswana(1/14)*	1	Donor	Single sample cluster	Out.Botswana		
27	Botswana(1/14)**	1	Donor	Single sample cluster	Out.Botswana		
28	Botswana(3/14)	3	Donor	No contribution	Out.Botswana		
29	South.Africa.1(1/3)	1	Donor	Single sample cluster	Out.South.Africa.1		
30	South.Africa.2(1/4)	1	Donor	Single sample cluster	Out.South.Africa.2		
31	Botswana(3/14)*	3	Donor	No contribution	Out.Botswana		
32	Botswana(5/14)	5	Donor	No contribution	Out.Botswana		
33	South.Africa.1(2/3)+South.Afri ca.2 (3/4)	5	Donor	No contribution	Out.South.Africa.1 Out.South.Africa.2		
34	Angola(1/19)+Namibia.1(1/15)	2	Donor	No contribution	Out.Angola Out.Namibia.1		
35	Angola(8/19)	8	Donor	No contribution	Out.Angola		
36	Ango-la(10/19)+Namibia.2(1/14)	11	Donor	No contribution	Out.Angola Out.Namibia.2		
37	Namibia.1(14/15)	14	Donor	No contribution	Out.Namibia.1		
38	Jordan.1(1/15)	1	Donor	Single sample cluster	Out.Jordan.1		
39	Israel.1(2/2)+Jordan.1(2/15)	4	Donor	Similar to **41**	Out.Israel.1 Out.Jordan.1		
40	Jordan.1(2/15)	2	Donor	Small cluster, similar **41**	Out.Jordan.1		
41	Jordan.1(7/15)+Yemen(2/2)	9	Surrogate		*EastMediterranean1*	*8*	
42	Jor-dan.1(1/15)+Jordan.2(3/3)+Pale stine(3/3)	7	Surrogate		*EastMediterranean2*	*9*	
43	Turkey.2(2/2)	2	Donor	Complex genetic profile	Out.Turkey.2		

44	Geor-gia(2/2)+Greece.1(1/2)+Greece.2(2/2)	5	Donor	Complex genetic profile	Out.Georgia Out.Greece.1 Out.Greece.2		
45	Iraq(2/2)+Israel.2(2/2)+Jordan.1(2/15)	6	Donor	Complex genetic profile	Out.Iraq, Out.Israel.2 Out.Jordan.1		
46	Morocco.2(7/7)	7	Surrogate		*Sephardic3*	*10*	
47	Libya.2(1/7)+Turkey.1(7/7)	8	Surrogate		*Sephardic1*	*11*	
48	Tunisia.2(4/6)	4	Surrogate (Merged)	Similar according to TVD and tree distance	*Sephardic2*	*12*	
49	Libya.2(6/7)+Tunisia.2(2/6)	8					
50	Libya.1(1/14)+Tunisia.1(2/14)	3	Surrogate (Merged)	Similar according to TVD and tree distance	*SouthMediterranean1*	*13*	
51	Libya.1(11/14)+Tunisia.1(3/14)	14					
52	Libya.1(2/14)+Tunisia.1(9/14)	11					
53	Morocco.1(3/11)	3	Surrogate (Merged)	Similar according to TVD and tree distance	*SouthMediterranean2*	*14*	
54	Morocco.1(8/11)	8					
55	Spain.4(2/15)	2	Donor	Similar to **56**, small	Out.Spain.4		
56	Spain.10(4/6)+Spain.11(5/8)+Spain.12(3/14)+Spain.14(1/7)+Spain.2(1/14)+Spain.4(13/15)+Spain.5(4/4)+Spain.6(4/8)+Spain.7(4/7)+Spain.9(5/12)	44	Surrogate		*CentralSouthSpain* Out.Spain.5 Out.Spain.10	*15*	2 inds excluded - inconsistent assignment
57	Spain.10(2/6)+Spain.12(6/14)+Spain.13(5/6)+Spain.17(6/6)+Spain.8(3/15)	22	Surrogate		*CentralNorthSpain* Out.Spain.8 Out.Spain.12 Out.Spain.17	*16*	4 inds excluded - inconsistent assignment
58	Spain.8(12/15)	12	Donor	Drifted, no contribution	Out.Spain.8		
59	Italy.2(3/3)	3	Donor	Complex genetic profile	Out.Italy.2		
60	Spain.1(2/8)+Spain.11(1/8)+Spain.12(5/14)+Spain.13(1/6)+Spain.14(6/7)+Spain.15(10/10)+Spain.16(7/8)+Spain.7(3/7)+Spain.9(1/12)	36	Surrogate		*Catalonia* Out.Spain.1 Out.Spain.11 Out.Spain.12	*17*	3 inds relocated to **56**, 4 inds excluded - inconsistent

61	Portugal.2(1/31)+Spain.11(2/8)+Spain.2(13/14)+Spain.3(2/2)+Spain.6(1/8)	19	Surrogate		*CanaryIslands*	*18*	1 ind relocated to **62**
62	Portugal.1(18/18)+Portugal.2(30/31)+Spain.1(6/8)+Spain.16(1/8)+Spain.6(3/8)+Spain.9(6/12)	64	Surrogate		*Portugal/WestSpain* Out.Spain.1 Out.Spain.9 Out.Spain.6 Out.Spain.16	*19*	3 inds relocated to **56**, 9 inds excluded - inconsistent assignment
63	France.1(1/2)+Spain.18(1/14)+Spain.19(8/8)	10	Surrogate (Merged)	Similar according to TVD and tree distance	*Basque*	*20*	
64	France.1(1/2)+Spain.18(13/14)	14					
65	Bulgaria(2/2)+Greece.1(1/2)+Italy.1(2/2)+Italy.5(15/15)	20	Surrogate		*Italy1* Out.Greece.1	*21*	1 Greece.1 ind removed
66	Italy.3(31/106)	31	Surrogate		*Italy2*	*22*	
67	Italy.3(75/106)+Italy.4(2/2)	77	Donor	No contribution	Out.Italy.3,Out.Italy.4		
68	UK.2(28/29)	28	Donor	Similar to **69**, no contrib.	Out.UK.2		
69	France.2(1/3)+NW.Europe(74/91)+UK.1(31/31)+UK.2(1/29)+UK.3(1/1)+UK.4(3/3)	111	Surrogate		*NorthWestEurope2* Out.UK.4 Out.NW.Europe Out.France.2	*23*	10 inds excluded - inconsistent assignment
70	Germany(6/37)+Hungary(1/2)+NW.Europe(10/91)	17	Donor	Similar to **69**, small contribution to CANDELA	Out.Germany Out.Hungary Out.NW.Europe		
71	UK.5(2/2)+UK.6(21/21)	23	Donor	No contribution	Out.UK.5, Out.UK.6		
72	France.2(2/3)+Germany(31/37)+Hungary(1/2)+NW.Europe(7/91)	41	Surrogate		*NorthWestEurope1* Out.Hungary Out.France.2 Out.NW.Europe	*24*	Non-Germany indivudals removed
73	Russia(2/2)	2	Surrogate		*NorthEastEurope1*	*25*	
74	Estonia(2/2)+Finland(7/99)	9	Surrogate		*NorthEastEurope2*	*26*	

75	Finland(29/99)	29	Surrogate (Merged)	Similar according to TVD and tree distance	*NorthEastEurope3*	*27*	
76	Finland(41/99)	41					
77	Finland(22/99)	22					
78	China.1(2/82)	2	Donor	Similar to **79**, small	Out.China.1		
79	China.1(72/82)	72	Surrogate		*China/Vietnam1*	*28*	
80	China.1(7/82)	7	Donor	Similar to **79**, small	Out.China.1		
81	Vietnam(91/95)	91	Surrogate		*China/Vietnam2*	*29*	
82	Japan(1/104)+Korea(1/2)	2	Donor	Samples represented by different clusters	Out.Japan Out.Korea		
83	China.3(1/31)+China.4(64/101)+Korea(1/2)	66	Surrogate		*ChinaHan* Out.China.3 Out.Korea	*30*	2 non China.4 inds removed
84	China.2(26/66)+China.3(2/31)+China.4(3/101)+Vietnam(4/95)	35	Donor	Similar to **84**, complex genetic background	Out.China.2 Out.China.3 Out.China.4 Out.Vietnam		
85	China.1(1/82)+China.2(40/66)+China.3(2/31)+China.4(29/101)	72	Donor	Contains several populations present in other clusters	Out.China.1 Out.China.2 Out.China.3, Out.China.4		
86	China.3(26/31)+China.4(5/101)	31	Donor	No contribution to CANDELA	Out.CHB Out.CHS.Fu.Jian		
87	Japan(72/104)	72	Surrogate (Merged)		*Japan*	*31*	
88	Japan(31/104)	31					
89	Chile.3(2/65)	2	Donor	Similar to **90**, small	Out.Chile.3		
90	Bolivia.2(6/12)+Chile.1(1/3)+Chile.3(27/65)	34	Surrogate (Merged)		*Quechua2* Out.Chile.3	*32*	3 inds excluded - inconsistent assignment
91	Bolivia.2(2/12)+Chile.3(23/65)	25					
92	Peru.3(5/5)	5	Removed	Removed as donor and recipient, because high drift			
93	Boli-	20	Surrogate		*Aymara*, Out.Chile.1,	*33*	4 inds excluded -

	via.1(10/12)+Chile.1(1/3)+Chile.3(1/65)+Peru.2(2/3)+Peru.4(6/17)				Out.Chile.3, Out.Bolivia.1		inconsistent assignment
94	Bolivia.1(2/12)+Bolivia.2(4/12)+Chile.1(1/3)+Chile.3(10/66)+Peru.4(1/17)	18	Donor	Whole cluster has inconsistent assignment	Out.Bolivia.1 Out.Bolivia.2 Out.Chile.1 Out.Chile.3 Out.Peru.4		
95	Argentina.1(10/19)+Chile.3(1/67)	11	Surrogate		*Colla*, Out.Chile.3	*34*	Chile.3 removed
96	Argentina.1(9/19)	9	Donor	Similar to **95**, no contrib.	Out.Argentina.1		
97	Peru.2(1/3)+Peru.4(8/17)	9	Surrogate		*Quechua1*	*35*	
98	Colombia.1(2/16)+Colombia.2(1/3)	3	Surrogate		*ChibchaPaez3*	*36*	
99	Costa.Rica.2(3/3)	3	Surrogate		*ChibchaPaez2*	*37*	
100	Costa.Rica.1(4/4)	4	Surrogate		*ChibchaPaez1*	*38*	
101	Colombia.5(4/4)	4	Surrogate		*ChibchaPaez5*	*39*	
102	Colombia.3(2/2)	2	Surrogate		*ChibchaPaez6*	*40*	
103	Colombia.4(4/4)	4	Removed	Removed as donor and recipient, because high drift			
104	Colombia.1(2/16)	2	Donor	Similar to **105**, drifted	Out.Colombia.1		
105	Colombia.1(11/16)	11	Surrogate, Merged with 106		*ChibchaPaez4*	*41*	
106	Colombia.1(1/16)+Colombia.2(2/3)	3	Surrogate, Merged with 105		*ChibchaPaez4*	*41*	
107	Peru.1(1/13)+Peru.4(2/16)	3	Surrogate		*AndesPiedmont*	*42*	
108	Argentina.2(2/2)+Chile.2(2/2)+Chile.3(1/65)	5	Surrogate		*Mapuche*	*43*	
109	Guatemala(5/5)+Mexico.9(2/2)	7	Surrogate		*Mayan*	*44*	
110	Brazil.1(1/3)	1	Removed	Single sample cluster, removed as donor and recipient, because high drift			
111	Brazil.1(2/3)	2	Removed	Removed as donor and recipient, because high drift			
112	Brazil.2(2/2)	2	Removed	Removed as donor and recipient, because high drift			

113	Paraguay(4/4)	4	Surrogate		*Amazon3*	*45*	
114	Colombia.7(3/3)	3	Removed	Removed as donor and recipient, because high drift			
115	Colombia.6(2/2)	2	Surrogate		*Amazon1*	*46*	
116	Peru.1(6/13)	6	Donor	Similar to **117**, no contrib	Out.Peru1	NA	
117	Peru.1(6/13)*	6	Surrogate		*Amazon2*	*47*	
118	Argenti-na.6(3/5)+Argentina.7(2/2)	5	Surrogate		*Chaco1*	*48*	
119	Argentina.6(2/5)	2	Donor	Similar to **118**, no contrib	Out.Argentina.6	NA	
120	Mexico.1(2/2)	2	Surrogate		*Pima*	*49*	
121	Mexi-co.10(8/22)+Mexico.2(2/20)	10	Surrogate		*Nahua1* Out.Mexico.10	*50*	1 ind excluded - inconsistent
122	Mexico.6(7/8)	7	Surrogate		*SouthMexico3*	*51*	
123	Mexico.8(6/8)	6	Surrogate		*SouthMexico2*	*52*	
124	Mexi-co.10(13/22)+Mexico.6(1/8)+Mexico.8(2/8)	16	Surrogate		*SouthMexico1*	*53*	
125	Mexi-co.10(1/22)+Mexico.2(18/20)	19	Surrogate		*Nahua2*	*54*	
126	Mexico.3(2/2)+Mexico.4(16/16)	18	Surrogate + Remove	Highly drifted population excluded (Mexico.4)	*Mixe* (Only Mexico.3)	*55*	
127	Argenti-na.3(1/13)+Argentina.5(3/3)	4	Surrogate (Merged)	Similar according to TVD and tree distance	*Chaco2*	*56*	
128	Argentina.3(5/13)	5					
129	Argenti-na.3(7/13)+Argentina.4(2/2)	9					

fS Clust: Cluster assigned by fineSTRUCTURE
Decision: Some reference samples were used only as "donors" for the subsequent ancestry inference. Others are also used as surrogates for the ancestral populations in SOURCEFIND analyses. Some were removed from the reference set.
Donor/Surrogate: This is the final grouping used for generating the "copying vectors" used for the sub-continental ancestry analyses. Groups in *italics* are the ones selected as surrogates as described in Supplementary Table 3.

Supplementary Table 3. Individuals from the 117 reference population samples included in the 56 clusters defined by fineSTRUCTURE.

n	Cluster label	Size	Individuals included (labels as in Supplementary Table 1)
1	EastAfrica1	10	Ethiopia(3/3), South.Sudan(7/8)
2	EastAfrica2	73	Kenya(73/73)
3	Namibia	6	Namibia.3(6/9)
4	SouthAfrica	18	South.Africa.3(18/19)
5	WestAfrica1	51	Gambia(51/111)
6	WestAfrica2	68	Sierra.Leone(68/69)
7	WestAfrica3	99	Nigeria.1(99/101)
8	EastMediterranean1	9	Jordan.1(7/15), Yemen(2/2)
9	EastMediterranean2	7	Jordan.1(1/15), Jordan.2(3/3), Palestine(3/3)
10	Sephardic3	7	Morocco.2(7/7)
11	Sephardic1	8	Libya.2(1/7), Turkey.1(7/7)
12	Sephardic2	12	Tunisia.2(6/6), Libya.2(6/7)
13	SouthMediterranean1	28	Tunisia.1(14/14), Libya.1(14/14)
14	SouthMediterranean2	11	Morocco.1(11/11)
15	CentralSouthSpain	48	Spain.2(1/14), Spain.4(13/15), Spain.5(3/4), Spain.6(4/8), Spain.7(4/7), Spain.9(9/12), Spain.10(3/6), Spain.11(5/8), Spain.12(5/14), Spain.14(1/7)
16	CentralNorthSpain	18	Spain.8(1/15), Spain.10(2/6), Spain.12(5/14), Spain.13(5/6), Spain.17(5/6)
17	Catalonia	29	Spain.7(3/7), Spain.12(2/14), Spain.13(1/6), Spain.14(6/7), Spain.15(10/10), Spain.16(7/8)
18	CanaryIslands	18	Spain.2(13/14), Spain.3(2/2), Spain.6(1/8), Spain.11(2/8)
19	Portugal/WestSpain	53	Portugal.1(18/18),Portugal.2(31/31), Spain.1(4/8)
20	Basque	24	Spain.18(14/14), Spain.19(8/8), France.1(2/2)
21	Italy1	19	Italy.5*(15/15), Italy.1(2/2), Bulgaria(2/2)
22	Italy2	31	Italy.3(31/106)
23	NorthWestEurope2	101	NW.Europe(68/91), UK.1(31/31), UK.2(1/29), UK.3(1/1)
24	NorthWestEurope1	31	Germany*(31/37)
25	NorthEastEurope1	2	Russia(2/2)
26	NorthEastEurope2	9	Finland(7/99), Estonia(2/2)
27	NorthEastEurope3	92	Finland (92/99)
28	China/Vietnam1	72	China.1(72/82)
29	China/Vietnam2	91	Vietnam(91/95)
30	ChinaHan	64	China.4(64/101)
31	Japan	103	Japan(103/104)
32	Quechua2	56	Chile.1(1/3), Bolivia.2(8/12), Chile.3*(47/65)
33	Aymara	16	Bolivia.1(8/12), Peru.4*(6/17), Peru.2(2/3)
34	Colla	10	Argentina.1(10/19)

35	Quechua1	9	Peru.4*(8/17), Peru.2(1/3)
36	ChibchaPaez3	3	Colombia.1(2/16), Colombia.2(1/3)
37	ChibchaPaez2	3	Costa.Rica.2(3/3)
38	ChibchaPaez1	4	Costa.Rica.1(4/4)
39	ChibchaPaez5	4	Colombia.5(4/4)
40	ChibchaPaez6	2	Colombia.3(2/2)
41	ChibchaPaez4	14	Colombia.1(12/16), Colombia.2(2/3)
42	AndesPiedmont	3	Peru.1(1/13), Peru.4*(2/17)
43	Mapuche	5	Chile.3*(1/65), Argentina.2(2/2), Chile.2(2/2)
44	Mayan	7	Mexico.9(2/2), Guatemala(5/5)
45	Amazon3	4	Paraguay(4/4)
46	Amazon1	2	Colombia.6(2/2)
47	Amazon2	6	Peru.1(6/13)
48	Chaco1	5	Argentina.6(3/5), Argentina.7(2/2)
49	Pima	2	Mexico.1(2/2)
50	Nahua1	9	Mexico.2(2/20), Mexico.10*(7/22)
51	SouthMexico3	7	Mexico.6(7/8)
52	SouthMexico2	6	Mexico.8(6/8)
53	SouthMexico1	16	Mexico.10*(13/22), Mexico.6(1/8), Mexico.8(2/8)
54	Nahua2	19	Mexico.2(18/20), Mexico.10*(1/22)
55	Mixe	2	Mexico.3(2/2)
56	Chaco2	18	Argentina.3(13/13), Argentina.4(2/2), Argentina.5(3/3)

n corresponds to the position (top to bottom) of a cluster in the tree of Supplementary Figure 3.

* Individuals from the CANDELA data that were considered reference samples (see methods). Italy.5: Brazilians of Italian descent, Germany: Brazilians of German descent, Chile.3: Native Americans in Chile, Mexico.10: Native Americans in Mexico, Peru.4: Native Americans in Peru.

Supplementary Table 4. Regression of Native American ancestry proportion on inferred admixture date.

(A)

Analysis	N_{ind}	Beta	se(Beta)	t-stat	p-value
all	3,340	-1.41	0.14	-10.4	< 1e-15
0.05 < *p* < 0.95	3,244	-1.56	0.13	-11.7	< 1e-15
0.1 < *p* < 0.9	3,049	-1.52	0.13	-12.1	< 1e-15
0.2 < *p* < 0.8	2,534	-1.21	0.11	-11.2	< 1e-15
Simulations (all)	1,297	-0.12	0.17	-1.04	0.30
Simulations, multiple events (all)	923	-0.11	0.03	-3.73	0.0002

(B)

Analysis	N_{ind}	Beta	se(Beta)	t-stat	p-value
all	3,274	-1.45	0.15	-9.7	< 1e-15
0.05 < *p* < 0.95	3,189	-1.62	0.14	-11.2	< 1e-15
0.1 < *p* < 0.9	3,000	-1.60	0.14	-11.8	< 1e-15
0.2 < *p* < 0.8	2,495	-1.29	0.12	-11.2	< 1e-15
Simulations (all)	1,083	-0.27	0.25	-1.1	0.28
Simulations, multiple events (all)	832	-0.10	0.04	-2.63	0.009

Inferred coefficients (Beta), standard errors (se(Beta)), t-statistics (t-stat) and p-values for a simple linear regression of total % Native American ancestry on inferred admixture date, for individuals inferred to have a single date of admixture between two sources best represented by European and Native American surrogates.
To test robustness, we restricted the regression to individuals (N_{ind}) whose inferred proportions *p* of Native and European ancestry *each* met the given criterion.
(A) All individuals. (B) Individuals inferred to have a single date of admixture between 5-17 generations ago.
"Simulations" and "Simulations, multiple events" refer to the simulations described in sections "Simulations with a single admixture event" and "Simulations with two sequential admixture events" of Supplementary Note 1 that consist of one and two separate admixture events, respectively.

Supplementary Table 5. Allele frequencies in the Central Andes and the Mapuche at index SNPs associated with facial features in the CANDELA sample.

				Allele frequency		N (haplotypes)		
Chromosomal Region	SNP	Gene region	Derived Allele	Central-Andes	Mapuche	Central-Andes	Mapuche	P-value
2q12	rs3827760	EDAR	G	0.961	0.995	879	595	2.18E-04
2q35	rs2395845	PAX3	A	0.388	0.683	896	635	6.09E-29
4q31	rs12644248	DCHS2	G	0.512	0.725	903	699	3.59E-17
6p21	rs1285029	SUPT3H/RUNX2	C	0.585	0.638	880	566	4.51E-02
7p13	rs17640804	GLI3	T	0.417	0.498	892	614	6.19E-03
20p11	rs927833	PAX1	C	0.700	0.503	888	616	7.41E-14

Supplementary Table 6. Proportion of inferred admixture events with given GLOBETROTTER conclusion, for all events inferred to have at least one admixing source group best-matched by the given reference group.

Source*	**n**	**One-date**	**One-date, multiway**	**Multiple-dates, recent**	**Multiple-dates, older**
Iberia	8167	0.4	0.09	0.24	0.26
INorthWest Europe & Italy	296	0.57	0.15	0.15	0.12
E.Mediterranean & Sephardic	99	0.41	0.04	0.25	0.29
Sub Saharan Africa	1704	0.02	0.28	0.52	0.18
East Asia	87	0.07	0.02	0.89	0.02
ALL SOURCES		3519	455+455**	2378	2378

*The sources have been defined according to those of the 56 clusters that were often inferred as sources by Globetrotter and grouped to represent different historical/demographic processes. Iberia includes: CanaryIslands, Portugal/WestSpain, CentralSouthSpain, CentralNorthSpain, Basque and Catalonia. NorthWestEurope & Italy includes: Italy1 and NorthWestEurope1. E.Mediterranean & Sephardic includes Sephardic1, EastMediterranean1 and EastMediterranean2), Sub Saharan Africa includes WestAfrica1, WestAfrica3, EastAfrica1, EastAfrica2, Namibia and SouthAfrica). East Asia includes Japan, ChinaHan, China/Vietnam1 and China/Vietnam2.
** The two events inferred in this scenario are simultaneous.

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