LETTER

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An early modern human from Romania with a recent Neanderthal ancestor

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Neanderthals are thought to have disappeared in Europe approximately 39,000–41,000 years ago but they have contributed 1–3% of the DNA of present-day people in Eurasia[1]. Here we analyse DNA from a 37,000–42,000-year-old[2] modern human from Peştera cu Oase, Romania. Although the specimen contains small amounts of human DNA, we use an enrichment strategy to isolate sites that are informative about its relationship to Neanderthals and present-day humans. We find that on the order of 6–9% of the genome of the Oase individual is derived from Neanderthals, more than any other modern human sequenced to date. Three chromosomal segments of Neanderthal ancestry are over 50 centimorgans in size, indicating that this individual had a Neanderthal ancestor as recently as four to six generations back. However, the Oase individual does not share more alleles with later Europeans than with East Asians, suggesting that the Oase population did not contribute substantially to later humans in Europe.

Between 45,000 and 35,000 years ago, anatomically modern humans spread across Europe, while the Neanderthals, present since before 300,000 years ago, disappeared. How this process occurred has long been debated[1,3–5]. Comparisons between the Neanderthal genome and the genomes of present-day humans have shown that Neanderthals contributed approximately 1–3% of the genomes of all people living today outside sub-Saharan Africa[6,7] suggesting that human populations ancestral to all non-Africans mixed with Neanderthals. The size of segments of Neanderthal ancestry in present-day humans suggests that this occurred between 37,000 and 86,000 years ago[8]. However, where and how often this occurred is not understood. For example, Neanderthals share more alleles with East Asians and Native Americans than with Europeans, which may reflect additional interbreeding in the ancestors of eastern non-Africans[9–12]. Surprisingly, analyses of present-day genomes have not yielded any evidence that Neanderthals mixed with modern humans in Europe, despite the fact that Neanderthals were numerous there and cultural interactions between the two groups have been proposed[13,14].

More direct insight into the interactions between modern and archaic humans can be obtained by studying genomes from modern humans who lived at a time when they could have met Neanderthals. Recent analyses of genomes from a ~43,000–47,000-year-old modern human from western Siberia[15] and a ~36,000–39,000-year-old modern human from eastern Europe[16] showed that Neanderthal gene flow into modern humans occurred before these individuals lived. The Siberian individual's genome contained some segments of Neanderthal ancestry as large as 6 million base pairs (bp), suggesting that some Neanderthal gene flow could have occurred a few thousand years before his death[15].

We report genome-wide data from a modern human mandible, Oase 1, found in 2002 in the Peştera cu Oase, Romania. The age of this specimen has been estimated to be ~37,000–42,000 years by direct radiocarbon dating[2,17,18]. Oase 1 is therefore one of the earliest modern humans in Europe. Its morphology is generally modern but some aspects are consistent with Neanderthal ancestry[19–21]. Subsequent excavations uncovered a cranium from another, probably contemporaneous individual, Oase 2, which also carries morphological traits that could reflect admixture with Neanderthals[17,19].

We prepared two DNA extracts from 25 mg and 10 mg of bone powder removed from the inferior right ramus of Oase 1. We treated an aliquot of each of these extracts with *Escherichia coli* uracil-DNA glycosylase (UDG), an enzyme that removes uracils from the interior parts of DNA molecules, but leaves a proportion of uracils at the ends of the molecules unaffected. Uracil residues occur in DNA molecules as a result of deamination of cytosine residues, and are particularly prevalent at the ends of ancient DNA molecules[9,22]. Among the DNA fragments sequenced from these two extracts, 0.18% and 0.06%, respectively, could be mapped to the human reference genome. We prepared three additional DNA libraries from the extract containing 0.18% human-like molecules, but omitted the UDG treatment to increase the number of molecules in which terminal C-to-T substitutions could be seen and used to identify putatively ancient fragments. Because the fraction of endogenous DNA is so small, we used hybridization to DNA probes to isolate human DNA fragments from the libraries[23]. Applying this strategy to the mitochondrial genome allowed the mitochondrial (mt)DNA from the five libraries to be sequenced to an average coverage of 803-fold (Supplementary Note 1). At the 3′ ends of the DNA fragments, cytosine residues appeared as thymine residues relative to the human mtDNA reference in 21% of fragments, reflecting appreciable levels of cytosine deamination. This suggests that at least some of the human mtDNA is of ancient origin. We determined mtDNA consensus sequences in two ways: using all mtDNA fragments, and using only deaminated fragments that carry C-to-T substitutions at either end relative to the consensus mtDNA sequence based on these fragments, an approach known to enrich for endogenous DNA[9,24–26]. The mtDNA sequence based on all fragments clusters with present-day Europeans (Extended Data Fig. 1) (Supplementary Note 1). In contrast, the mtDNA sequence based on deaminated fragments is related to a large group of present-day Eurasian mtDNAs (haplogroup N) but diverges from these before they diverged from each other. This Oase 1 mtDNA carries a few private mutations on the basis of which its age can be estimated to be 36,330 years before present (14,520–56,450; 95% confidence interval). Using six positions at which the mtDNA sequence differs from at least 99% of 311 present-day humans, we estimate the contamination

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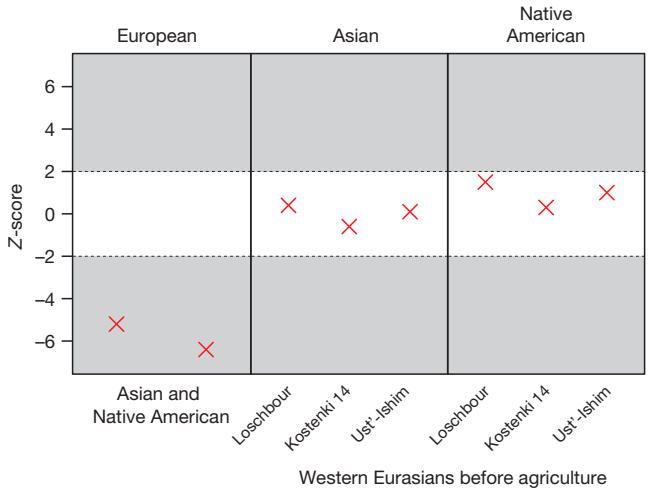

Figure 1 | Allele sharing between the Oase 1 individual and other genomes. Each point indicates the extent to which the Oase 1 genome shares alleles with one or other of a pair of genomes from different populations indicated above and below (see Extended Data Table 1 for numbers). *Z*-scores with an absolute value greater than 2 indicate an excess of allele sharing (grey).

among all mtDNA fragments to be 67% (95% confidence interval 65–69%). When we restrict to mtDNA fragments that carry terminal C-to-T substitutions, the contamination estimate is 4% (95% confidence interval of 2–9%) (Supplementary Note 1).

To isolate nuclear DNA from Oase 1, we used three sets of oligonucleotide probes that cover about two million sites that are single nucleotide polymorphisms (SNPs) in present-day humans and captured DNA molecules from the five libraries. Of the SNPs targeted, 51% (n = 1,038,619) were covered by at least one DNA fragment, and 13% (n = 271,326) were covered by at least one fragment with a terminal C-to-T substitution. To estimate nuclear DNA contamination, we tested whether Oase 1 DNA fragments with or without evidence of deamination share more alleles with present-day Europeans or with East Asians. We found that Europeans share significantly fewer alleles with Oase 1 fragments that are deaminated than with Oase 1 fragments that are not, consistent with European contamination of 17–30% (Supplementary Note 1). On the basis of these findings and those from mtDNA, we restricted all subsequent analyses to DNA fragments that carry terminal C-to-T substitutions. After doing this, we found that we captured targeted SNPs from the X and Y chromosomes at a similar rate, indicating that Oase 1 carried both an X and a Y chromosome and thus that he was male. The Y chromosome alleles belong to the F haplogroup, which is carried by most males in Eurasia today (Supplementary Note 2).

To determine the relationship of the Oase 1 individual to present-day populations, we first tested whether he shared more alleles with particular present-day individuals from different populations using *D*-statistics, which provides a robust estimate of admixture almost regardless of how SNPs for analysis are chosen[27]. We find that Oase 1 shared more alleles with present-day East Asians and Native Americans than with present-day Europeans, counter to what might naively be expected for an ancient individual from Europe (Fig. 1) ($5.2 \leq |Z| \leq 6.4$; Extended Data Table 1). However, it has been suggested that Europeans after the introduction of agriculture derive a part of their ancestry from a 'basal Eurasian' population that separated from the initial settlers of Europe and Asia before they split from each other[28]. Therefore, we replaced present-day Europeans with Palaeolithic and Mesolithic European individuals in these analyses. We then find that the Oase 1 individual shares equally many alleles with these early Europeans as with present-day East Asians and Native Americans (Fig. 1) ($|Z| \leq 1.5$ in Extended Data Table 1). Restricting this analysis to transversion polymorphisms, which are not susceptible to errors induced by cytosine deamination, does not influence this result (Extended Data Table 2 and Supplementary Note 3). This suggests that the Oase 1 individual belonged to a population that did not contribute much, or not at all, to later Europeans. This contrasts, for example, with the ~36,000–39,000-year-old Kostenki 14 individual from western Russia, who was more closely related to later Europeans than to East Asians ($1.9 \leq |Z| \leq 13.7$; Extended Data Table 1)[16].

To assess whether the ancestors of the Oase 1 individual mixed with Neanderthals, we tested whether the Altai Neanderthal genome shares more alleles with the Oase 1 genome than with sub-Saharan Africans. We find this to be the case ($|Z| = 7.7$; Supplementary Note 4). We then asked whether the amount of Neanderthal ancestry in the Oase 1 genome is similar to that in present-day non-Africans. Surprisingly, the Neanderthal genome shares more alleles with the Oase 1 individual than it does with any present-day people in Eurasia that we tested, indicating that he carries more Neanderthal-like DNA than present-day people ($5.0 \leq |Z| \leq 8.2$; Extended Data Table 3). We also observe more Neanderthal-like alleles in the Oase 1 individual when we compare him to four early modern humans: an 8,000-year-old individual from Luxembourg, and three individuals from Russia who vary in age between 24,000 and 45,000 years ($3.6 \leq |Z| \leq 6.8$; Extended Data Table 3). Thus, the Oase 1 individual appears to have carried more Neanderthal-like DNA than any other modern human analysed to date. This observation cannot be explained by residual present-day human contamination among the DNA fragments that carry terminal C-to-T substitutions, because all modern humans studied to date carry less Neanderthal ancestry than the Oase 1 genome, and thus contamination would lower, rather than increase, the apparent Neanderthal ancestry.

We estimated the proportion of Neanderthal DNA in the Oase 1 genome using three different statistics[7,29] (Supplementary Note 4). Although the results differ, they all yield point estimates between 6.0% and 9.4% (Table 1). For one of the statistics, none of the 90% confidence intervals for Neanderthal ancestry in the other modern

Table 1 | Estimated fraction of the Oase 1 genome that derives from Neanderthals

	Statistic 1 $\frac{f_4(\text{Denisova, Altai; Mbuti, X})}{f_4(\text{Denisova, Altai; Mbuti, Mezmaiskaya})}$			Statistic 2 $1-\frac{f_4(\text{Mbuti, Chimp; X, Denisova})}{f_4(\text{Mbuti, Chimp; Dinka, Denisova})}$			Statistic 3 $\frac{f_4(\text{X, Mbuti; Denisova, Chimp})}{f_4(\text{Altai, Mbuti; Denisova, Chimp})}$		
Sample	Proportion	s.e.m.	90% CI	Proportion	s.e.m.	90% CI	Proportion	s.e.m.	90% CI
Oase 1	8.1%	2.0%	4.8–11.3%	9.4%	1.1%	7.5–11.3%	6.0%	2.0%	2.8–9.3%
Ust'-Ishim	3.6%	0.9%	2.2–5.0%	5.5%	0.7%	4.3–6.6%	0.4%	1.2%	0.0–2.5%
Kostenki 14	3.8%	1.0%	2.1–5.5%	2.9%	0.8%	1.6–4.2%	1.7%	1.3%	0.0–3.9%
MA1	1.2%	1.1%	0.0–3.0%	3.5%	0.8%	2.2–4.8%	2.3%	1.3%	0.1–4.5%
Loschbour	1.3%	0.9%	0.0–2.8%	3.9%	0.7%	2.7–5.1%	0.5%	1.2%	0.0–2.6%
La Braña	3.1%	1.0%	1.4–4.7%	1.9%	0.7%	0.7–3.1%	1.4%	1.2%	0.0–3.4%
Stuttgart	3.0%	0.9%	1.5–4.4%	2.5%	0.7%	1.3–3.7%	0.4%	1.2%	0.0–2.4%
Han	2.2%	0.9%	0.6–3.7%	2.2%	0.8%	1.0–3.5%	1.0%	1.2%	0.0–3.1%
Dai	2.6%	0.9%	1.1–4.0%	1.0%	0.8%	0.0–2.3%	0.7%	1.2%	0.0–2.6%
French	3.0%	0.9%	1.6–4.5%	3.0%	0.7%	1.8–4.2%	0.2%	1.2%	0.0–2.2%

CI, confidence interval; s.e.m., standard error of the mean; negative values are truncated to 0%.

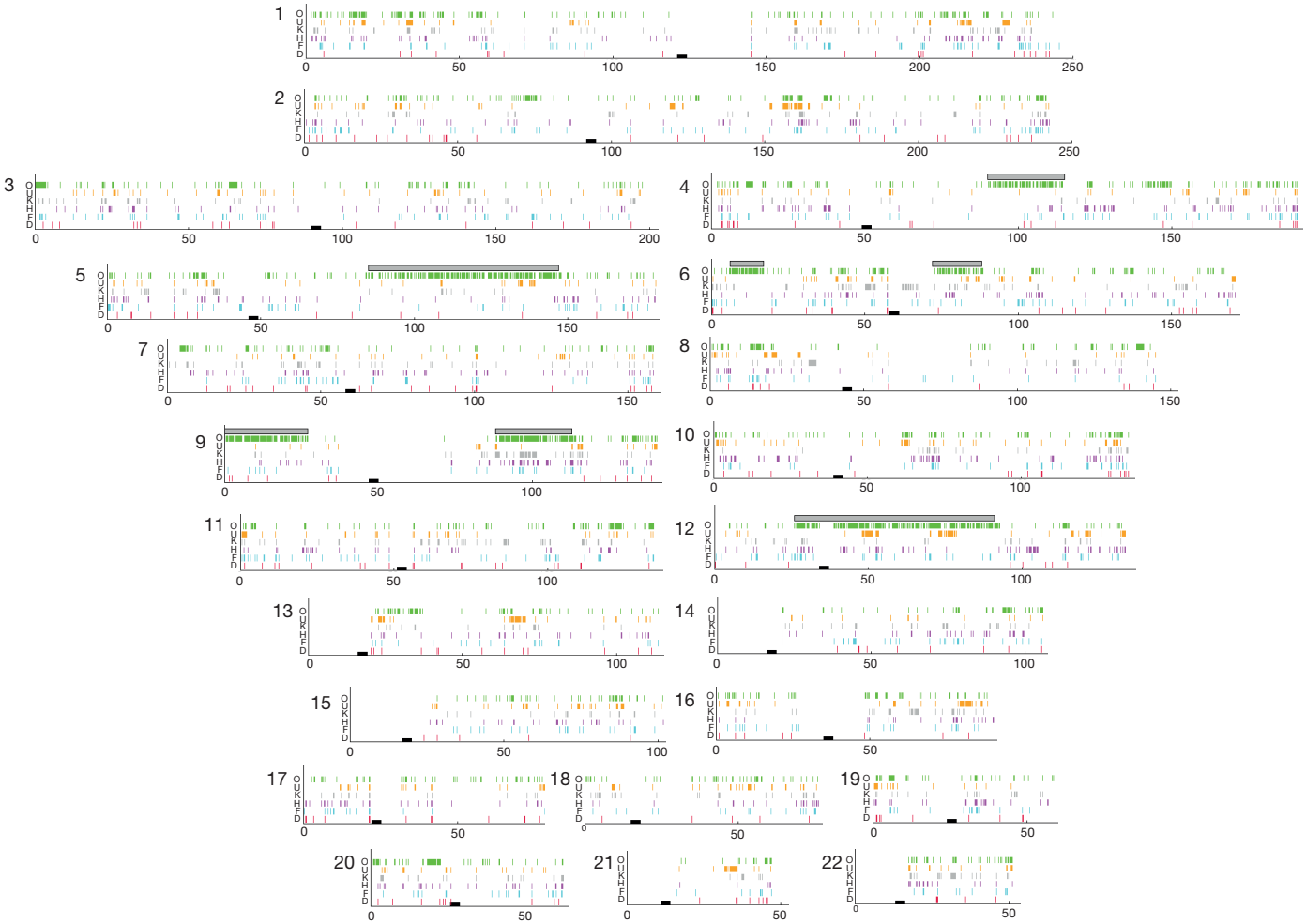

Figure 2 | Spatial distribution of alleles matching Neanderthals in modern humans. Coloured vertical lines indicate alleles shared with Neanderthals and no colour indicates alleles shared with the great majority of West Africans. D, Dinka; F, French; H, Han; K, Kostenki 14; O, Oase 1; U, Ust'-Ishim. The seven grey bars indicate segments of putative recent Neanderthal ancestry. This analysis is based on 78,055 sites. Numbers refer to chromosomes.

human samples overlap with the confidence interval in Oase 1. When we restrict analysis to transversion SNPs, the point estimates of Neanderthal ancestry are even higher (range of 8.4% to 11.3%) (Extended Data Table 4).

To study the spatial distribution of Neanderthal DNA across the Oase 1 genome, we designed capture probes for around 1.7 million nucleotide positions at which nearly all individuals in a sub-Saharan African population carry one allele whereas Neanderthal genomes carry a different allele. We used these probes to isolate DNA fragments from the Oase 1 individual. A total of 78,055 sites were covered by deaminated DNA fragments from the Oase 1 individual and were also covered by DNA fragments sequenced from the ~36,000–39,000-year-old Kostenki 14 individual from western Russia[16], the ~43,000–47,000-year-old individual from Ust'-Ishim in Siberia[15], and three present-day human genomes from China, France and Sudan (Supplementary Note 5). Because the Dinka from Sudan are thought to have little or no Neanderthal ancestry[7], we subtracted the number of alleles that match the Neanderthals in the Dinka individual (485) from the number in the other genomes to estimate the number of alleles attributable to Neanderthal ancestry. The resulting numbers of putative Neanderthal alleles are 3,746 in the Oase 1 individual, 1,586 and 1,121 in the Ust'-Ishim and Kostenki 14 individuals, respectively, and 1,322 and 1,033 in the Chinese and the European individuals (Extended Data Table 5). Thus, the Neanderthal contribution to the Oase 1 genome appears to be between 2.3- and 3.6-fold larger than to the other genomes analysed. Assuming that the Neanderthal contribution to the European individual is 2% (ref. 7), this suggests that 7.3% of the Oase 1 genome is of Neanderthal origin. When the numbers of alleles matching the Neanderthal genome are compared per chromosome (Extended Data Table 5), the highest numbers are always observed for the Oase 1 genome, except in the case of chromosome 21, in which the Ust'-Ishim individual carries a large segment of likely Neanderthal ancestry.

We plotted the positions of Neanderthal-like alleles across the Oase 1 genome (Fig. 2). We detect three segments that are over 50 centimorgans (cM) in size, suggesting that the Neanderthal contribution to the Oase 1 individual occurred so recently in his family tree that chromosomal segments of Neanderthal origin had little time to break up due to recombination. To estimate the date of the most recent Neanderthal contribution to the Oase 1 genome, we studied the size spans of seven segments of the genome that appeared to be recently derived from Neanderthals. Their genetic lengths suggest that the Oase 1 individual had a Neanderthal ancestor as a fourth-, fifth- or sixth-degree relative (Supplementary Note 5). This would predict that an average of 1.6% to 6.3% of the Oase 1 genome derived from this recent Neanderthal ancestor. Visual inspection of the Oase 1 genome suggests that in addition to these seven segments, other smaller segments also carry Neanderthal-like alleles (Fig. 2). When we remove the seven longest segments, the estimate of Neanderthal ancestry in Oase 1 drops from 7.3% to 4.8%, which is still around twice the 2.0–2.9% estimated for the French, Han, Kostenki and Ust'-Ishim individuals in this remaining part of the genome. This additional Neanderthal ancestry

could reflect an older Neanderthal admixture into the ancestors of Oase 1, or that we failed to find all segments of recent Neanderthal ancestry.

The Oase 1 genome shows that mixture between modern humans and Neanderthals was not limited to the first ancestors of present-day people to leave Africa, or to people in the Near East; it occurred later as well and probably in Europe. The fact that the Oase 1 individual had a Neanderthal ancestor removed by only four to six generations allows this Neanderthal admixture to be dated to less than 200 years before the time he lived. However, the absence of a clear relationship of the Oase 1 individual to later modern humans in Europe suggests that he may have been a member of an initial early modern human population that interbred with Neanderthals but did not contribute much to later European populations. To better understand the interactions between early modern and Neanderthal populations, it will be important to study other specimens that, like Oase 1, have been suggested to carry morphological traits suggestive of admixture with Neanderthals[30].

Online Content Methods, along with any additional Extended Data display items and Source Data, are available in the online version of the paper; references unique to these sections appear only in the online paper.

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Supplementary Information is available in the online version of the paper.

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Author Contributions N.P., K.P., M.M., J.K., D.R. and S.P. supervised the study. S.C. and O.T.M. collected and analysed archaeological material. Q.F., M.H. and B.N. performed laboratory work. Q.F., M.H., S.M., P.S., N.P., N.R., I.L., B.V., K.P., J.K. and D.R. analysed data. Q.F., S.M., M.M. and D.R. designed capture probes. D.R. and S.P. wrote the manuscript with the help of all co-authors.

Author Information The aligned sequences have been deposited in the European Nucleotide Archive under accession number PRJEB8987. Reprints and permissions information is available at www.nature.com/reprints. The authors declare no competing financial interests. Readers are welcome to comment on the online version of the paper. Correspondence and requests for materials should be addressed to D.R. (reich@genetics.med.harvard.edu) or S.P. (paabo@eva.mpg.de).

METHODS

DNA extraction and library preparation. We used a dentistry drill to remove two samples of bone powder from an area where a larger sample had previously been removed for carbon dating[2]. We prepared two extracts (E1406, E1843) from 25 mg and 10 mg of bone powder, respectively, as described[31]. We produced five libraries from the two extracts using a single-stranded library protocol[9,32] (Extended Data Table 6). We treated one library from each extract (A5227, A5252) with *E. coli* uracil-DNA glycosylase (UDG) and endonuclease VIII to remove deaminated cytosine residues from the interior parts of molecules[33]. We amplified all libraries by PCR for 35 cycles using AccuPrime Pfx DNA polymerase (Life Technologies)[34] and primers carrying library-specific indexes[35]. We determined library concentrations using a NanoDrop 2000 spectrophotometer.

Sequencing and DNA capture. We shotgun sequenced the UDG-treated libraries A5252 and A5227 and found that they contained 0.06% and 0.18% human DNA, respectively. We used hybridization to oligonucleotide probes to enrich the libraries for subsets of the nuclear genome containing panels of known SNPs as described[23], except that each SNP was targeted by four 52-nucleotide probes: two immediately flanking the SNP on both sides, and two centred on the SNP containing one or the other alternate allele, respectively. We used four panels of probes.

Panel 1 "390k": 394,577 SNPs, about 90% of which are on the Affymetrix Human Origins array[27]. See ref. 36 for SNPs and probes.

Panel 2 "840k": 842,630 SNPs constituting the rest of the SNPs on the Human Origins array, all SNPs on the Illumina 610-Quad array, all SNPs on the Affymetrix 50k array, and smaller numbers of SNPs chosen for other purposes. See Supplementary Data 1.

Panel 3 "1000k": 997,780 SNPs comprising all transversion polymorphisms seen in two Yoruba males from Nigeria sequenced to high coverage and transversion polymorphisms seen in the Altai Neanderthal genome. The design was restricted to SNPs that passed strict quality filters in the Neanderthal genome (Map35_99%)[7], and had chimpanzee alleles available. Probes were designed from chimpanzee flanking sequences. See Supplementary Data 2.

Panel 4 "Archaic": This panel contains SNPs where the West-African Yoruba population carry a high frequency of one allele while at least one archaic individual carries an alternative allele. To determine Yoruba allele frequencies, we examined data from all Yoruba individuals from the 1000 Genomes Project[37] covered by at least three sequences passing filters. At these sites we called majority alleles (drawing a random allele in the case of equal numbers of reads supporting both alleles). We furthermore restricted the analysis to sites at which ≥24 Yoruba individuals as well as the Altai Neanderthal and Denisovan genomes had allele calls (Map35_50% filter[7]). We then selected sites at which at most one alternative allele is seen among the Yoruba while at least one of four archaic genomes (Denisovan; Altai, Vindija and Mezmaiskaya Neanderthals) carry the alternative allele. Ancestral states were taken from the inferred ancestor of humans and chimpanzees (Ensembl Compara v.64)[38,39]. We used the following classes of sites. Class 1: 297,894 SNPs where Yoruba is derived and at least one ancestral allele is seen in the Altai, Vindija, Mezmaiskaya or Denisova genomes. Class 2: sites where Yoruba alleles are all or nearly all ancestral and derived alleles are seen in archaic genomes. Since such derived alleles often arise due to errors in an archaic genome, we restricted this class to the following three cases: (1) 1,321,774 SNPs where the high-coverage Altai Neandertal and/or Denisova genomes are homozygous derived; (2) 523,041 SNPs where the Altai and/or Denisova genomes are heterozygous but are not C-to-T or G-to-A substitutions relative to the ancestral allele; and (3) 30,735 SNPs that are homozygous ancestral in Altai and/or Denisova and at least one copy of the derived allele is observed in the Mezmaiskaya or Vindija Neanderthal genomes, and the derived allele represents a transversion that is also seen in the Simons Genome Diversity Panel (https://www.simonsfoundation.org/life-sciences/simons-genome-diversity-project/). After eliminating SNPs where capture probes covered ambiguous bases in the human (hg19) and chimpanzee (pantro2) genomes or overlapped for less than 35 nucleotides with mapable regions (Map35_50%)[7], this left us with a set of 1,749,385 SNPs (see Supplementary Data 3).

Sequencing of capture products and data processing. We sequenced capture products using 2 × 75 bp reads on an Illumina HiSeq2500 or an Illumina NextSeq500. We de-multiplexed the reads allowing one mismatch in each of the two indices (Extended Data Table 6), and merged paired reads into sequenced fragments requiring an overlap of at least 15 bp (allowing one mismatch) using a modified form of SeqPrep (https://github.com/jstjohn/SeqPrep). We used the bases with the higher quality (and score) to represent the overlap region. After removing adapters, we mapped merged fragments to hg19 using BWA (v.0.6.1) using the 'samse' command. We identified duplicated fragments on the basis of sharing the same orientation and end positions, in which case we kept the fragment with the highest quality (Extended Data Table 7).

To focus on putatively deaminated fragments we used fragments with C-to-T substitutions relative to the hg19 human genome reference sequence in the first 5′ or last two 3′ bases for the UDG-treated libraries, and to fragments with C-to-T substitutions relative to hg19 in the terminal three bases at either end of fragments from non-UDG-treated libraries (Supplementary Note 1 and Extended Data Table 8).

Merging the Oase 1 data with genome sequences. At each SNP covered at least once in Oase 1, we selected the majority allele (in case of a tie, we picked a random allele). We then merged the Oase 1 data with 25 genomes of present-day humans sequenced to 24–42× coverage[7]: the Altai Neanderthal[7], the Siberian Denisovan[9], a ~45,000-year-old modern human from Ust'-Ishim in Siberia[15], an ~8,000-year-old Mesolithic individual from Loschbour Cave, Luxembourg[28], and a ~7,000-year-old early farmer from Stuttgart, Germany[28] (Extended Data Table 9). All the genotype calls for the five deeply sequenced ancient genomes were performed in the same way. We restricted analyses to sites with a minimum root-mean-square mapping quality (MAPQ) of 30 in the 30 genomes. We added lower coverage shotgun data from the ~36,000-year-old Kostenki 14 from Russia[16], the ~24,000-year-old Mal'ta Siberian individual from Russia[40], an 8,000-year-old Mesolithic individual from La Braña Cave, Spain[41], a Neanderthal from Mezmaiskaya in Russia[7], and a pool of three Neanderthals from Vindija Cave in Croatia[6]. For these samples, we restricted to fragments with a map quality of MAPQ ≥ 37 to match the filter for the low-coverage Oase 1 data (Extended Data Table 9).

Population genetic analyses. To determine the relationship of Oase 1 to other modern humans, we used *D*-statistics to evaluate whether sets of four tested samples are consistent with being related to one another according to an unrooted tree[27] (Supplementary Note 3). We used *D*-statistics and f_4-statistic ratios[27] to test both whether there is excess archaic ancestry in Oase 1 compared with other modern humans, and to estimate proportions of Neanderthal ancestry[27] (Supplementary Note 4). We studied the genomic distribution of alleles that are likely to derive from Neanderthals in the sense of being shared with Neanderthal but either absent or at very low frequency in West Africans. We used the spatial distribution of these sites to identify stretches of likely Neanderthal ancestry in several individuals including Oase 1. We also used these data to estimate the number of generations since the most recent Neanderthal ancestor of Oase 1 (Supplementary Note 5).

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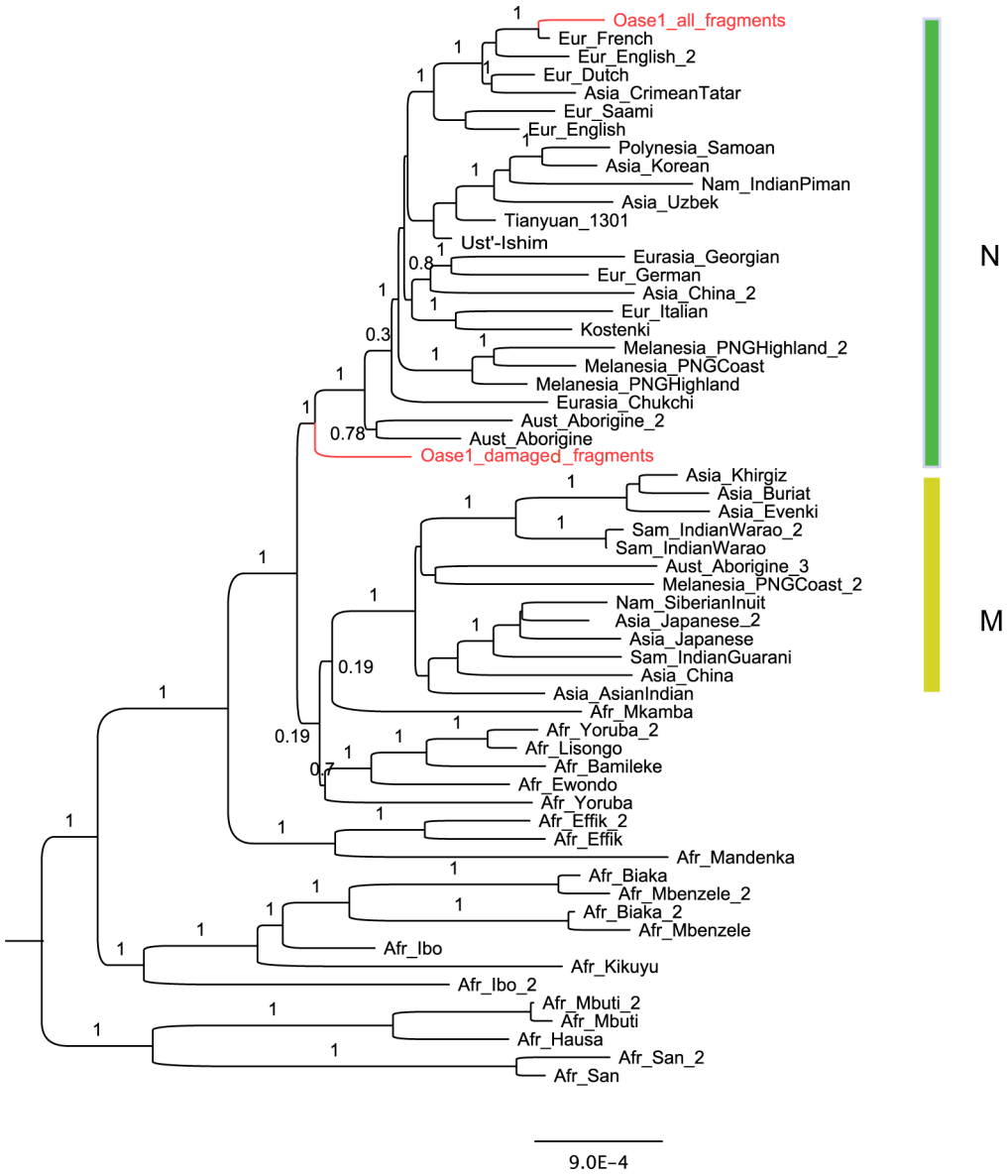

Extended Data Figure 1 | Mitochondrial DNA tree for Oase 1 and other modern humans. The consensus sequences for all Oase 1 fragments and for deaminated fragments are shown. The tree is rooted with a Neanderthal mtDNA (Vindija33.25).

Extended Data Table 1 | Allele sharing between early modern humans and other humans

		Oase 1		Ust'-Ishim		Kostenki 14	
Non-African$_1$	*Non-African$_2$*	D	Z	D	Z	D	Z
Oase 1	Ust'-Ishim					-0.0033	-3.8
Oase 1	Kostenki 14			-0.0037	-4.1		
Oase 1	MA1			-0.0032	-3.5	-0.0092	-9.8
Oase 1	Loschbour			-0.0032	-3.9	-0.0101	-12.2
Oase 1	East Asian			-0.0027	-3.8	-0.0011	-1.6
Oase 1	Native American			-0.0030	-4.1	-0.0039	-5.5
Ust'-Ishim	Kostenki 14	-0.0005	-0.6				
Ust'-Ishim	MA1	-0.0007	-0.8			-0.0059	-6.4
Ust'-Ishim	Loschbour	0.0002	0.3			-0.0068	-8.5
Ust'-Ishim	East Asian	0.0000	-0.1			0.0022	3.3
Ust'-Ishim	Native American	-0.0007	-1.0			-0.0006	-0.8
Kostenki 14	MA1	-0.0004	-0.6	0.0003	0.4		
Kostenki 14	Loschbour	0.0007	1.0	0.0006	0.8		
Kostenki 14	East Asian	0.0004	0.6	0.0011	1.6		
Kostenki 14	Native American	-0.0002	-0.3	0.0008	1.1		
MA1	Loschbour	0.0012	1.7	0.0005	0.7	-0.0012	-1.5
MA1	East Asian	0.0008	1.2	0.0007	1.1	0.0079	10.6
MA1	Native American	0.0001	0.1	0.0004	0.6	0.0051	7.0
Loschbour	East Asian	-0.0002	-0.4	0.0005	0.9	0.0090	13.7
Loschbour	Native American	-0.0009	-1.5	0.0002	0.3	0.0062	9.0
East Asian	Native American	-0.0006	-1.6	-0.0003	-0.8	-0.0028	-6.6
European	Oase 1			0.0004	0.6	0.0049	7.3
European	Ust'-Ishim	-0.0023	-3.5			0.0016	2.4
European	Kostenki 14	-0.0028	-4.7	-0.0033	-5.1		
European	MA1	-0.0033	-5.4	-0.0031	-5.1	-0.0041	-6.0
European	Loschbour	-0.0021	-4.5	-0.0027	-5.7	-0.0052	-9.1
European	East Asian	-0.0024	-5.2	-0.0022	-5.3	0.0039	9.2
European	Native American	-0.0030	-6.4	-0.0025	-5.9	0.0010	2.2
European	Stuttgart	-0.0007	-1.5	-0.0001	-0.2	-0.0002	-0.3
Stuttgart	Oase 1			0.0005	0.6	0.0051	6.7
Stuttgart	Ust'-Ishim	-0.0017	-2.3			0.0018	2.3
Stuttgart	Kostenki 14	-0.0021	-3.2	-0.0032	-4.6		
Stuttgart	MA1	-0.0027	-3.9	-0.0029	-4.2	-0.0041	-5.0
Stuttgart	Loschbour	-0.0015	-2.4	-0.0027	-4.6	-0.0050	-7.5
Stuttgart	East Asian	-0.0017	-2.9	-0.0022	-3.8	0.0040	6.8
Stuttgart	Native American	-0.0024	-3.9	-0.0025	-4.4	0.0012	1.9

We compute *D*(Non-African$_1$, Non-African$_2$; Early Modern Human, African) to test whether an early modern human (Oase 1, Ust'-Ishim, or Kostenki 14) shares more alleles with Non-African$_1$ (in which case the statistic is positive) or Non-African$_2$ (negative). We use a pool of six sub-Saharan African genomes (2 Mbuti, 2 Yoruba, 2 Dinka) as an outgroup; a pool of four genomes (2 French, 2 Sardinians) to represent Europeans; a pool of four genomes (2 Han, 2 Dai) to represent East Asians; and a pool of three genomes (2 Karitiana, 1 Mixe) to represent Native Americans. Results are based on 242,122 transition and transversion SNPs covered by at least one deaminated fragment in Oase 1, and covered in all other samples, although not necessarily MA1. For analyses involving MA1, a subset of 176,569 transversion SNPs was analysed.

Extended Data Table 2 | Allele sharing between early modern humans and other humans (transversions only)

		Oase 1		Ust'-Ishim		Kostenki 14	
Non-African$_1$	*Non-African$_2$*	D	Z	D	Z	D	Z
Oase 1	Ust'-Ishim					-0.0019	-2.1
Oase 1	Kostenki 14			-0.0031	-3.3		
Oase 1	MA1			-0.0026	-2.9	-0.0071	-6.5
Oase 1	Loschbour			-0.0023	-2.6	-0.0081	-8.8
Oase 1	East Asian			-0.0013	-1.9	0.0007	1.0
Oase 1	Native American			-0.0019	-2.7	-0.0018	-2.3
Ust'-Ishim	Kostenki 14	-0.0012	-1.4				
Ust'-Ishim	MA1	-0.0006	-0.7			-0.0050	-5.1
Ust'-Ishim	Loschbour	0.0003	0.4			-0.0062	-7.1
Ust'-Ishim	East Asian	0.0005	0.7			0.0026	3.8
Ust'-Ishim	Native American	-0.0003	-0.4			0.0001	0.1
Kostenki 14	MA1	0.0001	0.1	0.0002	0.3		
Kostenki 14	Loschbour	0.0015	2.0	0.0008	1.1		
Kostenki 14	East Asian	0.0017	2.3	0.0017	2.5		
Kostenki 14	Native American	0.0009	1.2	0.0012	1.6		
MA1	Loschbour	0.0019	2.2	0.0010	1.3	-0.0013	-1.3
MA1	East Asian	0.0011	1.4	0.0013	1.9	0.0075	8.5
MA1	Native American	0.0006	0.7	0.0007	1.1	0.0051	6.0
Loschbour	East Asian	0.0001	0.2	0.0009	1.5	0.0088	12.3
Loschbour	Native American	-0.0006	-0.9	0.0004	0.6	0.0063	8.4
East Asian	Native American	-0.0008	-1.7	-0.0006	-1.3	-0.0025	-5.3
European	Oase 1			-0.0005	-0.7	0.0029	3.9
European	Ust'-Ishim	-0.0023	-3.3			0.0010	1.4
European	Kostenki 14	-0.0035	-5.1	-0.0035	-5.2		
European	MA1	-0.0033	-4.5	-0.0033	-5.2	-0.0038	-4.8
European	Loschbour	-0.0020	-3.6	-0.0027	-5.1	-0.0052	-8.4
European	East Asian	-0.0018	-3.6	-0.0018	-4.0	0.0036	7.8
European	Native American	-0.0026	-4.8	-0.0023	-5.2	0.0011	2.1
European	Stuttgart	-0.0009	-1.7	-0.0010	-2.2	-0.0012	-2.3
Stuttgart	Oase 1			0.0005	0.7	0.0041	4.7
Stuttgart	Ust'-Ishim	-0.0014	-1.8			0.0022	2.6
Stuttgart	Kostenki 14	-0.0026	-3.3	-0.0025	-3.5		
Stuttgart	MA1	-0.0026	-3.1	-0.0023	-3.2	-0.0031	-3.4
Stuttgart	Loschbour	-0.0011	-1.6	-0.0017	-2.8	-0.0040	-5.2
Stuttgart	East Asian	-0.0010	-1.4	-0.0008	-1.3	0.0048	7.2
Stuttgart	Native American	-0.0017	-2.4	-0.0013	-2.2	0.0023	3.4

We compute *D*(Non-African$_1$, Non-African$_2$; Early Modern Human, African), to test whether an early modern human (Oase 1, Ust'-Ishim or Kostenki 14) shares more alleles with Non-African$_1$ (in which case the statistic is positive) or Non-African$_2$ (negative). We use a pool of six sub-Saharan African genomes (2 Mbuti, 2 Yoruba, 2 Dinka) as an outgroup; a pool of four genomes (2 French, 2 Sardinians) to represent Europeans; a pool of four genomes (2 Han, 2 Dai) to represent East Asians; and a pool of three genomes (2 Karitiana, 1 Mixe) to represent Native Americans. Statistics are as in Extended Data Table 1 but are based on 106,004 transversion SNPs covered by at least one deaminated fragment in Oase 1 and that also have coverage for all other samples, although not necessarily MA1. For analyses involving MA1, a subset of 76,715 transversion SNPs is analysed.

Extended Data Table 3 | Testing whether archaic genomes share more alleles with Oase 1 than with other modern humans

		Archaic = Altai				Archaic = Denisovan			
		Chimp		Mbuti		Chimp		Mbuti	
Test	Sites	D	Z	D	Z	D	Z	D	Z
Han	115,300	-0.0036	-5.1	-0.0071	-7.6	-0.0014	-2.2	-0.0049	-6.3
Dai	115,300	-0.0035	-5.0	-0.0077	-8.2	-0.0013	-2.1	-0.0056	-7.0
Karitiana	115,300	-0.0032	-4.3	-0.0063	-6.9	-0.0008	-1.3	-0.0040	-5.3
French	115,300	-0.0049	-6.9	-0.0074	-8.2	-0.0021	-3.4	-0.0047	-6.2
Sardinian	115,300	-0.0038	-5.1	-0.0071	-7.8	-0.0016	-2.5	-0.0050	-6.5
Papuan	115,300	-0.0026	-3.6	-0.0051	-5.4	0.0009	1.5	-0.0016	-2.1
Ust'-Ishim	115,100	-0.0026	-3.6	-0.0052	-5.5	-0.0009	-1.5	-0.0035	-4.4
Kostenki14	108,100	-0.0032	-4.1	-0.0059	-6.0	-0.0017	-2.4	-0.0044	-5.3
MA1	83,200	-0.0031	-3.6	-0.0050	-4.7	-0.0007	-0.9	-0.0028	-2.8
Loschbour	114,300	-0.0043	-5.7	-0.0066	-6.8	-0.0019	-2.9	-0.0043	-5.3
LaBrana	111,000	-0.0033	-4.2	-0.0072	-7.3	-0.0008	-1.2	-0.0047	-5.4
Stuttgart	114,000	-0.0037	-5.1	-0.0066	-7.1	-0.0013	-2.1	-0.0042	-5.6

The statistic *D*(Test, Oase 1; Archaic, Outgroup) is negative if the archaic genomes share more alleles with Oase 1 than with a test sample. The outgroups are either chimpanzee or a sub-Saharan African (Mbuti).

Extended Data Table 4 | Estimated fraction of the Oase 1 genome that derives from Neanderthals

	$\frac{f_4(Denisova,Altai;Mbuti,X)}{f_4(Denisova,Altai;Mbuti,Mezmaiskaya)}$			$1-\frac{f_4(Mbuti,Chimp;X,Denisova)}{f_4(Mbuti,Chimp;Dinka,Denisova)}$			$\frac{f_4(X,Mbuti;Denisova,Chimp)}{f_4(Altai,Mbuti;Denisova,Chimp)}$		
Sample	**Prop.**	**S.E.**	**90% CI**	**Prop.**	**S.E.**	**90% CI**	**Prop.**	**S.E.**	**90% CI**
Oase 1	11.3%	2.8%	6.7%-16%	10.9%	1.6%	8.3%-13.6%	8.4%	2.7%	4.0%-12.9%
Ust'-Ishim	2.9%	1.2%	1.0%-4.9%	6.0%	0.8%	4.7%-7.4%	4.2%	1.5%	1.8%-6.6%
Kostenki 14	3.0%	1.4%	0.7%-5.3%	3.0%	0.9%	1.6%-4.5%	6.2%	1.6%	3.6%-8.7%
MA1	1.5%	1.5%	0.0%-4.0%	3.6%	1.0%	1.9%-5.2%	5.5%	1.6%	2.8%-8.2%
Loschbour	1.1%	1.2%	0.0%-3.1%	4.8%	0.9%	3.3%-6.2%	3.6%	1.5%	1.2%-6.1%
LaBrana	3.7%	1.3%	1.4%-5.9%	2.4%	0.9%	0.9%-3.8%	4.8%	1.5%	2.4%-7.2%
Stuttgart	2.8%	1.2%	0.8%-4.8%	3.4%	0.9%	2.0%-4.9%	3.8%	1.5%	1.4%-6.2%
Han	1.0%	1.3%	0.0%-3.1%	2.8%	0.9%	1.3%-4.2%	3.6%	1.5%	1.2%-6.1%
Dai	2.1%	1.2%	0.2%-4.0%	1.3%	0.9%	0.0%-2.8%	3.8%	1.5%	1.4%-6.2%
French	1.6%	1.2%	0.0%-3.5%	3.3%	0.9%	1.9%-4.7%	2.7%	1.5%	0.3%-5.2%
Sardinian	2.7%	1.2%	0.8%-4.7%	2.3%	0.9%	0.8%-3.7%	3.7%	1.4%	1.3%-6.1%

Estimates are as in Table 1 but restrict to transversions. Present-day human genomes are from a data set reported previously[7].

Extended Data Table 5 | Counts of putative Neanderthal alleles in six modern humans

		Neanderthal allele counts						Neanderthal ancestry				
Chr	Sites	Oase 1	Ust'-Ishim	Kostenki 14	Han	French	Dinka	Oase 1	Ust'-Ishim	Kostenki 14	Han	French
1	6740	323	196	148	129	117	25	6.70%	3.84%	2.77%	2.34%	2.07%
2	7112	294	145	121	188	199	29	5.65%	2.47%	1.96%	3.39%	3.62%
3	5417	177	102	96	74	98	28	4.17%	2.07%	1.90%	1.29%	1.96%
4	4495	359	86	63	141	96	42	10.69%	1.48%	0.71%	3.34%	1.82%
5	4330	446	108	66	103	95	23	14.80%	2.97%	1.50%	2.80%	2.52%
6	4549	324	155	167	142	138	73	8.36%	2.73%	3.13%	2.30%	2.16%
7	4422	147	68	65	102	72	34	3.87%	1.16%	1.06%	2.33%	1.30%
8	4322	131	132	72	35	38	14	4.10%	4.14%	2.03%	0.74%	0.84%
9	3107	500	69	120	118	49	15	23.65%	2.63%	5.12%	5.02%	1.66%
10	4009	147	139	67	131	86	22	4.72%	4.42%	1.70%	4.12%	2.42%
11	4193	153	93	88	81	73	26	4.59%	2.42%	2.24%	1.99%	1.70%
12	3456	456	160	54	125	93	10	19.55%	6.58%	1.93%	5.04%	3.64%
13	2457	96	81	33	54	30	18	4.81%	3.89%	0.93%	2.22%	0.74%
14	2390	85	27	52	50	52	13	4.56%	0.89%	2.47%	2.35%	2.47%
15	2327	73	78	47	38	32	5	4.43%	4.75%	2.73%	2.15%	1.76%
16	3139	90	121	68	43	39	8	3.96%	5.45%	2.90%	1.69%	1.50%
17	2543	72	89	37	85	75	56	0.95%	1.97%	-1.13%	1.73%	1.13%
18	2305	57	58	59	27	29	5	3.42%	3.48%	3.55%	1.45%	1.58%
19	1769	79	49	33	43	35	12	5.74%	3.17%	1.80%	2.66%	1.97%
20	2492	107	29	62	56	43	12	5.78%	1.03%	3.04%	2.68%	1.88%
21	1026	36	53	22	8	11	10	3.84%	6.35%	1.77%	-0.30%	0.15%
22	1455	79	33	66	34	18	5	7.71%	2.92%	6.35%	3.02%	1.35%
All	78055	4231	2071	1606	1807	1518	485	7.27%	3.08%	2.18%	2.57%	"2%"
Subtract Dinka		3746	1586	1121	1322	1033	0					

The analysis is based on 78,055 sites covered by at least one deaminated fragment in Oase 1. To convert the counts to estimates of ancestry, we subtract the Dinka count as an estimate of the false positive rate and divide by the number of sites covered (as indicated for the whole genome on the bottom). This gives the rate of alleles per screened site on this chromosome for this individual. We then multiply this quantity by 2%/1.32% to recalibrate the 1.32% seen genome-wide in the French to an assumed 2% genome-wide Neanderthal ancestry in the French[7].

Extended Data Table 6 | Ancient DNA libraries made from the Oase 1 mandible

Metainformation						Sequencing results			All fragments			Deaminated fragments		
Library	Extract	UDG treatment	Index 1	Index 2	Extract used (µl)	Sequences going into alignment	Sequences ≥35bp mapped	After dup. removal	Coverage	% C→T 5' end	% C→T 3' end	Coverage	% C→T 5' end	% C→T 3' end
A5227	E1406	Yes	ACTTGCG	AACTCCG	8	206,982	118,976	34,486	112	8	19	5	19	36
A5252	E1843	Yes	GTAAGCC	TTGAAGT	40	74,384	46,394	31,368	114	7	25	5	18	55
A9032	E1406	No	ATAACGT	ACTATCA	6	9,321,903	5,904,210	51,810	178	20	21	12	31	39
A9033	E1406	No	AATAGGA	ACCAACT	6	7,932,271	4,816,314	55,878	193	21	20	13	36	38
A9034	E1406	No	ATCACGA	AACTCCG	6	10,422,467	6,861,634	59,883	207	20	20	14	35	38
						27,958,007	17,747,528	233,425	803	17	21	49	30	39

Extended Data Table 7 | Sequencing metrics on the five libraries for the four capture probe panels

Library	Panel	No. target SNPs	Fragments going into alignment	Fragments mapped to genome	Fragments on target after dup. removal and MAPQ37 filter	% SNPs hit at least once	Average coverage on SNPs
A9032	390k	393,577	10,849,144	2,235,955	133,564	26.5%	0.34
A9033	390k	393,577	17,159,085	2,808,704	73,824	15.9%	0.19
A9034	390k	393,577	16,902,935	3,256,438	142,520	27.7%	0.36
A5227	390k	393,577	63,441,719	22,124,247	195,161	36.0%	0.5
A5252	390k	393,577	60,181,844	14,278,978	180,626	33.3%	0.46
All 5	390k	393,577	168,534,727	44,704,322	724,653	73.0%	1.84
A9032	840k	842,630	25,105,625	3,801,435	178,015	17.6%	0.21
A9033	840k	842,630	29,196,969	4,655,434	183,093	17.9%	0.22
A9034	840k	842,630	35,780,652	5,968,851	200,767	19.3%	0.24
A5227	840k	842,630	28,209,496	4,276,439	152,411	15.3%	0.18
A5252	840k	842,630	20,286,540	1,630,343	106,943	11.2%	0.13
All 5	840k	842,630	138,579,282	20,332,502	818,648	51.7%	0.97
A9032	1000k	997,780	26,088,835	2,964,094	159,162	13.5%	0.16
A9033	1000k	997,780	26,641,358	4,490,372	158,614	13.3%	0.16
A9034	1000k	997,780	28,795,043	4,985,140	154,177	13.0%	0.15
A5227	1000k	997,780	25,848,311	4,395,413	71,537	6.4%	0.07
A5252	1000k	997,780	25,691,323	2,254,636	53,932	5.0%	0.05
All 5	1000k	997,780	133,064,870	19,089,655	596,107	36.1%	0.6
A9032	Archaic	1,749,385	19,329,832	2,086,208	205,095	10.0%	0.12
A9033	Archaic	1,749,385	24,629,023	2,768,355	237,818	11.4%	0.14
A9034	Archaic	1,749,385	31,200,466	3,783,805	257,351	12.2%	0.15
A5227	Archaic	1,749,385	27,659,125	3,606,375	195,356	9.6%	0.11
A5252	Archaic	1,749,385	31,472,143	2,435,080	136,637	6.8%	0.08
All 5	Archaic	1,749,385	134,290,589	14,679,823	1,022,046	34.6%	0.58
A9032	Combined	3,801,245	81,373,436	11,087,692	719,146	15.5%	0.19
A9033	Combined	3,801,245	97,626,435	14,722,865	698,890	15.1%	0.18
A9034	Combined	3,801,245	112,679,096	17,994,234	806,589	17.0%	0.21
A5227	Combined	3,801,245	145,158,651	34,402,474	666,195	14.2%	0.18
A5252	Combined	3,801,245	137,631,850	20,599,037	531,873	11.4%	0.14
All 5	Combined	3,801,245	574,469,468	98,806,302	3,406,685	45.5%	0.90

Extended Data Table 8 | Effect of filtering on amount of nuclear data available

Panel	Target SNPs	All fragments			Deaminated fragments only		
		No. SNPs hit ≥1×	% SNPs hit ≥1×	Average coverage	No. SNPs hit ≥1×	% SNPs hit ≥1×	Average coverage
Panels 1-3	2,051,902	1,038,619	50.6%	1.03	271,326	13.2%	0.16
Panel 4 subset*	954,849	361,681	37.9%	0.69	87,803	9.2%	0.11
Panels 1-4	3,801,245	1,685,891	44.4%	0.85	426,027	11.2%	0.13

Note that numbers differ from Extended Data Table 7 because only sites with base quality ≥20 were used.
* The Panel 4 subset excludes the sites where only the Denisovan genome differs from the African panel.

Extended Data Table 9 | Genomes merged with the Oase 1 data

Sample ID	Human	Data type	Mean	UDG-treated
Oase1	Modern	Low coverage	Capture	Mix of library types
Vindija	Archaic	Low coverage	1.3	No
Mezmaiskaya	Archaic	Low coverage	0.5	Yes
Altai	Archaic	High coverage	52	Yes
Denisova	Archaic	High coverage	31	Yes
Kostenki14	Modern	Low coverage	2.4	Mix of library types
MA1	Modern	Low coverage	1	No
LaBrana	Modern	Low coverage	3.4	No
Loschbour	Modern	High coverage	22	Yes
Stuttgart	Modern	High coverage	19	Yes
Ust'-Ishim	Modern	High coverage	42	Yes
$Dinka_A$	Modern	High coverage	28	..
$French_A$	Modern	High coverage	27	..
$Papuan_A$	Modern	High coverage	26	..
$Sardinian_A$	Modern	High coverage	25	..
Han_A	Modern	High coverage	28	..
$Yoruba_A$	Modern	High coverage	32	..
$Karitiana_A$	Modern	High coverage	26	..
San_A	Modern	High coverage	33	..
$Mandenka_A$	Modern	High coverage	25	..
Dai_A	Modern	High coverage	28	..
$Mbuti_A$	Modern	High coverage	24	..
Dai_B	Modern	High coverage	37	..
$French_B$	Modern	High coverage	42	..
Han_B	Modern	High coverage	35	..
$Mandenka_B$	Modern	High coverage	37	..
$Mbuti_B$	Modern	High coverage	37	..
$Papuan_B$	Modern	High coverage	42	..
San_B	Modern	High coverage	38	..
$Sardinian_B$	Modern	High coverage	38	..
$Yoruba_B$	Modern	High coverage	39	..
$Karitiana_B$	Modern	High coverage	35	..
$Mixe_B$	Modern	High coverage	42	..
$Australian_{B1}$	Modern	High coverage	42	..
$Australian_{B2}$	Modern	High coverage	37	..
$Dinka_B$	Modern	High coverage	35	..

For the 25 present-day humans, individuals ending with a subscript 'A' are from 'Panel A' reported in ref. 9 and individuals with a subscript 'B' are from 'Panel B' reported in ref. 7. Unless otherwise specified, we used Panel B individuals.