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POPULATION GENOMICS OF STONE AGE EURASIA

2 Morten E. Allentoft^{1,2,*}§, Martin Sikora^{1*}§, Alba Refoyo-Martínez¹§, Evan K. Irving-Pease¹§, Anders Fischer^{3,4}§,
3 William Barrie⁵§, Andrés Ingason^{6,1}§, Jesper Stenderup¹, Karl-Göran Sjögren³, Alice Pearson⁷, Barbara Mota^{8,9}, Bettina
4 Schulz Paulsson³, Alma Halgren¹⁰, Ruairidh Macleod^{1,5,11}, Marie Louise Schjellerup Jørgen¹², Fabrice Demeter^{1,13},
5 Maria Novosolov¹, Lasse Sørensen¹⁴, Poul-Otto Nielsen¹⁴, Rasmus H.A. Henriksen¹, Tharsika Vimala¹, Hugh McColl¹,
6 Ashot Margaryan^{15,16}, Melissa Ilardo¹⁷, Andrew Vaughn¹⁸, Morten Fischer Mortensen¹⁴, Anne Birgitte Nielsen¹⁹,
7 Mikkel Ulfeldt Hede²⁰, Peter Rasmussen¹⁴, Lasse Vinner¹, Gabriel Renaud²¹, Aaron Stern¹⁸, Theis Zetner Trolle
8 Jensen¹⁵, Niels Nørkjær Johannsen²², Gabriele Scorrano¹, Hannes Schroeder¹⁵, Per Lysdahl²³, Abigail Daisy Ramsøe¹,
9 Andrei Skorobogatov²⁴, Andrew Joseph Schork^{6,25}, Anders Rosengren^{6,1}, Anthony Ruter¹, Alan Outram²⁶, Aleksey A.
10 Timoshenko²⁷, Alexandra Buzhilova²⁸, Alfredo Coppa²⁹, Alisa Zubova³⁰, Ana Maria Silva^{31,59}, Anders J. Hansen¹,
11 Andrey Gromov³⁰, Andrey Logvin³², Anne Birgitte Gottfredsen¹, Bjarne Henning Nielsen³³, Borja González-Rabanal³⁴,
12 Carles Lalueza-Fox³⁵, Catriona J. McKenzie²⁶, Charleen Gaunitz¹, Concepción Blasco³⁶, Corina Liesau³⁶, Cristina
13 Martínez-Labarga³⁷, Dmitri V. Pozdnyakov²⁷, David Cuenca-Solana^{38,39}, David O. Lordkipanidze^{40,41}, Dmitri En'shin⁴²,
14 Domingo C. Salazar-García^{43,44}, T. Douglas Price⁴⁵, Dušan Borčić^{29,46}, Elena Kostyleva⁴⁷, Elizaveta V. Veselovskaya⁴⁸,
15 Emma R. Usmanova^{49,50}, Enrico Cappellini¹⁵, Erik Brinch Petersen⁵¹, Esben Kannegaard⁵², Francesca Radina⁵³, Fulya
16 Eylem Yediay¹, Henri Duda⁵⁴, Igor Gutiérrez-Zugasti³⁸, Inna Potekhina^{55,56}, Irina Shevnina³², Isin Altinkaya¹, Jean
17 Guilaine⁵⁷, Jesper Hansen⁵⁸, Joan Emili Aura Tortosa⁴³, João Zilhão^{59,60}, Jorge Vega⁶¹, Kristoffer Buck Pedersen⁶²,
18 Krzysztof Tunia⁶³, Lei Zhao¹, Liudmila N. Mylnikova²⁷, Lars Larsson⁶⁴, Laure Metz⁶⁵, Levon Yéppiskoposyan^{66,93},
19 Lisbeth Pedersen⁶⁷, Lucia Sarti⁶⁸, Ludovic Orlando⁶⁹, Ludovic Slimak⁶⁵, Lutz Klassen⁵², Malou Blank³, Manuel
20 González-Morales³⁸, Mara Silvestrini⁷⁰, Maria Vretemark⁷¹, Marina S. Nesterova²⁷, Marina Rykun⁷², Mario Federico
21 Rolfo⁷³, Marzena Szmyt⁷⁴, Marcin Przybyła⁷⁵, Mauro Calattini⁶⁸, Mikhail Sablin⁷⁶, Miluše Dobisiková⁷⁷, Morten
22 Meldgaard⁷⁸, Morten Johannsen⁷⁹, Natalia Berezina²⁸, Nick Card⁸⁰, Nikolai A. Saveliev⁸¹, Olga Poshekhonova⁴², Olga
23 Rickards³⁷, Olga V. Lozovskaya⁸², Otto Christian Uldum⁷⁹, Paola Aurino⁸³, Pavel Kosintsev^{84,85}, Patrice Courtaud⁵⁴,
24 Patricia Ríos³⁶, Peder Mortensen⁸⁶, Per Lotz^{87,88}, Per Åke Persson⁸⁹, Pernille Bangsgaard⁹⁰, Peter de Barros Damgaard¹,
25 Peter Vang Petersen¹⁴, Pilar Prieto Martínez⁹¹, Piotr Włodarczyk⁶³, Roman V. Smolyaninov⁹², Rikke Maring^{22,52},
26 Roberto Menduina⁶¹, Ruben Badalyan⁹¹, Rune Iversen⁵¹, Ruslan Turin²⁴, Sergey Vasilyev²⁷, Sidsel Wählin²³, Svetlana
27 Borutskaya²⁸, Svetlana Skochina⁴², Søren Anker Sørensen⁸⁷, Søren H. Andersen⁹⁴, Thomas Jørgensen⁸⁷, Yuri B.
28 Serikov⁹⁵, Vyacheslav I. Molodin²⁷, Vaclav Smrcka⁹⁶, Victor Merz⁹⁷, Vivek Appadurai⁶, Vyacheslav Moiseyev³⁰,
29 Yvonne Magnusson⁹⁸, Kurt H. Kjær¹, Niels Lynnerup¹², Daniel J. Lawson⁹⁹, Peter H. Sudmant^{10,18}, Simon
30 Rasmussen¹⁰⁰, Thorfinn Korneliussen¹@, Richard Durbin^{7,101}@, Rasmus Nielsen^{10,1}@, Olivier Delaneau⁸@, Thomas
31 Werge^{1,6,102}@, Fernando Racimo¹@, Kristian Kristiansen^{1,3}@, Eske Willerslev^{1,5,101,103}*@

Affiliations

35 ¹Lundbeck Foundation GeoGenetics Centre, Globe Institute, University of Copenhagen, Copenhagen, Denmark. ²Trace
36 and Environmental DNA (TrEnD) Laboratory, School of Molecular and Life Sciences, Curtin University, Perth,
37 Australia. ³Department of Historical Studies, University of Gothenburg, Gothenburg, Sweden. ⁴Sealand Archaeology,
38 Gl. Roesnaesvej 27, 4400 Kalundborg, Denmark. ⁵GeoGenetics Group, Department of Zoology, University of
39 Cambridge, Cambridge, UK. ⁶Institute of Biological Psychiatry, Mental Health Services, Copenhagen University
40 Hospital, Roskilde, Denmark. ⁷Department of Genetics, University of Cambridge, Cambridge, UK. ⁸Department of
41 Computational Biology, University of Lausanne, Switzerland. ⁹Swiss Institute of Bioinformatics, University of
42 Lausanne, Switzerland. ¹⁰Department of Integrative Biology, University of California, Berkeley, USA. ¹¹Research
43 department of Genetics, Evolution and Environment, University College London, London, UK. ¹²Laboratory of
44 Biological Anthropology, Department of Forensic Medicine, University of Copenhagen, Copenhagen, Denmark.
45 ¹³Muséum national d'Histoire naturelle, CNRS, Université de Paris, Muséum de l'Homme, Paris, France. ¹⁴The National
46 Museum of Denmark, Ny Vestergade 10, Copenhagen, Denmark. ¹⁵Section for Evolutionary Genomics, GLOBE
47 Institute, University of Copenhagen, Copenhagen, Denmark. ¹⁶Centre for Evolutionary Hologenomics, University of
48 Copenhagen, Copenhagen, Denmark. ¹⁷Anthropology Department, University of Utah, USA. ¹⁸Center for
49 Computational Biology, University of California, Berkeley, USA. ¹⁹Department of Geology, Lund University, Lund,
50 Sweden. ²⁰Tårnby Gymnasium og HF, Kastrup, Denmark. ²¹Department of Health Technology, Section of
51 Bioinformatics, Technical University of Denmark, Kongens Lyngby, Denmark. ²²Department of Archaeology and
52 Heritage Studies, Aarhus University, Aarhus, Denmark. ²³Vendsyssel Historiske Museum, DK-9800 Hjørring,
53 Denmark. ²⁴Terra Ltd., Letchik Zlobin St. 20, Voronezh, 394055, Russian Federation. ²⁵Neurogenomics Division, The
54 Translational Genomics Research Institute (TGEN), Phoenix, AZ, USA. ²⁶Department of Archaeology, University of
55 Exeter, Exeter, UK. ²⁷Institute of Archaeology and Ethnography, Siberian Branch of the Russian Academy of Sciences,
56 Novosibirsk, Russian Federation. ²⁸Research Institute and Museum of Anthropology, Lomonosov Moscow State
57 University, Mokhovaya str. 11, Moscow, Russian Federation. ²⁹Department of Environmental Biology, Sapienza
58 University of Rome, Rome, Italy. ³⁰Peter the Great Museum of Anthropology and Ethnography (Kunstkamera), Russian
59 Academy of Sciences, Saint Petersburg, Russian Federation. ³¹CIAS, Department of Life Science, University of

60 Coimbra, Coimbra, Portugal. ³²Kostanay Regional University A. Baitursynov, Kostanay, Kazakhstan.
61 ³³Vesthimmerlands Museum, Søndergade 44, Aars, Denmark. ³⁴Grupo EvoAdapta, Departamento de Ciencias
62 Históricas, Universidad de Cantabria, Santander, Spain. ³⁵Institute of Evolutionary Biology, CSIC-Universitat Pompeu
63 Fabra, Barcelona, Spain. ³⁶Departamento de Prehistoria y Arqueología Department, Universidad Autónoma de Madrid,
64 Madrid, Spain. ³⁷Department of Biology, University of Rome "Tor Vergata", Rome, Italy. ³⁸Instituto Internacional de
65 Investigaciones Prehistóricas de Cantabria, Universidad de Cantabria, Santander, Spain. ³⁹Centre de Recherche en
66 Archéologie, Archeosciences, Histoire (CREAAH), UMR-6566 CNRS, Rennes, France. ⁴⁰Georgian National Museum,
67 Tbilisi, Georgia. ⁴¹Tbilisi State University, Tbilisi, Georgia. ⁴²IPND, Tyumen Scientific Centre, Siberian Branch of the
68 Russian Academy of Sciences, Tyumen, Russian Federation. ⁴³Departament de Prehistòria, Arqueologia i Història
69 Antiga, Universitat de València, València, Spain. ⁴⁴Department of Geological Sciences, University of Cape Town, Cape
70 Town, South Africa. ⁴⁵Laboratory for Archaeological Chemistry, Department of Anthropology, University of
71 Wisconsin-Madison, Madison, USA. ⁴⁶Department of Anthropology, New York University, New York, USA. ⁴⁷Institute
72 of Humanities, Ivanovo State University, Ivanovo, Russian Federation. ⁴⁸Institute of Ethnology and Anthropology,
73 Russian Academy of Sciences, Moscow, Russian Federation. ⁴⁹Saryarka Archaeological Institute, Buketov Karaganda
74 University, Karaganda, Kazakhstan. ⁵⁰South Ural State University, Chelyabinsk, Russia. ⁵¹The Saxo Institute,
75 University of Copenhagen, Copenhagen, Denmark. ⁵²Museum Østjylland, Stemannsgade 2, Randers, Denmark.
76 ⁵³Soprintendenza Archeologia Belle Arti e Paesaggio per la Città Metropolitana di Bari, Via Pier l'Eremita, 25, 70122,
77 Bari, Italy. ⁵⁴UMR 5199 PACEA, CNRS, Université de Bordeaux, 33615 Pessac, France. ⁵⁵Institute of Archaeology,
78 National Academy of Sciences of Ukraine, Kyiv, Ukraine. ⁵⁶National University of Kyiv-Mohyla Academy, Kyiv,
79 Ukraine. ⁵⁷Collège de France, 75231 Paris cedex 05, France. ⁵⁸Odense City Museums, Overgade 48, Odense, Denmark.
80 ⁵⁹UNIARQ, University of Lisbon, Lisbon, Portugal. ⁶⁰ICREA, University of Barcelona, Barcelona, Spain. ⁶¹ARGEA
81 Consultores SL, C. de San Crispin, Madrid, Spain. ⁶²Museum Sydøstdanmark, Algade 97, 4760 Vordingborg, Denmark.
82 ⁶³Institute of Archaeology and Ethnology, Polish Academy of Sciences, Kraków, Poland. ⁶⁴Department of Archaeology
83 and Ancient History, Lund University, Lund, Sweden. ⁶⁵CNRS UMR 5608, Toulouse Jean Jaurès University, Maison
84 de la Recherche, 5 Allées Antonio Machado, 31058 Toulouse, Cedex 9, France. ⁶⁶Institute of Molecular Biology,
85 National Academy of Sciences, Yerevan, Armenia. ⁶⁷HistorieUdvikler, Gl. Roesnaesvej 27, DK-4400 Kalundborg,
86 Denmark. ⁶⁸Department of history and cultural heritage, University of Siena, Siena, Italy. ⁶⁹Centre d'Anthropobiologie
87 et de Génomique de Toulouse, CNRS UMR 5288, Université Paul Sabatier, Toulouse, France. ⁷⁰Soprintendenza per i
88 Beni Archeologici delle Marche, Via Birarelli 18, 60100, Ancona, Italy. ⁷¹Västergötlands museum, Stadsträdgården,
89 Skara, Sweden. ⁷²Cabinet of Anthropology, Tomsk State University, Tomsk, Russian Federation. ⁷³Department of
90 History, Humanities and Society, University of Rome "Tor Vergata", Rome, Italy. ⁷⁴Institute for Eastern Research,
91 Adam Mickiewicz University in Poznań, Poznań, Poland. ⁷⁵Institute of Archaeology, Jagiellonian University, Ul.
92 Gołębia 11, 31-007, Kraków, Poland. ⁷⁶Zoological Institute of Russian Academy of Sciences, Universitetskaya nab. 1,
93 199034, St. Petersburg, Russian Federation. ⁷⁷Department of Anthropology, Czech National Museum, Prague, Czech
94 Republic. ⁷⁸Department of Health and Nature, University of Greenland, Greenland. ⁷⁹The Viking Ship Museum,
95 Vindeboder 12, Roskilde, Denmark. ⁸⁰Archaeology Institute, University of Highlands and Islands, Scotland, UK.
96 ⁸¹Scientific Research Center "Baikal region", Irkutsk State University; 1, K. Marx st., Irkutsk, 664003, Russian
97 Federation. ⁸²Laboratory for Experimental Traceology, Institute for the History of Material Culture of the Russian
98 Academy of Sciences, Dvortsovaya nab., 18, 191186, St. Petersburg, Russian Federation. ⁸³Soprintendenza
99 Archeologia, Belle Arti e Paesaggio per la provincia di Cosenza, Cosenza, Italy. ⁸⁴Paleoecology Laboratory, Institute of
100 Plant and Animal Ecology, Ural Branch of the Russian Academy of Sciences, Ekaterinburg, Russian Federation.
101 ⁸⁵Department of History of the Institute of Humanities, Ural Federal University, Ekaterinburg, Russian Federation.
102 ⁸⁶Centre for the Study of Early Agricultural Societies, Department of Cross-Cultural and Regional Studies, University
103 of Copenhagen, 2300 Copenhagen, Denmark. ⁸⁷Museum Nordsjælland, Frederiksgade 9, 3400 Hillerød. ⁸⁸Museum
104 Vestsjælland, Klosterstræde 18, 4300 Holbæk, Denmark. ⁸⁹Museum of Cultural History, University of Oslo, P.O. Box
105 6762. St. Olavs Plass NO-0130 Oslo, Norway. ⁹⁰ArchaeoScience, GLOBE Institute, University of Copenhagen,
106 Copenhagen, Denmark. ⁹¹Department of History, University of Santiago de Compostela, Spain. ⁹²Lipetsk Regional
107 Scientific Public Organisation "Archaeological Research", Lipetsk, Russian Federation. ⁹²Institute of Archaeology and
108 Ethnography, National Academy of Sciences, Yerevan, Armenia. ⁹³Russian-Armenian University, Yerevan, Armenia.
109 ⁹⁴Moesgaard Museum, Moesgård Allé 15, Højbjerg, Denmark. ⁹⁵Nizhny Tagil State Socio-Pedagogical Institute,
110 Nizhny Tagil, Russia. ⁹⁶Institute for History of Medicine, First Faculty of Medicine, Charles University, Prague, Czech
111 Republic. ⁹⁷Centre for Archaeological Research Toraighyrov University, Pavlodar, Kazakhstan. ⁹⁸Malmö Museer,
112 Malmöhusvägen 6, Malmö, Sweden. ⁹⁹Institute of Statistical Sciences, School of Mathematics, University of Bristol,
113 Bristol, UK. ¹⁰⁰Novo Nordisk Foundation Centre for Protein Research, Faculty of Health and Medical Sciences,
114 University of Copenhagen, Copenhagen N, Denmark. ¹⁰¹Wellcome Sanger Institute, Wellcome Genome Campus,
115 Cambridge, UK. ¹⁰²Department of Clinical Medicine, University of Copenhagen, 2200 Copenhagen N, Denmark.
116 ¹⁰³MARUM, University of Bremen, Bremen, Germany.

117
118 * Corresponding authors; email: morten.allentoft@curtin.edu.au, martin.sikora@sund.ku.dk, ew482@cam.ac.uk
119 § Joint first authors

120 @ Joint last authors

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122

123 **Summary**

124

125 **The transitions from foraging to farming and later to pastoralism in Stone Age Eurasia (c. 11-**
126 **3 thousand years before present, BP) represent some of the most dramatic lifestyle changes in**
127 **human evolution. We sequenced 317 genomes of primarily Mesolithic and Neolithic**
128 **individuals from across Eurasia combined with radiocarbon dates, stable isotope data, and**
129 **pollen records. Genome imputation and co-analysis with previously published shotgun**
130 **sequencing data resulted in >1600 complete ancient genome sequences offering fine-grained**
131 **resolution into the Stone Age populations. We observe that: 1) Hunter-gatherer groups were**
132 **more genetically diverse than previously known, and deeply divergent between western and**
133 **eastern Eurasia. 2) We identify hitherto genetically undescribed hunter-gatherers from the**
134 **Middle Don region that contributed ancestry to the later Yamnaya steppe pastoralists; 3) The**
135 **genetic impact of the Neolithic transition was highly distinct, east and west of a boundary**
136 **zone extending from the Black Sea to the Baltic. Large-scale shifts in genetic ancestry**
137 **occurred to the west of this “Great Divide”, including an almost complete replacement of**
138 **hunter-gatherers in Denmark, while no substantial ancestry shifts took place during the same**
139 **period to the east. This difference is also reflected in genetic relatedness within the**
140 **populations, decreasing substantially in the west but not in the east where it remained high**
141 **until c. 4,000 BP; 4) The second major genetic transformation around 5,000 BP happened at a**
142 **much faster pace with Steppe-related ancestry reaching most parts of Europe within 1,000-**
143 **years. Local Neolithic farmers admixed with incoming pastoralists in eastern, western, and**
144 **southern Europe whereas Scandinavia experienced another near-complete population**
145 **replacement. Similar dramatic turnover-patterns are evident in western Siberia; 5) Extensive**
146 **regional differences in the ancestry components involved in these early events remain visible**
147 **to this day, even within countries. Neolithic farmer ancestry is highest in southern and eastern**
148 **England while Steppe-related ancestry is highest in the Celtic populations of Scotland, Wales,**
149 **and Cornwall (this research has been conducted using the UK Biobank resource); 6) Shifts in**
150 **diet, lifestyle and environment introduced new selection pressures involving at least 21**
151 **genomic regions. Most such variants were not universally selected across populations but**
152 **were only advantageous in particular ancestral backgrounds. Contrary to previous claims, we**
153 **find that selection on the FADS regions, associated with fatty acid metabolism, began before**
154 **the Neolithisation of Europe. Similarly, the lactase persistence allele started increasing in**
155 **frequency before the expansion of Steppe-related groups into Europe and has continued to**
156 **increase up to the present. Along the genetic cline separating Mesolithic hunter-gatherers**
157 **from Neolithic farmers, we find significant correlations with trait associations related to skin**
158 **disorders, diet and lifestyle and mental health status, suggesting marked phenotypic**
159 **differences between these groups with very different lifestyles. This work provides new**
160 **insights into major transformations in recent human evolution, elucidating the complex**
161 **interplay between selection and admixture that shaped patterns of genetic variation in**
162 **modern populations.**

163

164

165 **Introduction**

166 The transition from hunting and gathering to farming represents one of the most dramatic shifts in
167 lifestyle and diet in human evolution with lasting effects on the modern world. For millions of years
168 our ancestors relied on hunting and foraging for survival but c.12,000 years ago in the Fertile

169 Crescent of the Near East, plant cultivation and animal husbandry were developed¹⁻³. This
170 ultimately resulted in a more sedentary lifestyle accompanied by increasing population sizes and
171 higher social complexity. Expanding populations and the adoption of herding, carried farming
172 practices into Europe and parts of SW Asia in the following millennia, and farming was also
173 developed independently in other parts of the World. Today, 50% of the Earth's habitable land is
174 used for agriculture and very few hunter-gatherers remain^{4,5}. Understanding the changes to the
175 human gene pool during this shift from hunter-gathering to farming between the Mesolithic and
176 Neolithic periods is central to understanding ourselves and the events that led to a major
177 transformation of our planet.

178
179 While the Neolithisation process has been studied extensively with ancient DNA (aDNA)
180 technology, several key questions remain unaddressed. Population movements during the Neolithic
181 can be traced in the gene pools across the European continent as farming was introduced from the
182 Near East. Several regional studies have testified to varying degrees of reproductive interaction
183 with local Mesolithic groups, ranging from genetic continuity⁶ to gradual population admixture⁷⁻¹⁰
184 to almost complete replacement¹¹. However, our knowledge of the population structure in the
185 Mesolithic period and how it was formed is limited, partly because of a paucity of data from
186 skeletons older than 8,000 years, compromising resolution into subsequent demographic transitions.
187 Moreover, the spatiotemporal mapping of population dynamics east of Europe, including Siberia,
188 Central- and North Asia during the same time period remains patchy. In these regions the
189 'Neolithic' typically refers to new forms of lithic material culture, and/or the presence of
190 ceramics¹². For instance, the Neolithic cultures of the Central Asian Steppe possessed pottery, but
191 retained a hunter-gatherer economy alongside stone blade technology similar to the preceding
192 Mesolithic cultures¹³. The archaeological record testifies to a boundary, ranging from the eastern
193 Baltic to the Black Sea, east of which hunter-gatherer societies persist for much longer than in
194 western Europe¹⁴. The population genomic implications of this "Great Divide" is, however, largely
195 unknown. Southern Scandinavia represents another enigma in the Neolithisation debate¹⁵. The
196 introduction of farming reached a 1,000-year standstill at the doorstep to Southern Scandinavia
197 before finally progressing into Denmark around 6,000 BP. It is not known what caused this delay
198 and whether the transition to farming in Denmark, was facilitated by the migration of people (demic
199 diffusion), similar to the rest of Europe^{11,16,17} or mostly involved cultural diffusion^{18,19}. Starting at
200 around 5,000 BP, a new ancestry component emerged on the eastern European plains associated
201 with Yamnaya Steppe pastoralists culture and swept across Europe mediated through expansion of
202 the Corded Ware complex (CWC) and related cultures^{20,21}. The genetic origin of the Yamnaya and
203 the fine-scale dynamics of the formation and expansion of the CWC are largely unresolved
204 questions of central importance to clarify the formation of the present day European gene pool.

205
206 Rapid dietary changes and expansion into new climate zones represent shifts in environmental
207 exposure, impacting the evolutionary forces acting on the gene pool. The Neolithisation can
208 therefore be considered as a series of large-scale selection pressures imposed on humans from
209 around 12,000 years ago. Moreover, close contact with livestock and higher population densities
210 have likely enhanced exposure and transmission of infectious diseases, introducing new challenges
211 to our survival^{22,23}. While signatures of selection can be identified from patterns of genetic diversity
212 in extant populations^{24,25}, this can be challenging in species such as humans, which show very wide
213 geographic distributions and have thus been exposed to highly diverse and changing local
214 environments through space and time. In the complex mosaic of ancestries that constitute a modern
215 human genome any putative signatures of selection may therefore misrepresent the timing and
216 magnitude of the actual event unless we can use ancient DNA to chart the individual ancestry
217 components back into the evolutionary past.

218

219 To investigate these formative processes in Eurasian prehistory, we conducted the largest ancient
220 DNA study to date on human Stone Age skeletal material. We sequenced low-coverage genomes of
221 317 radiocarbon-dated (AMS) primarily Mesolithic and Neolithic individuals, covering major parts
222 of Eurasia. We combined these with published shotgun-sequenced data to impute a dataset of
223 >1600 diploid ancient genomes. Genomic data from 100 AMS-dated individuals from Denmark
224 supported detailed analyses of the Stone Age population dynamics in Southern Scandinavia. When
225 combined with genetically-predicted phenotypes, proxies for diet ($\delta^{13}\text{C}/\delta^{15}\text{N}$), mobility ($^{87}\text{Sr}/^{86}\text{Sr}$)
226 and vegetation cover (pollen) we could connect this with parallel shifts in phenotype, subsidence
227 and landscape. To test for traces of divergent selection in health and lifestyle-related genetic
228 variants, we used the imputed ancient genomes to reconstruct polygenic risk scores for hundreds of
229 complex traits in the ancient Eurasian populations. Additionally, we used a novel chromosome
230 painting technique based on tree sequences, in order to model ancestry-specific allele frequency
231 trajectories through time. This allowed us to identify many new phenotype-associated genetic
232 variants with hitherto unknown evidence for positive selection in Eurasia throughout the Holocene.
233

234 **Results/Discussion**

235 *Samples and data*

236 In this study we present genomic data from 317 ancient individuals (Fig 1, Extended data fig. 2,
237 Supplement Table I). A total of 272 were radiocarbon dated within the project, while 39 dates were
238 derived from literature and 15 were dated by archaeological context. Dates were corrected for
239 marine and freshwater reservoir effects (Supplementary Note 8) and ranged from the Upper
240 Palaeolithic (UP) c. 25,700 calibrated years before present (cal. BP) to the mediaeval period (c.
241 1200 cal. BP). However, 97% of the individuals (N=309) span 11,000 cal. BP to 3,000 cal. BP, with
242 a heavy focus on individuals associated with various Mesolithic and Neolithic cultures.
243

244 Geographically, the sampled skeletons cover a vast territory across Eurasia, from Lake Baikal to the
245 Atlantic coast, from Scandinavia to the Middle East, and they derive from a variety of contexts,
246 including burial mounds, caves, bogs and the seafloor (Supplementary Notes 6-7). Broadly, we can
247 divide our research area into three large regions: 1) central, western and northern Europe, 2) eastern
248 Europe including western Russia and Ukraine, and 3) the Urals and western Siberia. Our samples
249 cover many of the key Mesolithic and Neolithic cultures in Western Eurasia, such as the
250 Maglemose and Ertebølle cultures in Scandinavia, the Cardial in the Mediterranean, the Körös and
251 Linear Pottery (LBK) in SE and Central Europe, and many archaeological cultures in Ukraine,
252 western Russia, and the trans-Ural (e.g. Veretye, Lyalovo, Volosovo, Kitoi). Our sampling was
253 particularly dense in Denmark from where we present a detailed and continuous sequence of 100
254 genomes spanning from the early Mesolithic to the Bronze Age. Dense sample sequences were also
255 obtained from Ukraine, Western Russia, and the trans-Ural, spanning from the Early Mesolithic
256 through the Neolithic, up to c. 5,000 BP.
257

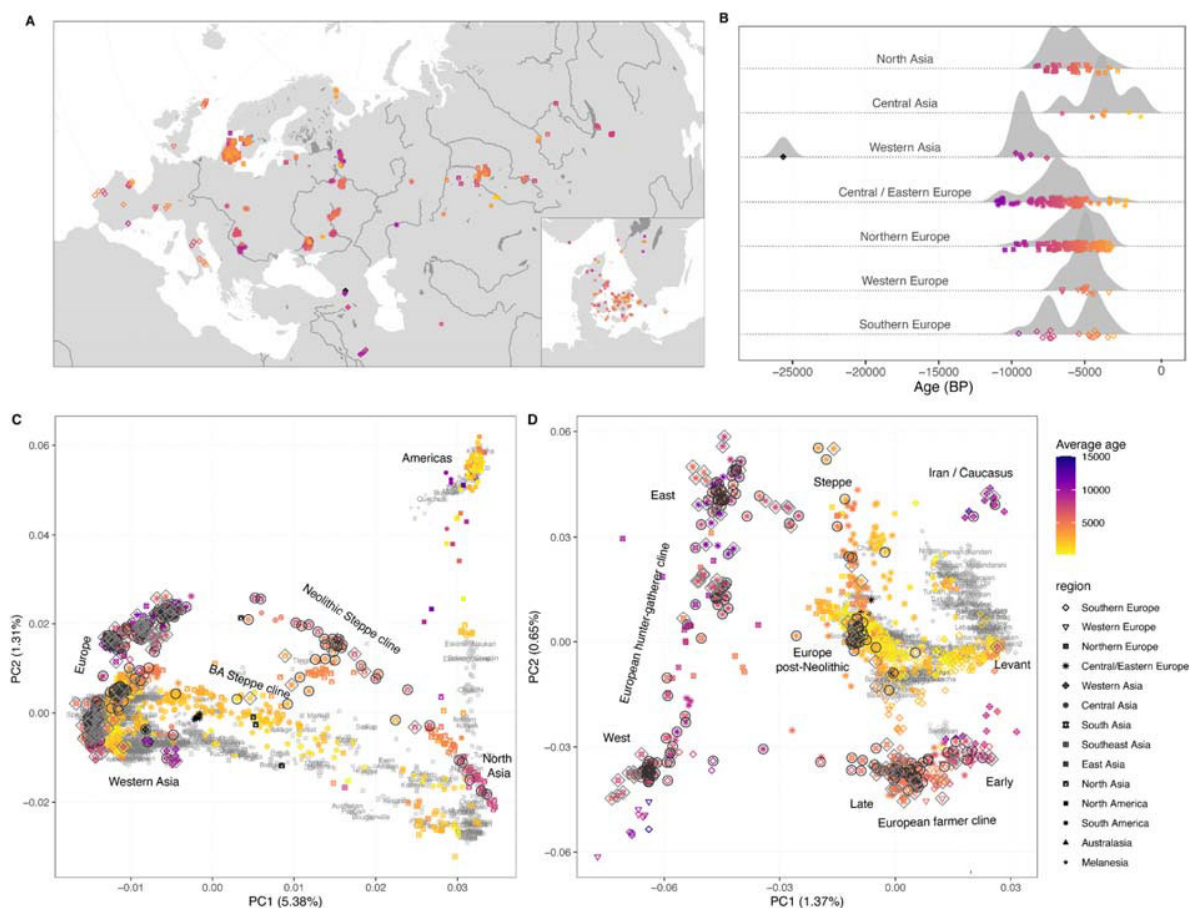
258 We extracted ancient DNA from tooth cementum or petrous bone and shotgun sequenced the 317
259 genomes to a depth of genomic coverage ranging from 0.01X to 7.1X (mean = 0.75X, median =
260 0.26X), with 81 individuals having >1X coverage. Using a new imputation method designed for
261 low-coverage sequencing data²⁶, we performed genotype imputation based on the 1,000 Genomes
262 phased data as a reference panel. We also imputed >1,300 previously published shotgun-sequenced
263 ancient genomes. This resulted in a “raw” dataset containing 8.5 million common Single Nucleotide
264 Polymorphisms (SNPs) (>1% MAF and imputation info score > 0.5) from 1,664 imputed diploid
265 ancient genomes. This number includes 42 high-coverage ancient genomes (Table S2.1,
266 Supplementary Note 2) that were down-sampled to values between 0.1X and 4X for validation.

267 This demonstrated that 1-fold genome coverage provides remarkably high imputation accuracy
268 ($r^2 > 0.95$ at common variants with MAF above 5%) and closely matches what is obtained for
269 modern samples (Extended Fig. 1A-D). African genomes, however, exhibit lower imputation
270 accuracy as a result of the poor representation of this ancestry in the reference panel. For European
271 genomes, this translates into genotyping error rates usually below 5% for the most challenging
272 genotypes to impute (heterozygous genotypes or with two copies of the non-reference allele;
273 Supplementary Fig. S2.1-S2.2). Imputation accuracy also depends on minor allele frequency and
274 genomic coverage (Supplementary Fig. S2.3). We find that coverage values as low as 0.1x and
275 0.4X are sufficient to obtain r^2 imputation accuracy of 0.8 and 0.9 at common variants
276 (MAF $\geq 10\%$), respectively. As further validation, we increased genomic coverage to 27.5X, 18.9X
277 and 5.4X on a previously published trio (mother, father, son) from the Late Neolithic mass burial at
278 Koszyce in Poland²⁷. This allowed for a validation of imputed genotypes and haplotypes using
279 Mendel's rules of inheritance. We obtained Mendelian error rates from 0.1% at 4X to 0.55% at
280 0.1X (Extended Fig. 1E). Similarly, we obtained switch error rates between 2% and 6%. Altogether,
281 our validation analysis showed that ancient European genomes can be imputed confidently from
282 coverages above 0.4X and highly valuable data can still be obtained with coverages as low as 0.1X
283 when using specific QC on the imputed data, although at very low coverage a bias arise towards the
284 major allele (see Supplementary Note 2). We filtered out samples with poor coverage or variant
285 sites with low MAF in downstream analyses depending on the specific data quality requirements.
286 For most analyses we use a subset of 1,492 imputed ancient genomes (213 sequenced in this study)
287 after filtering individuals with very low coverages ($< 0.1X$) and/or low imputation quality (average
288 genotype probability < 0.8) and close relatives. This dataset allows us to characterise the ancient
289 cross-continental gene pools and the demographic transitions with unprecedented resolution.

290
291 We performed broad-scale characterization of this dataset using principal component analysis
292 (PCA) and model-based clustering (ADMIXTURE), recapitulating and providing increased
293 resolution into previously described ancestry clines in ancient Eurasian populations (Fig. 1;
294 Extended Data Fig. 2; Supplementary Note 3d). Strikingly, inclusion of the imputed ancient
295 genomes in the inference of the principal components reveals much higher variance among the
296 ancient groups than previously anticipated using projection onto a PC-space inferred from modern
297 individuals alone (Extended Data Fig. 2). This is particularly notable in a PCA of West Eurasian
298 individuals, where genetic variation among all present-day populations is confined within a small
299 central area of the PCA (Extended Data Fig. 2C, D). These results are consistent with much higher
300 genetic differentiation between ancient Europeans than present-day populations reflecting lower
301 effective population sizes and genetic isolation among ancient groups.

302
303 To obtain a finer-scale characterization of genetic ancestries across space and time, we assigned
304 imputed ancient individuals to genetic clusters by applying hierarchical community detection on a
305 network of pairwise identity-by-descent (IBD)-sharing similarities²⁸ (Extended Data Fig. 3;
306 Supplementary Note 3c). The obtained clusters capture fine-scale genetic structure corresponding to
307 shared ancestry within particular spatiotemporal ranges and/or archaeological contexts, and were
308 used as sources and/or targets in supervised ancestry modelling (Extended Data Fig. 4;
309 Supplementary Note 3i). We focus our subsequent analyses on three panels of putative source
310 clusters reflecting different temporal depths: "deep", using a set of deep ancestry source groups
311 reflecting major ancestry poles; "postNeol", using diverse Neolithic and earlier source groups; and
312 "postBA", using Late Neolithic and Bronze Age source groups (Extended Data Fig. 4).

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Fig 1. Sample overview and broad scale genetic structure. (A), (B) Geographic and temporal distribution of the 317 ancient genomes reported here. Age and geographic region of ancient individuals are indicated by plot symbol colour and shape, respectively. Random jitter was added to geographic coordinates to avoid overplotting. (C), (D) Principal component analysis of 3,316 modern and ancient individuals from Eurasia, Oceania, and the Americas (C), as well as restricted to 2,126 individuals from western Eurasia (west of Urals) (D). Principal components were defined using both modern and imputed ancient genomes passing all filters, with the remaining low-coverage ancient genomes projected. Ancient genomes sequenced in this study are indicated with black circles (imputed genomes passing all filters, n=213) or grey diamonds (pseudo-haploid projected genomes, n=104). Genomes of modern individuals are shown in grey, with population labels corresponding to their median coordinates.

327 *Deep population structure of western Eurasians*

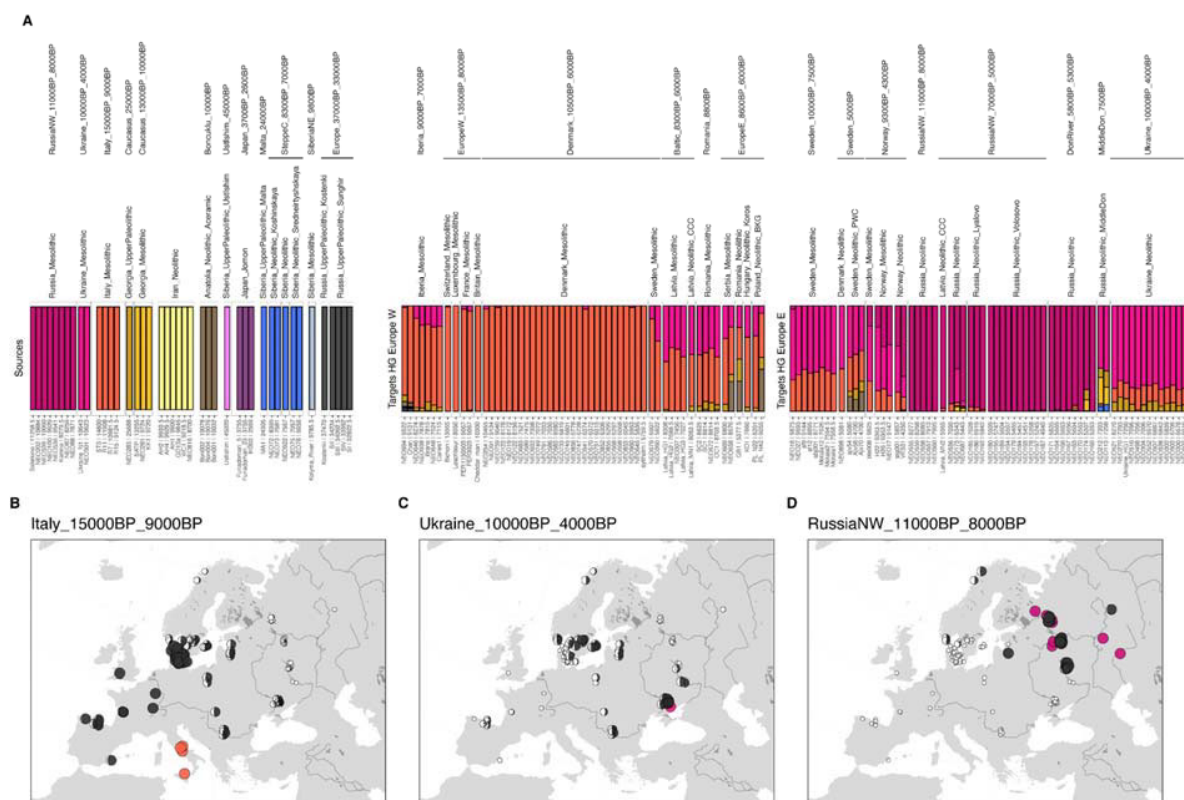
328 Our study comprises the largest genomic dataset on European hunter-gatherers to date, including
329 113 imputed hunter-gatherer genomes of which 79 were sequenced in this study. Among them, we
330 report a 0.83X genome of an Upper Palaeolithic (UP) skeleton from Kotias Klde Cave in Georgia,
331 Caucasus (NEO283), directly dated to 26,052 - 25,323 cal BP (95%). In the PCA of all non-African
332 individuals, it occupies a position distinct from other previously sequenced UP individuals, shifted
333 towards west Eurasians along PC1 (Supplementary Note 3d). Using admixture graph modelling, we
334 find that this Caucasus UP lineage derives from a mixture of predominantly West Eurasian UP
335 hunter-gatherer ancestry (76%) with ~24% contribution from a “basal Eurasian” ghost population,
336 first observed in West Asian Neolithic individuals²⁹ (Extended Data Fig. 5A). Models attempting to
337 reconstruct major post-LGM clusters such as European hunter-gatherers and Anatolian farmers
338 without contributions from this Caucasus UP lineage provided poor admixture graph fits or were
339 rejected in *qpAdm* analyses (Extended Data Fig. 5B,C). These results thus suggest a central role of

340 the descendants related to this Caucasus UP lineage in the formation of later West Eurasian
341 populations, consistent with recent genetic data from the nearby Dzudzuana Cave, also in
342 Georgia³⁰.

343
344 We performed supervised admixture modelling using a set of twelve possible source clusters
345 representing Mesolithic hunter-gatherers from the extremes of the HG cline, as well as temporal or
346 geographical outgroups of deep Eurasian lineages (Fig 2A). We replicate previous results of broad-
347 scale genetic structure correlated to geography in European hunter-gatherers after the LGM¹⁷, while
348 also revealing novel insights into their fine-scale structure. Ancestry related to southern European
349 hunter-gatherers (source: Italy_15000BP_9000 BP) predominates in western Europe. This includes
350 Denmark, where our 28 sequenced and imputed hunter-gatherer genomes derive almost exclusively
351 from this cluster, with remarkable homogeneity across a 5,000 year transect (Fig. 3A). In contrast,
352 hunter-gatherer individuals from the eastern and far northern reaches of Europe show the highest
353 proportions of Russian hunter-gatherer ancestry (source: RussiaNW_11000BP_8000BP; Fig. 2B,
354 D), with genetic continuity until ~5,000 BP in Russia. Ancestry related to Mesolithic hunter-
355 gatherer populations from Ukraine (source: Ukraine_10000BP_4000BP) is carried in highest
356 proportions in hunter-gatherers from a geographic corridor extending from south-eastern Europe
357 towards the Baltic and southern Scandinavia. Swedish Mesolithic individuals derive up to 60% of
358 their ancestry from that source (Fig. 2C). Our results thus indicate northwards migrations of at least
359 three distinct waves of hunter-gatherer ancestry into Scandinavia: a predominantly southern
360 European source into Denmark; a source related to Ukrainian and south-eastern European hunter-
361 gatherers into the Baltic and southern Sweden; and a northwest Russian source into the far north,
362 before venturing south along the Atlantic coast of Norway³¹ (Fig. 2). These movements are likely to
363 represent post glacial expansions from refugia areas shared with many plant and animal species^{32,33}.

364
365 Despite the major role of geography in shaping European hunter-gatherer structure, we also
366 document more complex local dynamics. On the Iberian Peninsula, the earliest individuals,
367 including a ~9,200-year-old hunter-gatherer (NEO694) from Santa Maira (eastern Spain),
368 sequenced in this study, show predominantly southern European hunter-gatherer ancestry with a
369 minor contribution from UP hunter-gatherer sources (Fig. 3). In contrast, later individuals from
370 Northern Iberia are more similar to hunter-gatherers from eastern Europe, deriving ~30-40% of
371 their ancestry from a source related to Ukrainian hunter-gatherers^{34,35}. The earliest evidence for this
372 gene flow is observed in a Mesolithic individual from El Mazo, Spain (NEO646) that was dated,
373 calibrated and reservoir-corrected to c. 8,200 BP (8365-8182 cal BP, 95%) but context-dated to
374 slightly older (8550-8330 BP, see³⁶). The younger date coincides with some of the oldest Mesolithic
375 geometric microliths in northern Iberia, appearing around 8,200 BP at this site³⁶. In southern
376 Sweden, we find higher amounts of southern European hunter-gatherer ancestry in late Mesolithic
377 coastal individuals (NEO260 from Evensås; NEO679 from Skateholm) than in the earlier
378 Mesolithic individuals from further inland, suggesting either geographic genetic structure in the
379 Swedish Mesolithic population or a possible eastward expansion of hunter-gatherers from
380 Denmark, where this ancestry prevailed (Fig. 3). An influx of southern European hunter-gatherer-
381 related ancestry in Ukrainian individuals after the Mesolithic (Fig. 3) suggests a similar eastwards
382 expansion in south-eastern Europe¹⁷. Interestingly, two herein reported ~7,300-year-old imputed
383 genomes from the Middle Don River region in the Pontic-Caspian steppe (Golubaya Krinitisa,
384 NEO113 & NEO212) derive ~20-30% of their ancestry from a source cluster of hunter-gatherers
385 from the Caucasus (Caucasus_13000BP_10000BP) (Fig. 3). Additional lower coverage (non-
386 imputed) genomes from the same site project in the same PCA space (Fig. 1D), shifted away from
387 the European hunter-gatherer cline towards Iran and the Caucasus. Our results thus document
388 genetic contact between populations from the Caucasus and the Steppe region as early as 7,300
389 years ago, providing documentation of continuous admixture prior to the advent of later nomadic

390 Steppe cultures, in contrast to recent hypotheses, and also further to the west than previously
 391 reported^{17,37}.
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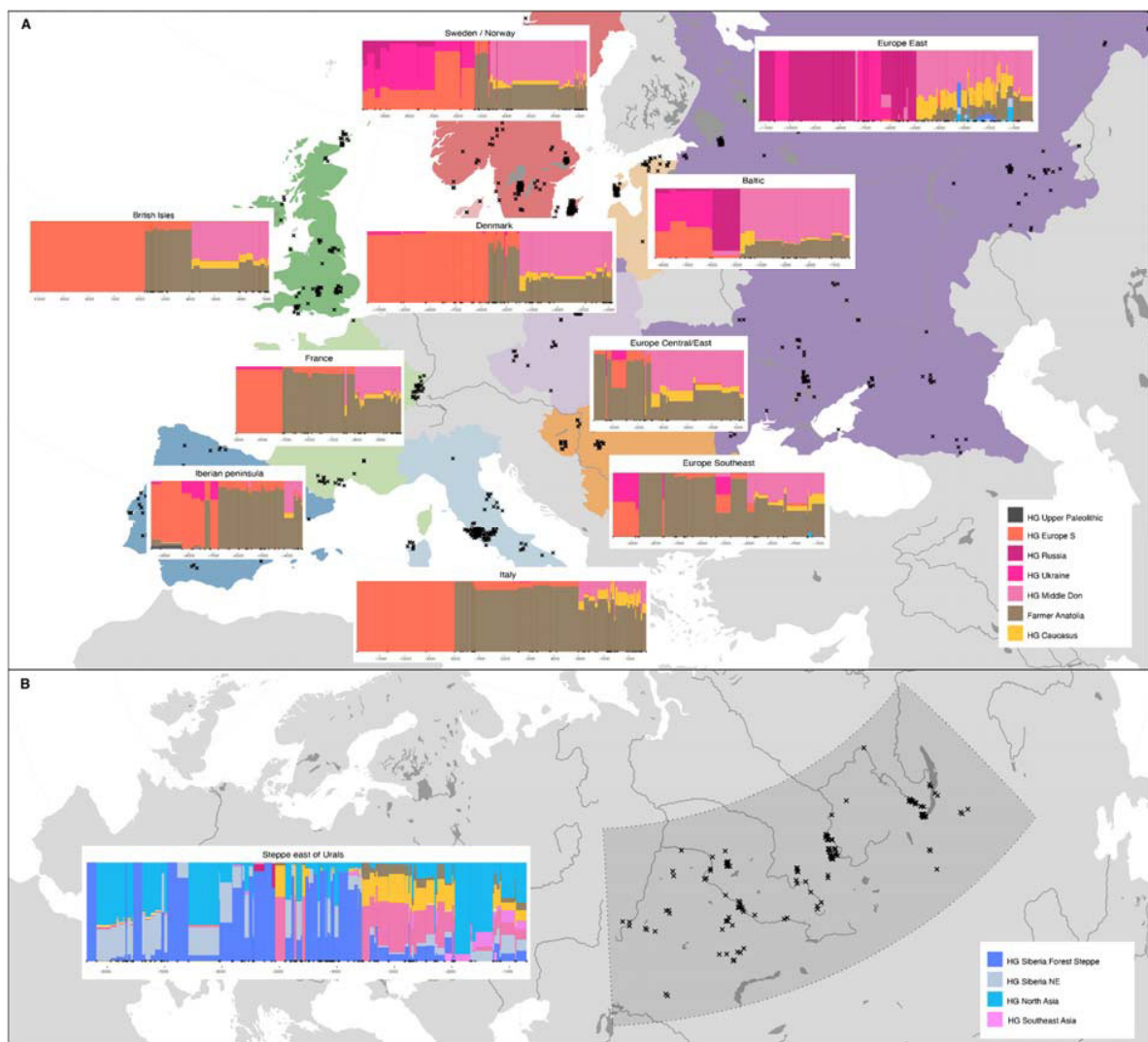
393
 394 **Fig 2. Genetic structure of European hunter-gatherers** (A) Ancestry proportions in 113 imputed ancient genomes
 395 representing European hunter-gatherer contexts (right) estimated from supervised non-negative least squares analysis
 396 using deep Eurasian source groups (left). Individuals from target groups are grouped by genetic clusters. (B)-(D) Moon
 397 charts showing spatial distribution of ancestry proportions in European hunter-gatherers deriving from three deep
 398 Eurasian source groups; Italy_15000BP_9000BP; Ukraine_10000BP_4000BP; RussiaNW_11000BP_8000BP (source
 399 origins shown with coloured symbol). Estimated ancestry proportions are indicated by both size and amount of fill of
 400 moon symbols.
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 402

403 *Major genetic transitions in Europe*

404 Previous ancient genomics studies have documented multiple episodes of large-scale population
 405 turnover in Europe within the last 10,000 years^{6,11,14,16,17,20,21,34,38-41}. The 317 genomes reported here
 406 fill important knowledge gaps, particularly in northern and eastern Europe, allowing us to track the
 407 dynamics of these events at both continental and regional scales.
 408

409 Our analyses reveal profound differences in the spatiotemporal Neolithisation dynamics across
 410 Europe. Supervised admixture modelling (“deep” set) and spatiotemporal kriging⁴² document a
 411 broad east-west distinction along a boundary zone running from the Black Sea to the Baltic. On the
 412 western side of this “Great Divide”, the Neolithic transition is accompanied by large-scale shifts in
 413 genetic ancestry from local hunter-gatherers to Neolithic farmers with Anatolian-related ancestry
 414 (Boncuklu_10000BP; Fig. 3; Extended Data Fig. 4, 6). The arrival of Anatolian-related ancestry in
 415 different regions spans an extensive time period of over 3,000 years, from its earliest evidence in
 416 the Balkans (Lepenski Vir) at ~8,700 BP¹⁷ to c. 5,900 BP in Denmark. On the eastern side of this
 417 divide, no ancestry shifts can be observed during this period. In the East Baltic region (see also⁴³),

418 Ukraine and Western Russia local hunter-gatherer ancestry prevails until ~5,000 BP without
419 noticeable input of Neolithic Anatolian-related farmer ancestry (Fig. 3; Extended Data Fig. 4, 6).
420 This Eastern genetic continuity is in remarkable congruence with the archaeological record showing
421 persistence of pottery-using hunter-gatherer-fisher groups in this wide region, and delayed
422 introduction of cultivation and husbandry by several thousand years (Supplementary Note 5).
423
424 From approximately 5,000 BP, an ancestry component appears on the eastern European plains in
425 Early Bronze Age Steppe pastoralists associated with the Yamnaya culture and it rapidly spreads
426 across Europe through the expansion of the Corded Ware complex (CWC) and related cultures^{20,21}.
427 We demonstrate that this “steppe” ancestry (Steppe_5000BP_4300BP) can be modelled as a
428 mixture of ~65% ancestry related to herein reported hunter-gatherer genomes from the Middle Don
429 River region (MiddleDon_7500BP) and ~35% ancestry related to hunter-gatherers from Caucasus
430 (Caucasus_13000BP_10000BP) (Extended Data Fig. 4). Thus, Middle Don hunter-gatherers, who
431 already carry ancestry related to Caucasus hunter-gatherers (Fig. 2), serve as a hitherto unknown
432 proximal source for the majority ancestry contribution into Yamnaya genomes. The individuals in
433 question derive from the burial ground Golubaya Krinitsa (Supplementary Note 3). Material culture
434 and burial practices at this site are similar to the Mariupol-type graves, which are widely found in
435 neighbouring regions of Ukraine, for instance along the Dnepr River. They belong to the group of
436 complex pottery-using hunter-gatherers mentioned above, but the genetic composition at Golubaya
437 Krinitsa is different from the remaining Ukrainian sites (Fig 2A, Extended Data Fig. 4). We find
438 that the subsequent transition of the Late Neolithic and Early Bronze Age European gene pool
439 happened at a faster pace than during the Neolithisation, reaching most parts of Europe within a
440 ~1,000-year time period after first appearing in eastern Baltic region ~4,800 BP (Fig. 3). In line
441 with previous reports we observe that beginning c. 4,200 BP, steppe-related ancestry was already
442 dominant in samples from France and the Iberian peninsula, while it reached Britain only 400 years
443 later^{11,38,44}. Strikingly, because of the delayed Neolithisation in Southern Scandinavia these
444 dynamics resulted in two episodes of large-scale genetic turnover in Denmark and southern Sweden
445 within a 1,000-year period (Fig. 3).
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Fig. 3. Genetic transects of Eurasia. Regional timelines of genetic ancestry compositions within the past 15,000 years in western Eurasia (top) and the Eurasian Steppe belt east of the Urals (bottom). Ancestry proportions in 972 imputed ancient genomes from these regions (covering c. 12,000 BP to 500 BP), inferred using supervised admixture modelling with “deep” hunter-gatherer ancestry source groups. Geographic areas included in timelines are indicated with fill colour (west Eurasia) and grey shading (eastern Steppe region). Excavation locations of the ancient skeletons are indicated with black crosses. Coloured bars within the timelines represent ancestry proportions for temporally consecutive individuals, with the width corresponding to their age difference. Individuals with identical age were offset along the time axis by adding random jitter, ages. We note that the inclusion of only shotgun-sequenced samples may affect the exact timing of events in some regions from where such data are sparse.

460 We next investigated fine-grained ancestry dynamics underlying these transitions. We replicate
461 previous reports^{11,16,17,21,41,45,46} of widespread, but low-level admixture between Neolithic farmers
462 and local hunter-gatherers resulting in a resurgence of HG ancestry in many regions of Europe
463 during the middle and late Neolithic (Extended Data Fig. 7). Estimated hunter-gatherer ancestry
464 proportions among early Neolithic people rarely exceed 10%, with notable exceptions observed in
465 individuals from south-eastern Europe (Iron Gates), Sweden (Pitted Ware Culture) as well as herein
466 reported early Neolithic genomes from Portugal (western Cardial), estimated to harbour 27% – 43%
467 Iberian hunter-gatherer ancestry (Iberia_9000BP_7000BP). The latter result, suggesting extensive
468 first-contact admixture, is in agreement with archaeological inferences derived from modelling the

469 spread of farming along west Mediterranean Europe⁴⁷. Individuals associated with Neolithic
470 farming cultures from Denmark show some of the highest overall hunter-gatherer ancestry
471 proportions (up to ~25%), mostly derived from Western European-related hunter-gatherers
472 (EuropeW_13500BP_8000BP) supplemented with marginal contribution from local Danish groups
473 in some individuals (Extended Data Fig. 7D; Supplementary Note 3f). We estimated the timing of
474 the admixture using the linkage-disequilibrium-based method DATES⁴⁸ at ~6,000 BP. Both lines of
475 evidence thus suggest that a significant part of the hunter-gatherer admixture observed in Danish
476 Neolithic individuals occurred already before the arrival of the incoming Neolithic people in the
477 region (Extended Data Fig. 7), and further imply Central Europe as a key region in the resurgence
478 of HG ancestry. Interestingly, the genomes of two ~5,000-year-old Danish male individuals
479 (NEO33, NEO898) were entirely composed of Swedish hunter-gatherer ancestry, and formed a
480 cluster with Pitted Ware Culture (PWC) individuals from Ajvide on the Baltic island of Gotland
481 (Sweden)^{49–51}. Of the two individuals, NEO033 also displays an outlier Sr-signature (Fig. 4),
482 potentially suggesting a non-local origin matching his unusual ancestry. Overall, our results
483 demonstrate direct contact across the Kattegat and Öresund during Neolithic times (Extended Data
484 Fig. 3, 4), in line with archaeological finds from Zealand (east Denmark) showing cultural affinities
485 to PWC on the Swedish west coast^{52–55}.

486
487 Further, we find evidence for regional stratification in early Neolithic farmer ancestries in
488 subsequent Neolithic groups. Specifically, southern European early farmers appear to have provided
489 major genetic ancestry to mid- and late Neolithic groups in Western Europe, while central European
490 early farmer ancestry is mainly observed in subsequent Neolithic groups in eastern Europe and
491 Scandinavia (Extended Data Fig. 7D-F). These results are consistent with distinct migratory routes
492 of expanding farmer populations as previously suggested⁸. For example, similarities in material
493 culture and flint mining activities could suggest that the first farmers in South Scandinavia
494 originated from or had close social relations with the central European Michelsberg Culture⁵⁶.

495
496 The second continental-wide and CWC-mediated transition from Neolithic farmer ancestry to
497 Steppe-related ancestry was found to differ markedly between geographic regions. The contribution
498 of local Neolithic farmer ancestry to the incoming groups was high in eastern, western and southern
499 Europe, reaching >50% on the Iberian Peninsula (“postNeol” set; Extended Data Fig. 4, 6B, C)³⁴.
500 Scandinavia, however, portrays a dramatically different picture, with a near-complete replacement
501 of the local Neolithic farmer population inferred across all sampled individuals (Extended Data Fig.
502 7B, C). Following the second transition, Neolithic Anatolian-related farmer ancestry remains in
503 Scandinavia, but the source is now different. It can be modelled as deriving almost exclusively from
504 a genetic cluster associated with the Late Neolithic Globular Amphora Culture (GAC)
505 (Poland_5000BP_4700BP; Extended Data Fig. 4). Strikingly, after the Steppe-related ancestry was
506 first introduced into Europe (Steppe_5000BP_4300BP), it expanded together with GAC-related
507 ancestry across all sampled European regions (Extended Data Fig. 7I). This suggests that the spread
508 of steppe-related ancestry throughout Europe was predominantly mediated through groups that were
509 already admixed with GAC-related farmer groups of the eastern European plains. This finding has
510 major implications for understanding the emergence of the CWC. A stylistic connection from GAC
511 ceramics to CWC ceramics has long been suggested, including the use of amphora-shaped vessels
512 and the development of cord decoration patterns⁵⁷. Moreover, shortly prior to the emergence of the
513 earliest CWC groups, eastern GAC and western Yamnaya groups exchanged cultural elements in
514 the forest-steppe transition zone northwest of the Black Sea, where GAC ceramic amphorae and
515 flint axes were included in Yamnaya burials, and the typical Yamnaya use of ochre was included in
516 GAC burials⁵⁸, indicating close interaction between the groups. Previous ancient genomic data from
517 a few individuals suggested that this was limited to cultural influences and not population
518 admixture⁵⁹. However, in the light of our new genetic evidence it appears that this zone, and

519 possibly other similar zones of contact between GAC and Yamnaya (or other closely-related
520 steppe/forest-steppe groups) were key in the formation of the CWC through which steppe-related
521 ancestry and GAC-related ancestry co-dispersed far towards the west and the north^{cf. 60}. This
522 resulted in regionally diverse situations of interaction and admixture^{61,62} but a significant part of the
523 CWC dispersal happened through corridors of cultural and demic transmission which had been
524 established by the GAC during the preceding period^{63,64}.

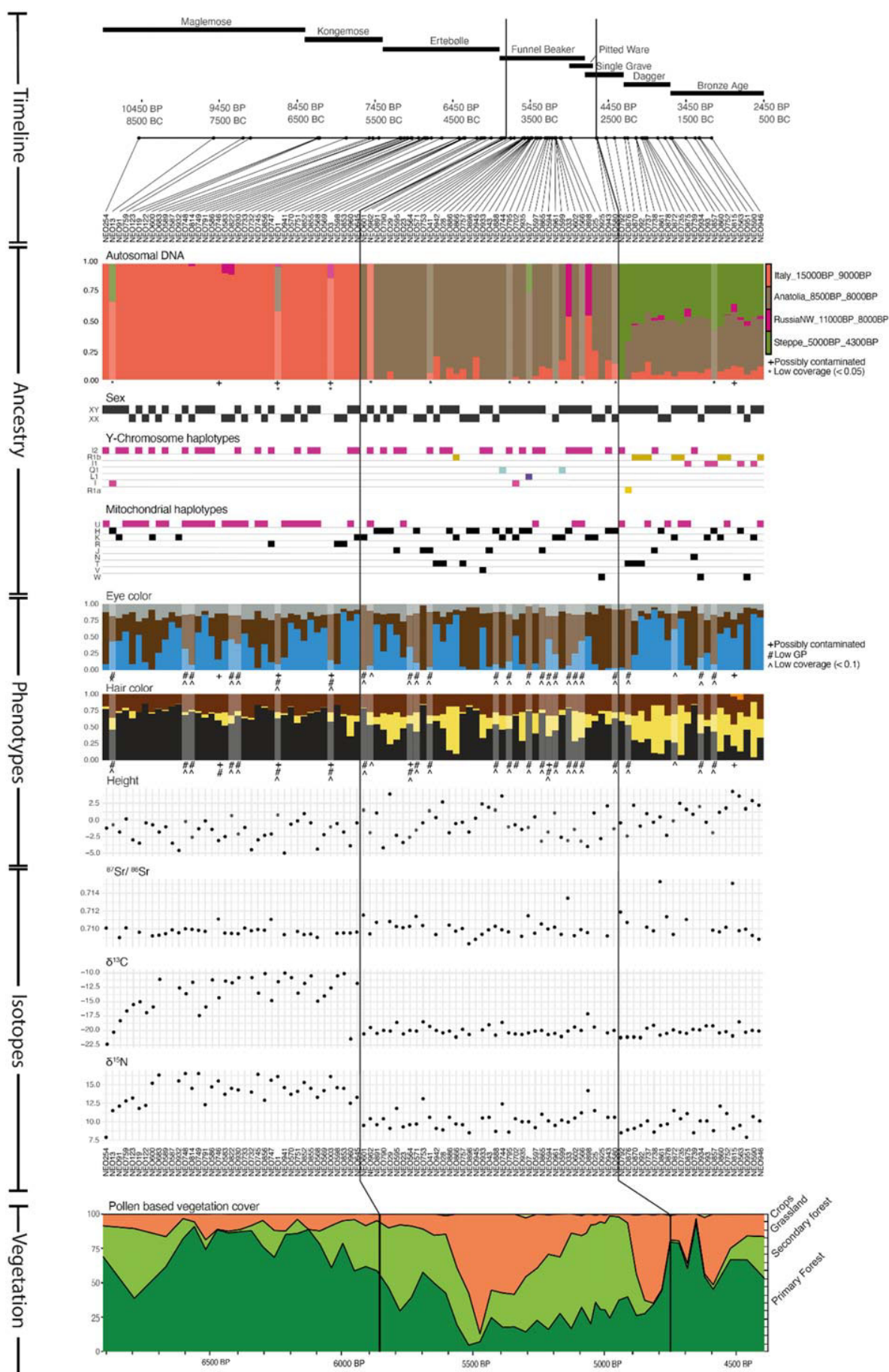
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527 *Fine-scale structure and multiproxy analysis of Danish transect*

528 We present a detailed and continuous sequence of multiproxy data from Denmark, from the Early
529 Mesolithic Maglemose, via the Kongemose and Late Mesolithic Ertebølle epochs, the Early and
530 Middle Neolithic Funnel Beaker Culture and the Single Grave Culture, to Late Neolithic and
531 Bronze Age individuals (Fig. 4). To integrate multiproxy data from as many skeletons as possible
532 we made use of non-imputed data for the admixture analyses (Supplementary Note S3d) which
533 were not restricted to the >0.1X coverage cut-off used elsewhere. This provided genetic profiles
534 from 100 Danish individuals (Fig 4), spanning c. 7,300 years from the earliest known skeleton in
535 Denmark (the Mesolithic “Koelbjerg Man” (NEO254, 10,648-10,282 cal. BP, 95% probability
536 interval) and formerly known as the “Koelbjerg Woman”⁶⁵), to a Bronze Age skeleton from Hove Å
537 (NEO946) dated to 3322-2967 cal. BP (95%). Two temporal shifts in genomic admixture
538 proportions confirm the major population genetic turnovers (Fig. 4) that was inferred from imputed
539 data (Fig. 3). The multiproxy evidence, however, unveils the dramatic concomitant changes in all
540 investigated phenotypic, environmental and dietary parameters (Fig. 4).

541



543

544 **Fig 4. Environmental, dietary, phenotypic and ancestry shifts in Denmark through time.** Two dramatic population
545 turnovers are evident from chronologically-sorted multiproxy data representing 100 Danish Stone Age and early Bronze
546 Age skeletons sequenced in this study. The figure shows concomitant changes in several investigated parameters
547 including (from the top) admixture proportions from non-imputed autosomal genome-wide data, Y-chromosomal and
548 mitochondrial haplogroups, genetic phenotype predictions (based on imputed data) as well as $^{87}\text{Sr}/^{86}\text{Sr}$ and $\delta^{13}\text{C}$ and
549 $\delta^{15}\text{N}$ isotope data as possible proxies for mobility and diet, respectively. Predicted height values represent differences
550 (in cm) from the average height of the present-day Danish population, based on genotypes at 310 height-associated loci
551 (Supplementary Note 4f). Probabilities for the indicated natural eye and hair colours are based on genotypes at 18
552 pigmentation-associated loci (Supplementary Note 4f) with grey denoting probability of intermediate eye colour
553 (including grey, green and hazel). Lower panel shows changes in vegetation as predicted from pollen analyses at Lake
554 Højby in Zealand (Supplementary Note 12). Black vertical lines mark the first presence of Anatolian farmer ancestry
555 and Steppe-related ancestry, respectively.

556

557

558 During the Danish Mesolithic, individuals from the Maglemose, Kongemose and Ertebølle cultures
559 displayed a remarkable genetic homogeneity across a 5,000 year transect deriving their ancestry
560 almost exclusively from a southern European source (source: Italy_15000BP_9000BP) that later
561 predominates in western Europe (Fig. 2). These cultural transitions occurred in genetic continuity,
562 apparent in both autosomal and uniparental markers, which rules out demic diffusion and supports
563 the long-held assumption of a continuum of culture and population^{e.g. 66–68}. Genetic predictions
564 indicate blue eye pigmentation with high probability in several individuals throughout the duration
565 of the Mesolithic (Supplementary Note 4f), consistent with previous findings^{11,20,45}. In contrast,
566 none of the analysed Mesolithic individuals displayed high probability of light hair pigmentation.
567 Height predictions for Mesolithic individuals generally suggest slightly lower or perhaps less
568 variable genetic values than in the succeeding Neolithic period. However, we caution that the
569 relatively large genetic distance to modern individuals included in the GWAS panel make these
570 scores poorly applicable to Mesolithic individuals (Supplementary Note 4c) and are dependent on
571 the choice of GWAS filters used. Unfortunately, only a fraction of the 100 Danish skeletons
572 included were suitable for stature estimation by actual measurement, why these values are not
573 reported.

574

575 Stable isotope $\delta^{13}\text{C}$ values in collagen inform on the proportion of marine versus terrestrial protein,
576 while $\delta^{15}\text{N}$ values reflect the trophic level of protein sources^{69,70}. Both the Koelbjerg Man and the
577 second earliest human known from Denmark, (Tømmerupgårds Mose – not part of the present
578 study; see⁷¹) showed more depleted dietary isotopic values, representing a lifestyle of inland hunter-
579 fisher-gatherers of the early Mesolithic forest. A second group consisted of coastal fisher-hunter-
580 gatherers dating to the late half of the Maglemose epoch onwards (Supplementary Figs. S10.1 and
581 S10.2). During this period global sea-level rise gradually changed the landscape of present-day
582 Denmark from an interior part of the European continent to an archipelago, where all human groups
583 had ample access to coastal resources within their annual territories. Increased $\delta^{13}\text{C}$ and $\delta^{15}\text{N}$ values
584 imply that from the late Maglemose marine foods gradually increased in importance, to form the
585 major supply of proteins in the final Ertebølle period^{71,cf. 72}. Interestingly, rather stable $^{87}\text{Sr}/^{86}\text{Sr}$
586 isotope ratios throughout the Mesolithic indicate limited mobility, in agreement with the evidence
587 for genetic continuity reported here and modelled in previous work^{73,74 Fig. 3}, and/or dietary sources
588 from homogeneous environments.

589

590 The arrival of Neolithic farmer-related ancestry at c. 5,900 BP in Denmark resulted in a population
591 replacement with very limited genetic contribution from the local hunter-gatherers. The shift is
592 abrupt and brings changes in all the measured parameters. This is a clear case of demic diffusion,
593 which settles a long-standing debate concerning the neolithisation process in Denmark^{15,56,75,76}, at
594 least at a broader population level. The continuing use of coastal kitchen middens well into the

595 Neolithic^{77,78} remains, however, an enigma, although this may represent sites where local remnants
596 of Mesolithic groups survived in partly acculturated form, or it could be middens taken over by the
597 newcomers. Concomitant shifts in both autosomal and uniparental genetic markers show that the
598 migration by incoming farmers was not clearly sex-biased but more likely involved nuclear family
599 units. Diet shifted abruptly to terrestrial sources evidenced by $\delta^{13}\text{C}$ values around -20 ‰ and $\delta^{15}\text{N}$
600 values around 10 ‰ in line with archaeological evidence that domesticated crops and animals were
601 now providing the main supply of proteins (Supplementary Note 6). Isotope values remained stable
602 at these levels throughout the following periods, although with somewhat greater variation after c.
603 4,500 BP. However, five Neolithic and Early Bronze Age individuals have $\delta^{13}\text{C}$ and $\delta^{15}\text{N}$ values
604 indicating intake of high trophic marine food. This is most pronouncedly seen for NEO898
605 (Svinninge Vejle) who was one of the two aforementioned Danish Neolithic individuals displaying
606 typical Swedish PWC hunter-gatherer ancestry. A higher variability in $^{87}\text{Sr}/^{86}\text{Sr}$ values can be seen
607 with the start of the Neolithic and this continues in the later periods, which suggests that the
608 Neolithic farmers in Denmark consumed food from more diverse landscapes and/or they were more
609 mobile than the preceding hunter-gatherers (Supplementary Note 11). The Neolithic transition also
610 marks a considerable rise in frequency of major effect alleles associated with light hair
611 pigmentation⁷⁹, whereas polygenic score predictions for height are generally low throughout the
612 first millennium of the Neolithic (Funnel Beaker epoch), echoing previous findings based on a
613 smaller set of individuals^{45,80}.

614
615 We do not know how the Mesolithic Ertebølle population disappeared. Some may have been
616 isolated in small geographical pockets of brief existence and/or adapted to a Neolithic lifestyle but
617 without contributing much genetic ancestry to subsequent generations. The most recent individual
618 in our Danish dataset with Mesolithic WHG ancestry is “Dragsholm Man” (NEO962), dated to
619 5,947-5,664 cal. BP (95%) and archaeologically assigned to the Neolithic Funnel Beaker farming
620 culture based on his grave goods^{81,82}. Our data confirms a typical Neolithic diet matching the
621 cultural affinity but contrasting his WHG ancestry. Thus, Dragsholm Man represents a local person
622 of Mesolithic ancestry who lived in the short Mesolithic-Neolithic transition period and adopted a
623 Neolithic culture and diet. A similar case of very late Mesolithic WHG ancestry in Denmark was
624 observed when analysing human DNA obtained from a piece of chewed birch pitch dated to 5,858–
625 5,661 cal. BP (95%)⁸³.

626
627 The earliest example of Anatolian Neolithic ancestry in our Danish dataset is observed in a bog
628 skeleton of a female from Viksø Mose (NEO601) dated to 5,896-5,718 cal. BP (95%) (and hence
629 potentially contemporaneous with Dragsholm Man) whereas the most recent Danish individual
630 showing Anatolian ancestry without any Steppe-related ancestry is NEO943 from Stenderup Hage,
631 dated to 4,818-4,415 cal. BP (95%). Using Bayesian modelling we estimate the duration between
632 the first appearance of Anatolian ancestry to the first appearance of Steppe-related ancestry in
633 Denmark to be between 876 and 1100 years (95% probability interval, Supplementary Note 9)
634 indicating that the typical Neolithic ancestry was dominant for less than 50 generations in Denmark.
635 From this point onwards the steppe-ancestry was introduced, signalling the rise of the late Neolithic
636 Corded Ware derived cultures in Denmark (i.e. Single Grave Culture), followed by the later
637 Neolithic Dagger epoch and Bronze Age cultures. While this introduced a major new component in
638 the Danish gene pool, it was not accompanied by apparent shifts in diet. Our complex trait
639 predictions indicate an increase in “genetic height” occurring concomitant with the introduction of
640 Steppe-related ancestry, which is consistent with Steppe individuals (e.g., Yamnaya) being
641 genetically taller on average⁴⁵ and with previous results from other European regions^{80,84}.

642
643 These major population turnovers were accompanied by significant environmental changes, as
644 apparent from high-resolution pollen diagrams from Lake Højby in Northwest Zealand

645 reconstructed using the Landscape Reconstruction Algorithm (LRA⁸⁵ (Supplementary Note 8).
646 While the LRA has previously been applied at low temporal resolution regional scale e.g. ^{86,87}, and at
647 local scale to Iron Age and later pollen diagrams e.g. ^{88,89}, this is the first time this quantitative
648 method is applied at local scale to a pollen record spanning the Mesolithic and Neolithic periods in
649 Denmark. Comparison with existing pollen records show that the land cover changes demonstrated
650 here reflect the general vegetation development in eastern Denmark, while the vegetation on the
651 sandier soils of western Jutland maintains a more open character throughout the sequence
652 (Supplementary Note 12). We find that during the Mesolithic (i.e. before c. 6,000 BP) the
653 vegetation was dominated by primary forest trees (*Tilia*, *Ulmus*, *Quercus*, *Fraxinus*, *Alnus* etc.).
654 The forest composition changed towards more secondary, early successional trees (*Betula* and then
655 *Corylus*) in the earliest Neolithic, but only a minor change in the relationship between forest and
656 open land is recorded. From c. 5,650 BP deforestation intensified, resulting in a very open
657 grassland-dominated landscape. This open phase was short-lived, and secondary forest expanded
658 from 5,500 to 5,000 BP, until another episode of forest clearance gave rise to an open landscape
659 during the last part of the Funnel Beaker epoch. We thus conclude that the agriculture practice was
660 characterised by repeated clearing of the forest with fire, followed by regrowth. This strategy
661 changed with the onset of the Single Grave Culture, when the forest increased again, but this time
662 dominated by primary forest trees, especially *Tilia* and *Ulmus*. This reflects the development of a
663 more permanent division of the landscape into open grazing areas and forests. In contrast, in
664 western Jutland this phase was characterised by large-scale opening of the landscape, presumably as
665 a result of human impact aimed at creating pastureland⁹⁰.

666
667 Finally, we investigated the fine-scale genetic structure in southern Scandinavia after the
668 introduction of Steppe-related ancestry using a temporal transect of 38 Late Neolithic and Early
669 Bronze Age Danish and southern Swedish individuals. Although the overall population genomic
670 signatures suggest genetic stability, patterns of pairwise IBD-sharing and Y-chromosome
671 haplogroup distributions indicate at least three distinct ancestry phases during a ~1,000-year time
672 span: i) An early stage between ~4,600 BP and 4,300 BP, where Scandinavians cluster with early
673 CWC individuals from Eastern Europe, rich in Steppe-related ancestry and males with an R1a Y-
674 chromosomal haplotype (Extended Data Fig. 8A, B); ii) an intermediate stage until c. 3,800 BP,
675 where they cluster with central and western Europeans dominated by males with distinct sub-
676 lineages of R1b-L51 (Extended Data Fig. 8C, D; Supplementary Note 3b) and includes Danish
677 individuals from Borreby (NEO735, 737) and Madesø (NEO752) with distinct cranial features
678 (Supplementary Note 6); and iii) a final stage from c. 3,800 BP onwards, where a distinct cluster of
679 Scandinavian individuals dominated by males with I1 Y-haplogroups appears (Extended Data Fig.
680 8E). Using individuals associated with this cluster (Scandinavia_4000BP_3000BP) as sources in
681 supervised ancestry modelling (see “postBA”, Extended Data Fig. 4), we find that it forms the
682 predominant source for later Iron- and Viking Age Scandinavians, as well as ancient European
683 groups outside Scandinavia who have a documented Scandinavian or Germanic association (e.g.,
684 Anglo-Saxons, Goths; Extended Data Fig. 4). Y-chromosome haplogroup I1 is one of the dominant
685 haplogroups in present-day Scandinavians, and we document its earliest occurrence in a ~4,000-
686 year-old individual from Falköping in southern Sweden (NEO220). The rapid expansion of this
687 haplogroup and associated genome-wide ancestry in the early Nordic Bronze Age indicates a
688 considerable reproductive advantage of individuals associated with this cluster over the preceding
689 groups across large parts of Scandinavia.

690
691

692 *Hunter-gatherer resilience east of the Urals*

693 In contrast to the significant number of ancient hunter-gatherer genomes from western Eurasia
694 studied to date, genomic data from hunter-gatherers east of the Urals remain sparse. These regions
695 are characterised by an early introduction of pottery from areas further east and are inhabited by
696 complex hunter-gatherer-fisher societies with permanent and sometimes fortified settlements
697 (Supplementary Note 5; ⁹¹).

698
699 Here, we substantially expand the knowledge on ancient Stone Age populations of this region by
700 reporting new genomic data from 38 individuals, 28 of which date to pottery-associated hunter-
701 gatherer contexts e.g. ⁹² between 8,300-5,000 BP (Supplementary Table II). The majority of these
702 genomes form a previously only sparsely sampled ^{48,93} “Neolithic Steppe” cline spanning the
703 Siberian Forest Steppe zones of the Irtysh, Ishim, Ob, and Yenisei River basins to the Lake Baikal
704 region (Fig. 1C; Extended Data Fig. 2A, 3E). Supervised admixture modelling (using the “deep” set
705 of ancestry sources) revealed contributions from three major sources in these hunter gatherers from
706 east of Urals: early West Siberian hunter-gatherer ancestry (SteppeC_8300BP_7000BP) dominated
707 in the western Forest Steppe; Northeast Asian hunter-gatherer ancestry (Amur_7500BP) was
708 highest at Lake Baikal; and Paleosiberian ancestry (SiberiaNE_9800BP) was observed in a cline of
709 decreasing proportions from northern Lake Baikal westwards across the Forest Steppe (Extended
710 Data Fig. 4, 9). ⁹³

711
712 We used these Neolithic hunter-gatherer clusters (“postNeol” ancestry source set, Extended Data
713 Fig. 4) as putative source groups in more proximal admixture modelling to investigate the
714 spatiotemporal dynamics of ancestry compositions across the Steppe and Lake Baikal after the
715 Neolithic period. We replicate previously reported evidence for a genetic shift towards higher
716 Forest Steppe hunter-gatherer ancestry (SteppeCE_7000BP_3600BP) in late Neolithic and early
717 Bronze Age individuals (LNBA) at Lake Baikal ^{93,94}. However, ancestry related to this cluster is
718 already observed at ~7,000 BP in herein-reported Neolithic hunter-gatherer individuals both at Lake
719 Baikal (NEO199, NEO200), and along the Angara river to the north (NEO843). Both male
720 individuals at Lake Baikal belonged to Y-chromosome haplogroup Q1, characteristic of the later
721 LNBA groups in the same region. (Extended Data Fig. 3, 6A). Together with an estimated date of
722 admixture of ~6,000 BP for the LNBA groups, these results suggest gene flow between hunter-
723 gatherers of Lake Baikal and the south Siberian forest steppe regions already during the early
724 Neolithic. This is consistent with archaeological interpretations of contact. In this region, bifacially
725 flaked tools first appeared near Baikal ⁹⁵ from where the technique spread far to the west. We find
726 its reminiscences in Late Neolithic archaeological complexes (Shiderty 3, Borly, Sharbakty 1, Ust-
727 Narym, etc.) in Northern and Eastern Kazakhstan, around 6,500-6,000 BP ^{96,97}. Our herein-reported
728 genomes also shed light on the genetic origins of the early Bronze Age Okunevo culture in the
729 Minusinsk Basin in Southern Siberia. In contrast to previous results, we find no evidence for Lake
730 Baikal hunter-gatherer ancestry in the Okunevo ^{93,94}, suggesting that they instead originate from a
731 three-way mixture of two different genetic clusters of Siberian forest steppe hunter-gatherers and
732 Steppe-related ancestry (Extended Data Fig. 4D). We date the admixture with Steppe-related
733 ancestry to ~4,600 BP, consistent with gene flow from peoples of the Afanasievo culture that
734 existed near Altai and Minusinsk Basin during the early eastwards’ expansion of Yamnaya-related
735 groups ^{20,94}.

736
737 From around 3,700 BP, individuals across the Steppe and Lake Baikal regions display markedly
738 different ancestry profiles (Fig. 3; Extended Data Fig. 4D, 9). We document a sharp increase in
739 non-local ancestries, with only limited ancestry contributions from local hunter-gatherers. The early
740 stages of this transition are characterised by influx of Yamnaya-related ancestry, which decays over

741 time from its peak of ~70% in the earliest individuals. Similar to the dynamics in western Eurasia,
742 Yamnaya-related ancestry is here correlated with late Neolithic GAC-related farmer ancestry
743 (Poland_5000BP_4700BP; Extended Data Fig. 9G), recapitulating the previously documented
744 eastward expansion of admixed Western Steppe pastoralists from the Sintashta and Andronovo
745 complexes during the Bronze Age^{20,48,98}. However, GAC-related ancestry is notably absent in
746 individuals of the Okunevo culture, providing further support for two distinct eastward migrations
747 of Western Steppe pastoralists during the early (Yamnaya) and later (Sintashta, Andronovo) Bronze
748 Age. The later stages of the transition are characterised by increasing Central Asian
749 (Turkmenistan_7000 BP_5000BP) and Northeast Asian-related (Amur_7500BP) ancestry
750 components (Extended Data Fig. 9G). Together, these results show that deeply structured hunter-
751 gatherer ancestry dominated the eastern Eurasian Steppe substantially longer than in western
752 Eurasia, before successive waves of population expansions swept across the Steppe within the last
753 4,000 years, including a large-scale introduction of domesticated horse lineages concomitant with
754 new equestrian equipment and spoke-wheeled chariotry^{20,48,98,99}.
755

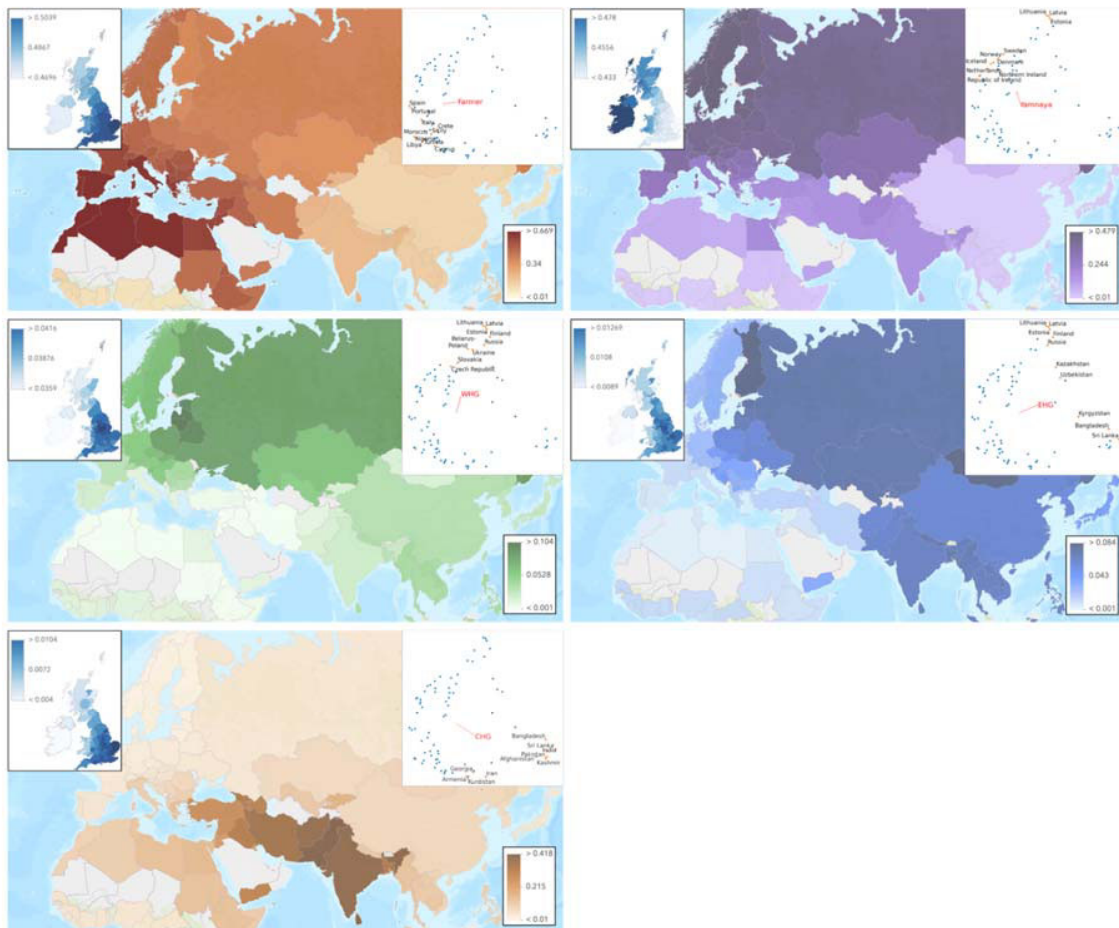
756 *Genetic legacy of Stone Age Europeans*

757 To investigate the distribution of Stone Age and Early Bronze Age ancestry components in modern
758 populations, we used ChromoPainter¹⁰⁰ to “paint” the chromosomes of individuals in the UK
759 Biobank (<https://www.ukbiobank.ac.uk>) using a panel of 10 ancient donor populations
760 (Supplementary Note 3h). Painting was done following the pipeline of Margaryan et al.¹⁰¹ based on
761 GLOBETROTTER¹⁰², and admixture proportions were estimated using Non-Negative Least
762 squares. Haplotypes in the modern genomes are assigned to the genetically closest ancient
763 population as measured by meiosis events, which favours more recent matches in time. Therefore,
764 ancestry proportions assigned to the oldest groups (e.g. WHG) should be interpreted as an excess of
765 this ancestry, which cannot be explained by simply travelling through more recent ancient
766 populations up to present times.
767

768 First, we selected non-British individuals from the UK Biobank if their country of birth was
769 European, African, or Asian. Because many of these individuals are admixed or British, we set up a
770 pipeline (Supplementary Note 3g) to select individuals of a typical ancestral background for each
771 country. This resulted in 24,511 individuals from 126 countries, who were then chromosome
772 painted to assess the average admixture proportions for each ancestry per country.
773

774 The various hunter-gatherer ancestries are not homogeneously distributed amongst modern
775 populations (Fig. 5). WHG-related ancestry is highest in present-day individuals from the Baltic
776 States, Belarus, Poland, and Russia; EHG-related ancestry is highest in Mongolia, Finland, Estonia
777 and Central Asia; and CHG-related ancestry is maximised in countries east of the Caucasus, in
778 Pakistan, India, Afghanistan and Iran, in accordance with previous results¹⁰³. The CHG-related
779 ancestry likely reflects both Caucasus hunter-gatherer and Iranian Neolithic signals, explaining the
780 relatively high levels in south Asia¹⁰⁴. Consistent with expectations^{105,106}, Neolithic Anatolian-
781 related farmer ancestry is concentrated around the Mediterranean basin, with high levels in southern
782 Europe, the Near East, and North Africa, including the Horn of Africa, but is less frequent in
783 Northern Europe. This is in direct contrast to the Steppe-related ancestry, which is found in high
784 levels in northern Europe, peaking in Ireland, Iceland, Norway, and Sweden, but decreases further
785 south. There is also evidence for its spread into southern Asia. Overall, these results refine global
786 patterns of spatial distributions of ancient ancestries amongst modern populations.
787

788 The availability of a large number of modern genomes (n=408,884) from self-identified “white”
789 British individuals who share similar PCA backgrounds ¹⁰⁷ allowed us to further examine the
790 distribution of ancient ancestries at high resolution in Britain (Supplementary Note 3h). Although
791 regional ancestry distributions differ by only a few percent, we find clear evidence of geographical
792 heterogeneity across the United Kingdom as visualised by assigning individuals to their birth
793 county and averaging ancestry proportions per county (Fig. 5, inset boxes). The proportion of
794 Neolithic farmer ancestry is highest in southern and eastern England today and lower in Scotland,
795 Wales, and Cornwall. Steppe-related ancestry is inversely distributed, peaking in the Outer
796 Hebrides and Ireland, a pattern only previously described for Scotland ¹⁰⁸. This regional pattern was
797 already evident in the Pre-Roman Iron Age and persists to the present day even though immigrating
798 Anglo-Saxons had relatively less Neolithic farmer ancestry than the Iron-Age population of
799 southwest Briton (Extended Data Fig. 4). Although this Neolithic farmer/steppe-related dichotomy
800 mirrors the modern ‘Anglo-Saxon’/‘Celtic’ ethnic divide, its origins are older, resulting from
801 continuous migration from a continental population relatively enhanced in Neolithic farmer
802 ancestry, starting as early as the Late Bronze Age ¹⁰⁹. By measuring haplotypes from these
803 ancestries in modern individuals, we are able to show that these patterns differentiate Wales and
804 Cornwall as well as Scotland from England. We also found higher levels of WHG-related ancestry
805 in central and Northern England. These results demonstrate clear ancestry differences within an
806 ‘ethnic group’ (white British) traditionally considered relatively homogenous, which highlights the
807 need to account for subtle population structure when using resources such as the UK Biobank
808 genomes.
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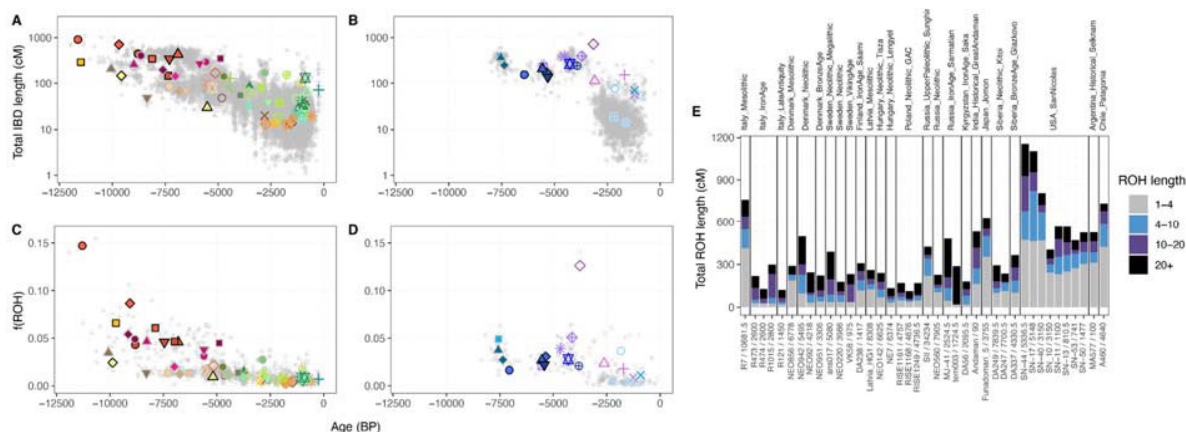
Fig 5. The genetic legacy of Stone Age ancestry in modern populations.

From top left clockwise: Neolithic Farmer, Yamnaya, Caucasus hunter-gatherer, Eastern hunter-gatherer, Western hunter-gatherer. Panels show average admixture proportion in modern individuals per country estimated using NNLS (large maps), average per county within the UK (top left insert), and PCA (PC2 vs PC1) of admixture proportions, with the top 10 highest countries by admixture fraction labelled and PCA loadings for that ancestry.

817 *Sociocultural insights*

818 We used patterns of pairwise IBD sharing between individuals and runs of homozygosity (ROH)
819 within individuals (measured as the fraction of the genome within a run of homozygosity $f(\text{ROH})$)
820 to examine our data for temporal shifts in relatedness within genetic clusters. Both measures show
821 clear trends of a reduction of within-cluster relatedness over time, in both western and eastern
822 Eurasia (Fig. 6). This pattern is consistent with a scenario of increasing effective population sizes
823 during this period¹¹⁰. Nevertheless, we observe notable differences in temporal relatedness patterns
824 between western and eastern Eurasia, mirroring the wider difference in population dynamics
825 discussed above. In the west, within-group relatedness changes substantially during the Neolithic
826 transition (~9,000 to ~6,000 BP), where clusters of Neolithic farmer-associated individuals show
827 overall reduced IBD sharing and $f(\text{ROH})$ compared to clusters of HG-associated individuals (Fig.
828 6A,C). In the east, genetic relatedness remains high until ~4,000 BP, consistent with a much longer
829 persistence of smaller localised hunter-gatherer groups (Fig. 6B,D).
830

831 Next, we examined the data for evidence of recent parental relatedness, by identifying individuals
 832 harbouring a large fraction of their genomes (> 50cM) in long (>20cM) ROH segments¹¹¹. We only
 833 detect 39 such individuals out of a total sample of 1,540 imputed ancient genomes (Fig. 6E), in line
 834 with recent results indicating that close kin mating was not common in human prehistory
 835 ^{41,103,111,112}. With the exception of eight ancient American individuals from the San Nicolas Islands
 836 in California¹¹³, no obviously discernible spatiotemporal or cultural clustering was observed among
 837 the individuals with recent parental relatedness. Interestingly, an ~1,700-year-old Sarmatian
 838 individual from Temyaysovo (tem003)¹¹⁴ was found homozygous for almost the entirety of
 839 chromosome 2, but without evidence of ROHs elsewhere in the genome, suggesting an ancient case
 840 of uniparental disomy. Among several noteworthy familial relationships (see Supplementary Fig.
 841 S3c.2), we report a Mesolithic father/son burial at Ertebølle (NEO568/NEO569), as well as a
 842 Mesolithic mother/daughter burial at Dragsholm (NEO732/NEO733).
 843
 844



845 **Fig 6. Patterns of co-ancestry.** (A)-(D) Panels show within-cluster genetic relatedness over time, measured either as
 846 the total length of genomic segments shared IBD between individuals (A, B) or the proportion of individual genomes
 847 found in a run of homozygosity $f(\text{ROH})$ (C, D). Results for both measures are shown separately for individuals from
 848 western (A, C) or eastern Eurasia (B, D). Small grey dots indicate estimates for individual pairs (A, B) or individuals
 849 (C, D), with larger coloured symbols indicating median values within genetic clusters. (E) Distribution of ROH lengths
 850 for 39 individuals with evidence for recent parental relatedness (>50 cM total in ROHs > 20 cM).
 851
 852
 853

854 *Pathogenic structural variants in ancient vs. modern-day humans*

855
 856 Rare, recurrent copy-number variants (CNVs) are known to cause neurodevelopmental disorders
 857 and are associated with a range of psychiatric and physical traits with variable expressivity and
 858 incomplete penetrance^{115,116}. To understand the prevalence of pathogenic structural variants over
 859 time we examined 50 genomic regions susceptible to recurrent CNV, known to be the most
 860 prevalent drivers of human developmental pathologies¹¹⁷. The analysis included 1442 ancient
 861 imputed genomes passing quality control for CNV analysis (Supplementary Note 4i) and 1093
 862 modern human genomes for comparison^{118,119}. We identified CNVs in ancient individuals at ten
 863 loci using a read-depth based approach and digital Comparative Genomic Hybridization¹²⁰
 864 (Supplementary Table S4i.1; Supplementary Figs. S4i.1-S4i.20). Although most of the observed
 865 CNVs (including duplications at 15q11.2 and *CHRNA7*, and CNVs spanning parts of the TAR locus
 866 and 22q11.2 distal) have not been unambiguously associated with disease in large studies, the
 867 identified CNVs include deletions and duplications that have been associated with developmental
 868 delay, dysmorphic features, and neuropsychiatric abnormalities such as autism (most notably at
 869 1q21.1, 3q29, 16p12.1 and the DiGeorge/VCFS locus, but also deletions at 15q11.2 and

870 duplications at 16p13.11). The individual harbouring the 16p13.1 deletion, RISE586²⁰, a 4,000 BP
871 woman aged 20-30 from the Únětice culture (modern day Czech Republic), had almost complete
872 skeletal remains, which allowed us to test for the presence of various skeletal abnormalities
873 associated with the 16p13.11 microdeletion¹²¹. RISE586 exhibited a hypoplastic tooth,
874 spondylolysis of the L5 vertebrae, incomplete coalescence of the S1 sacral bone, among other
875 minor skeletal phenotypes. The skeletal phenotypes observed in this individual are relatively
876 common (~10%) in European populations and are not specific to 16p13.1 thus do not indicate
877 strong penetrance of this mutation in RISE586^{122–125}. However, these results do highlight our
878 ability to link putatively pathogenic genotypes to phenotypes in ancient individuals. Overall, the
879 carrier frequency in the ancient individuals is similar to that reported in the UK Biobank genomes
880 (1.25% vs 1.6% at 15q11.2 and *CHRNA7* combined, and 0.8% vs 1.1% across the remaining loci
881 combined)¹²⁶. These results suggest that large, recurrent CNVs that can lead to several pathologies
882 were present at similar frequencies in the ancient and modern populations included in this study.
883

884 *Ancestry-stratified patterns of natural selection in the last 13,000 years*

885
886 The Neolithic transition led to a fundamental change in lifestyle, diet and exposure to pathogens
887 that imposed drastically new selection pressures on human populations. To detect genetic candidate
888 targets of selection, we used a set of 1,015 imputed ancient genomes from West Eurasia that were
889 fitted to a four-way admixture model of demographic history in this region (Supplementary Note 3i)
890 and identified phenotype-associated variants with evidence for directional selection over the last
891 13,000 years, with a special focus on the Neolithic transition (Supplementary Note 4a). We adapted
892 CLUES¹²⁷ to model time-series data (Supplementary Note 4a) and used it to infer allele frequency
893 trajectories and selection coefficients for 33,323 quality-controlled phenotype-associated variants
894 ascertained from the GWAS Catalogue¹²⁸. An equal number of putatively neutral, frequency-paired
895 variants were used as a control set. To control for possible confounders, we built a causal model to
896 distinguish direct effects of age on allele frequency from indirect effects mediated by read depth,
897 read length, and/or error rates (Supplementary Note 4b), and developed a mapping bias test used to
898 evaluate systematic differences between data from ancient and present-day populations
899 (Supplementary Note 4a). Because admixture between groups with differing allele frequencies can
900 confound interpretation of allele frequency changes through time, we also applied a novel
901 chromosome painting technique, based on inference of a sample's nearest neighbours in the
902 marginal trees of a tree sequence (Supplementary Note 3i). This allowed us to accurately assign
903 ancestral path labels to haplotypes found in both ancient and present-day individuals. By
904 conditioning on these haplotype path labels, we could infer selection trajectories while controlling
905 for changes in admixture proportions through time (Supplementary Note 4a).
906

907 Our analysis identified no genome-wide significant ($p < 5e-8$) selective sweeps when using
908 genomes from present-day individuals alone (1000 Genomes Project populations GBR, FIN and
909 TSI), although trait-associated variants were enriched for signatures of selection compared to the
910 control group ($p < 2.2e-16$, Wilcoxon signed-rank test). In contrast, when using imputed aDNA
911 genotype probabilities, we identified 11 genome-wide significant selective sweeps in the GWAS
912 variants, and none in the control group, consistent with selection acting on trait-associated variants
913 (Supplementary Note 4a, Supplementary Figs. S4a.4 to S4a.14). However, when conditioned on
914 one of our four ancestral histories—genomic regions arriving in present day genomes through
915 Western hunter-gatherers (WHG), Eastern hunter-gatherers (EHG), Caucasus hunter-gatherers
916 (CHG) or Anatolian farmers (ANA)—we identified 21 genome-wide significant selection peaks
917 (including the 11 from the pan-ancestry analysis) (Fig. 7). This suggests that admixture between
918 ancestral populations has masked evidence of selection at many trait associated loci in modern
919 populations.

933 trajectories for the top SNPs across all ancestries (grey shading for the marginal ancestries indicates approximate
934 temporal extent of the pre-admixture population).

935

936 *Selection on diet-associated loci*

937

938 We find strong changes in selection associated with lactose digestion after the introduction of
939 farming, but prior to the expansion of the Yamnaya pastoralists into Europe around 5,000 years ago
940 ^{20,21}, settling controversies regarding the timing of this selection ^{129–132}. The strongest overall signal
941 of selection in the pan-ancestry analysis is observed at the *MCM6 / LCT* locus (rs4988235; $p=9.86e-$
942 31 ; $s=0.020$), where the derived allele results in lactase persistence ^{133,134} (Supplementary Note 4a).
943 The trajectory inferred from the pan-ancestry analysis indicates that the lactase persistence allele
944 began increasing in frequency only c. 7,000 years ago, and has continued to increase up to present
945 times (Fig. 7). Our ancestry-stratified analysis shows, however, that selection at the *MCM6/LCT*
946 locus is much more complex than previously thought. In the pan-ancestry analysis, this sweep is led
947 by the lactase persistence SNP rs4988235, whereas in the ancestry-stratified analysis, this signal is
948 primarily driven by sweeps in two of the ancestral backgrounds (EHG and CHG), each of which
949 differ in their most significant SNPs (Fig. 7). Conversely, in the WHG background, we find no
950 evidence for selection at rs4988235, but strong selection at rs12465802 within the last c. 2,000
951 years. Overall, our results suggest that there were multiple, asynchronous selective sweeps in this
952 genomic region in recent human history, and possibly targeting different loci.

953

954 We also find strong selection in the *FADS* gene cluster — *FADS1* (rs174546; $p=2.65e-10$; $s=0.013$)
955 and *FADS2* (rs174581; $p=1.87e-10$; $s=0.013$) — which are associated with fatty acid metabolism
956 and known to respond to changes in diet from a more/less vegetarian to a more/less carnivorous diet
957 ^{135–140}. In contrast to previous results ^{138–140}, we find that much of the selection associated with a
958 more vegetarian diet occurred in Neolithic populations before they arrived in Europe, but then
959 continued during the Neolithic (Fig. 7). The strong signal of selection in this region in the pan-
960 ancestry analysis is driven primarily by a sweep occurring on the EHG, CHG and ANA haplotypic
961 backgrounds (Fig. 7). Interestingly, we find no evidence for selection at this locus in the WHG
962 background, and most of the allele frequency rise in the EHG background occurs after their
963 admixture with CHG (around 8ka, ¹⁴¹), within whom the selected alleles were already close to
964 present-day frequencies. This suggests that the selected alleles may already have existed at
965 substantial frequencies in early farmer populations in the Middle East and among Caucasus Hunter
966 gatherers (associated with the ANA and CHG and backgrounds, respectively) and were subject to
967 continued selection as eastern groups moved northwards and westwards during the late Neolithic
968 and Bronze Age periods.

969

970 When specifically comparing selection signatures differentiating ancient hunter-gatherer and farmer
971 populations ¹⁴², we also observe a large number of regions associated with lipid and sugar
972 metabolism, and various metabolic disorders (Supplementary Note 4e). These include, for example,
973 a region in chromosome 22 containing *PATZ1*, which regulates the expression of *FADS1*, and
974 *MORC2*, which plays an important role in cellular lipid metabolism ^{143–145}. Another region in
975 chromosome 3 overlaps with *GPR15*, which is both related to immune tolerance and to intestinal
976 homeostasis ^{146–148}. Finally, in chromosome 18, we recover a selection candidate region spanning
977 *SMAD7*, which is associated with inflammatory bowel diseases such as Crohn's disease ^{149–151}.
978 Taken together these results suggest that the transition to agriculture imposed a substantial amount
979 of selection for humans to adapt to our new diet and that some diseases observed today in modern
980 societies can likely be understood as a consequence of this selection.

981

982 *Selection on immunity-associated variants*

983

984 In addition to diet-related selection, we observe selection in several loci associated with
985 immunity/defence functions and with autoimmune disease (Supplementary Note 4a). Some of these
986 selection events occurred earlier than previously claimed and are likely associated with the
987 transition to agriculture and may help explain the high prevalence of autoimmune diseases today.
988 Most notably, we detect a 33 megabase (Mb) wide selection sweep signal in chromosome 6
989 (chr6:19.1–50.9 Mb), spanning the human leukocyte antigen (HLA) region (Supplementary Note
990 4a). The selection trajectories of the variants within this locus support multiple independent sweeps,
991 occurring at different times and with differing intensities. The strongest signal of selection at this
992 locus in the pan-ancestry analysis is at an intergenic variant, located between *HLA-A* and *HLA-W*
993 (rs7747253; $p=8.86e-17$; $s=-0.018$), associated with heel bone mineral density¹⁵², the derived allele
994 of which rapidly reduced in frequency, beginning c. 8,000 years ago (Extended Data Fig. 10). In
995 contrast, the signal of selection at *C2* (rs9267677; $p=9.82e-14$; $s=0.04463$), also found within this
996 sweep, and associated with educational attainment¹⁵³, shows a gradual increase in frequency
997 beginning c. 4,000 years ago, before rising more rapidly c. 1,000 years ago. This highlights the
998 complex temporal dynamics of selection at the HLA locus, which not only plays a role in the
999 regulation of the immune system, but also has association with many other non-immune-related
1000 phenotypes. The high pleiotropy in this region makes it difficult to determine which selection
1001 pressures may have driven these increases in frequencies at different periods of time. However,
1002 profound shifts in lifestyle in Eurasian populations during the Holocene, including a change in diet
1003 and closer contact with domestic animals, combined with higher mobility and increasing population
1004 sizes, are likely drivers for strong selection on loci involved in immune response.

1005

1006 We also identified selection signals at the *SLC22A4* (rs35260072; $p=1.15e-10$; $s=0.018$) locus,
1007 associated with increased itch intensity from mosquito bites¹⁵⁴, and find that the derived variant has
1008 been steadily rising in frequency since c. 9,000 years ago (Extended Data Fig. 11). However, in the
1009 same *SLC22A4* candidate region as rs35260072, we find that the frequency of the previously
1010 reported SNP rs1050152 plateaued c. 1,500 years ago, contrary to previous reports suggesting a
1011 recent rise in frequency⁴⁵. Similarly, we detect selection at the *HECTD4* (rs11066188; $p=3.02e-16$;
1012 $s=0.020$) and *ATXN2* (rs653178; $p=1.92e-15$; $s=0.019$) locus, associated with celiac disease and
1013 rheumatoid arthritis¹⁵⁵, which has been rising in frequency for c. 9,000 years (Extended Data Fig.
1014 12), also contrary to previous reports of a more recent rise in frequency⁴⁵. Thus, several disease-
1015 associated loci previously thought to be the result of recent adaptation may have been subject to
1016 selection for a longer period of time.

1017

1018 *Selection on the 17q12.13 locus*

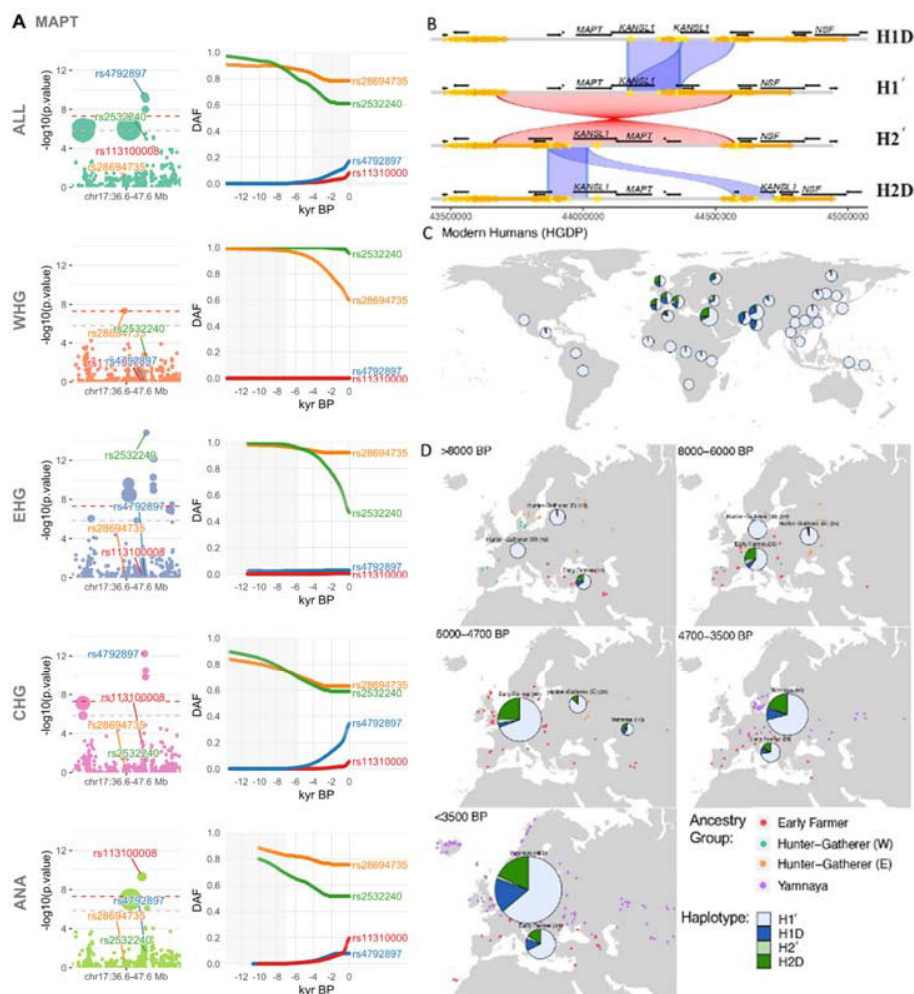
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1020 We further detect signs of strong selection in a 12 Mb sweep in chromosome 17 (chr17:36.1–48.1
1021 Mb), spanning a locus on 17q21.3 implicated in neurodegenerative and developmental disorders
1022 (Supplementary Note 4a). The locus includes an inversion and other structural polymorphisms with
1023 indications of a recent positive selection sweep in some human populations^{156,157}. Specifically,
1024 partial duplications of the *KANSL1* gene likely occurred independently on the inverted (H2) and
1025 non-inverted (H1) haplotypes (Fig. 8B) and both are found in high frequencies (15-25%) among
1026 current European and Middle Eastern populations but are much rarer in Sub-Saharan African and
1027 East Asian populations. We used both SNP genotypes and WGS read depth information to
1028 determine inversion (H1/H2) and *KANSL1* duplication (d) status in the ancient individuals studied
1029 here (see Supplementary Note 4g).

1030

1031 The H2 haplotype is observed in two of three previously published genomes¹⁵⁸ of Anatolian
1032 aceramic Neolithic individuals (Bon001 and Bon004) from around 10,000 BP, but data were
1033 insufficient to identify *KANSLI* duplications. The oldest evidence for *KANSLI* duplications is
1034 observed in an Iranian early Neolithic individual (AH1 from 9,900 BP²) followed by two Georgian
1035 Mesolithic individuals (NEO281 from 9,724 BP and KK1⁶ from 9,720 BP) all of whom are
1036 heterozygous for the inversion and carry the inverted duplication. The *KANSLI* duplications are
1037 also detected in two Russian Neolithic individuals: NEO560 from 7,919 BP (H1d) and NEO212
1038 from 7,390 BP (H2d). With both H1d and H2d having spread to large parts of Europe with
1039 Anatolian Neolithic Farmer ancestry, their frequency seems unchanged in most of Europe as
1040 Steppe-related ancestry becomes dominant in large parts of the subcontinent (Extended Data Fig.
1041 8D). The fact that both H1d and H2d are found in apparently high frequencies in both early
1042 Anatolian Farmers and the earliest Yamnaya/Steppe-related ancestry groups suggests that any
1043 selective sweep acting on the H1d and H2d variants would probably have occurred in populations
1044 ancestral to both.

1045
1046 We note that the strongest signal of selection observed in this locus is at *MAPT* (rs4792897;
1047 $p=4.65e-10$; $s=0.03$ (Fig. 8A; Supplementary Note 4a), which codes for the tau protein¹⁵⁹ and is
1048 involved in a number of neurodegenerative disorders, including Alzheimer's disease and
1049 Parkinson's disease^{160–164}. However, the region is also enriched for evidence of reference bias in
1050 our imputed dataset—especially around the *KANSLI* gene—due to complex structural
1051 polymorphisms (Supplementary Note 4i).



1052

1053 **Fig 8. Selection at the *MAPT* / 17q21.31 inversion locus.** A) Results for the pan-ancestry analysis (ALL) plus the four
1054 marginal ancestries: Western hunter-gatherers (WHG), Eastern hunter-gatherers (EHG), Caucasus hunter-gatherers
1055 (CHG) and Anatolian farmers (ANA). Grey shading for the marginal ancestries indicates approximate temporal extent
1056 of the pre-admixture population. B) Haplotypes of the 17q21.31 locus: the ancestral (non-inverted) H1 17q21.31 and
1057 the inverted H2 haplotype. Duplications of the *KANSL1* gene have occurred independently on both lineages yielding
1058 H1D and H2D haplotypes. C) Frequency of the 17q21.31 inversion and duplication haplotypes across modern-day
1059 global populations (Human Genome Diversity Project ¹¹⁹). D) Change in the frequency of the 17q21.31 inversion
1060 haplotype through time.

1061

1062 *Selection on pigmentation-associated variants*

1063

1064 Our results identify strong selection for lighter skin pigmentation in groups moving northwards and
1065 westwards, in agreement with the hypothesis that selection is caused by reduced UV exposure and
1066 resulting vitamin D deficiency. We find that the most strongly selected alleles reached near-fixation
1067 several thousand years ago, suggesting that this was not associated with recent sexual selection as
1068 proposed ^{165,166} (Supplementary Note 4a).

1069

1070 In the pan-ancestry analysis we detect strong selection at the *SLC45A2* locus (rs35395; $p=4.13e-23$;
1071 $s=0.022$) locus ^{167,168}, with the selected allele (responsible for lighter skin), increasing in frequency
1072 from c. 13,000 years ago, until plateauing c. 2,000 years ago (Fig. 7). The dominating hypothesis is
1073 that high melanin levels in the skin are important in equatorial regions owing to its protection

1074 against UV radiation, whereas lighter skin has been selected for at higher latitudes (where UV
1075 radiation is less intense) because some UV penetration is required for cutaneous synthesis of
1076 vitamin D^{169,170}. Our findings confirm pigmentation alleles as major targets of selection during the
1077 Holocene^{45,171,172} particularly on a small proportion of loci with large effect sizes¹⁶⁸.

1078
1079 Additionally, our results provide unprecedentedly detailed information about the duration and
1080 geographic spread of these processes (Fig. 7) suggesting that an allele associated with lighter skin
1081 was selected for repeatedly, probably as a consequence of similar environmental pressures
1082 occurring at different times in different regions. In the ancestry-stratified analysis, all marginal
1083 ancestries show broad agreement at the *SLC45A2* locus (Fig. 7) but differ in the timing of their
1084 frequency shifts. The ANA ancestry background shows the earliest evidence for selection, followed
1085 by EHG and WHG around c. 10,000 years ago, and CHG c. 2,000 years later. In all ancestry
1086 backgrounds except WHG, the selected haplotypes reach near fixation by c. 3,000 years ago, whilst
1087 the WHG haplotype background contains the majority of ancestral alleles still segregating in
1088 present-day Europeans. This finding suggests that selection on this allele was much weaker in
1089 ancient western hunter-gatherer groups during the Holocene compared to elsewhere. We also detect
1090 strong selection at the *SLC24A5* (rs1426654; p=6.45e-09; s=0.019) which is also associated with
1091 skin pigmentation^{167,173}. At this locus, the selected allele increased in frequency even earlier than
1092 *SLC45A2* and reached near fixation c. 3,500 years ago (Supplementary Note 4a). Selection on this
1093 locus thus seems to have occurred early on in groups that were moving northwards and westwards,
1094 and only later in the Western hunter-gatherer background after these groups encountered and
1095 admixed with the incoming populations.

1096 1097 *Selection among major axes of ancient population variation*

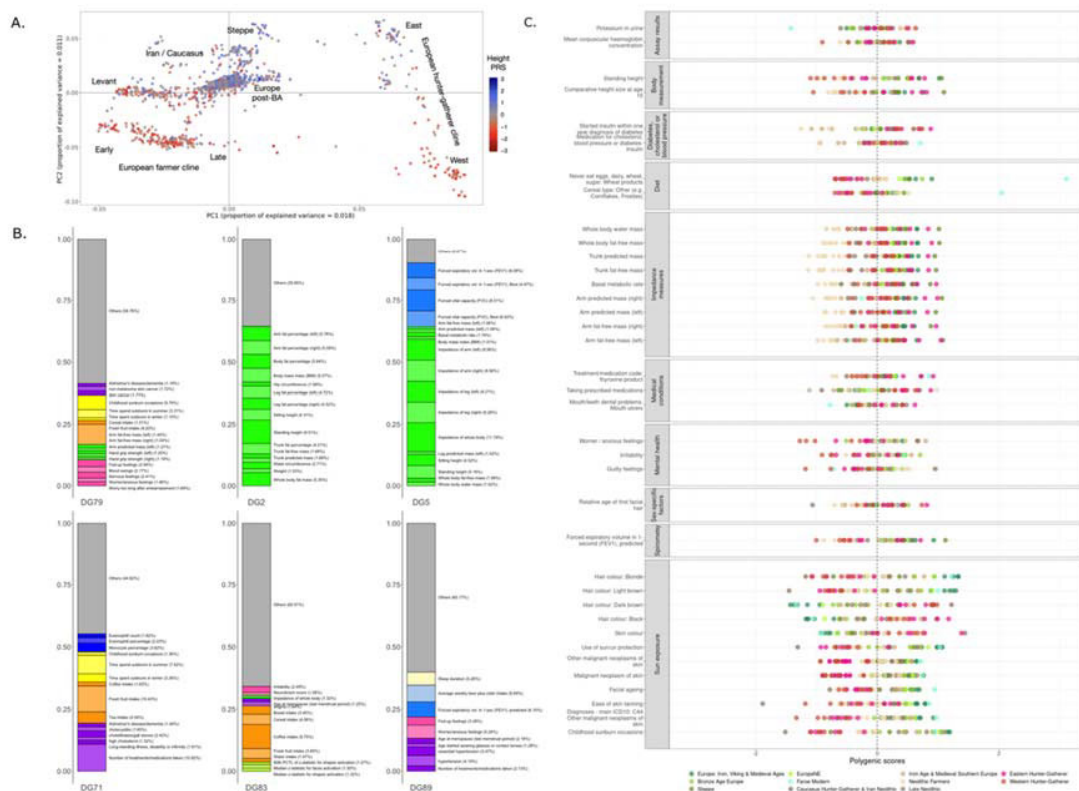
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1099 Beyond patterns of genetic change at the Mesolithic-Neolithic transition, much genetic variability
1100 observed today reflects high genetic differentiation in the hunter-gatherer groups that eventually
1101 contributed to modern European genetic diversity¹⁴². Indeed, a substantial number of loci
1102 associated with cardiovascular disease, metabolism and lifestyle diseases trace their genetic
1103 variability prior to the Neolithic transition, to ancient differential selection in ancestry groups
1104 occupying different parts of the Eurasian continent (Supplementary Note 4d). These may represent
1105 selection episodes that preceded the admixture events described above, and led to differentiation
1106 between ancient hunter-gatherer groups in the late Pleistocene and early Holocene. One of these
1107 overlaps with the *SLC24A3* gene which is a salt sensitivity gene significantly expressed in obese
1108 individuals^{174,175}. Another spans *ROPNI* and *KALRN*, two genes involved in vascular disorders^{176–}
1109¹⁷⁸. A further region contains *SLC35F3*, which codes for a thiamine transport and has been
1110 associated with hypertension in a Han Chinese cohort^{179,180}. Finally, there is a candidate region
1111 containing several genes (*CH25H*, *FAS*) associated with obesity and lipid metabolism^{181–183} and
1112 another peak with several genes (*ASXL2*, *RAB10*, *HADHA*, *GPR113*) involved in glucose
1113 homeostasis and fatty acid metabolism^{184–193}. These loci predominantly reflect ancient patterns of
1114 extreme differentiation between Eastern and Western Eurasian genomes, and may be candidates for
1115 selection after the separation of the Pleistocene populations that occupied different environments
1116 across the continent (roughly 45,000 years ago¹⁰³).

1117 1118 *Genetic trait reconstruction and the phenotypic legacy of ancient Europeans*

1119
1120 When comparing modern European genomes in the UK Biobank to ancient Europeans, we find
1121 strong differentiation at certain sets of trait-associated variants, and differential contribution of
1122 different ancestry groups to various traits. We reconstructed polygenic scores for phenotypes in
1123 ancient individuals, using effect size estimates obtained from GWASs performed using the

1124 >400,000 UK Biobank genomes¹⁰⁷ (<http://www.nealelab.is/uk-biobank>) and looked for
1125 overdispersion among these scores across ancient populations, beyond what would be expected
1126 under a null model of genetic drift¹⁹⁴ (Supplementary Note 4c). We stress that polygenic scores and
1127 Q_X statistic may both be affected by population stratification, so these results should be interpreted
1128 with caution^{195–198}. The most significantly overdispersed scores are for variants associated with
1129 pigmentation, anthropometric differences and disorders related to diet and sugar levels, including
1130 diabetes (Fig. 9). We also find psychological trait scores with evidence for overdispersion related to
1131 mood instability and irritability, with Western Hunter-gatherers generally showing smaller genetic
1132 scores for these traits than Neolithic Farmers. Intriguingly, we find highly inconsistent predictions
1133 of height based on polygenic scores in western hunter-gatherer and Siberian groups computed using
1134 effect sizes estimated from two different - yet largely overlapping - GWAS cohorts (Supplementary
1135 Note 4c), highlighting how sensitive polygenic score predictions are to the choice of cohort,
1136 particularly when ancient populations are genetically divergent from the reference GWAS cohort
1137¹⁹⁸. Taking this into account, we do observe that the Eastern hunter-gatherer and individuals
1138 associated with the Yamnaya culture have consistently high genetic values for height, which in turn
1139 contribute to stature increases in Bronze Age Europe, relative to the earlier Neolithic populations
1140^{45,80,199}.

1141
1142 We performed an additional analysis to examine the data for strong alignments between axes of
1143 trait-association²⁰⁰ and ancestry gradients, rather than relying on particular choices for population
1144 clusters (Supplementary Note 4e). Along the population structure axis separating ancient East Asian
1145 and Siberian genomes from Steppe and Western European genomes (Fig. 1), we find significant
1146 correlations with trait-association components related to impedance, body measurements, blood
1147 measurements, eye measurement and skin disorders. Along the axis separating Mesolithic hunter-
1148 gatherers from Anatolian and Neolithic farmer individuals, we find significant correlations with
1149 trait-association components related to skin disorders, diet and lifestyle traits, mental health status,
1150 and spirometry-related traits (Fig. 9). Our findings show that these phenotypes were genetically
1151 different among ancient groups with very different lifestyles. However, we note that the realised
1152 value of these traits is highly dependent on environmental factors and gene-environment
1153 interactions, which we do not model in this analysis.
1154



1155

1156 **Fig. 9** A. First two principal components of a PCA of ancient Western Eurasian samples, coloured by height polygenic
 1157 scores. B. Top 6 UK Biobank trait-association components from DeGAs that have the highest correlation ($P < 5e-3$)
 1158 with the principal component separating ancient farmers from hunter-gatherer populations (PC1 in Panel A). C. Top UK
 1159 Biobank traits with highest overdispersion in polygenic scores among ancient populations, out of a total of 320 sets of
 1160 trait-associated SNPs tested ($Q_X > 79.4$, $P < 0.05/320$).

1161

1162 In addition to the above reconstructions of genetic traits among the ancient individuals, we also
 1163 estimated the contribution from different ancestral populations (EHG, CHG, WHG, Yamnaya and
 1164 Anatolian farmer) to variation in polygenic phenotypes in present-day individuals, leveraging the
 1165 exceptional resolution offered by the UK Biobank genomes¹⁰⁷ to investigate this. We calculated
 1166 ancestry-specific polygenic risk scores based on the chromosome painting of the >400,000 UKB
 1167 genomes (Supplementary Note 4h); this allowed us to identify if any of the ancient ancestry
 1168 components were over-represented in modern UK populations at loci significantly associated with a
 1169 given trait, and also avoids exporting risk scores over space and time. Working with large numbers
 1170 of imputed ancient genomes provides high statistical power to use ancient populations as “ancestral
 1171 sources”. We focused on phenotypes whose polygenic scores were significantly over-dispersed in
 1172 the ancient populations (Supplementary Note 4c), as well as a single high effect variant, ApoE4,
 1173 known to be a significant risk factor in Alzheimer’s Disease^(201,202). We emphasise that this
 1174 approach makes no reference to ancient phenotypes but describes how these ancestries contributed
 1175 to the modern genetic landscape. In light of the ancestry gradients within the British Isles and
 1176 Eurasia (Fig. 5), these results support the hypothesis that ancestry-mediated geographic variation in
 1177 disease risks and phenotypes is commonplace. It points to a way forward for disentangling how
 1178 ancestry contributed to differences in risk of genetic disease – including metabolic and mental
 1179 health disorders – between present-day populations.

1180

1181 Taken together, these analyses help to settle the famous discussion of selection in Europe relating to
1182 height ^{45,80,203}. The finding that steppe individuals have consistently high genetic values for height
1183 (Supplementary Note 4c), is mirrored by the UK Biobank results, which find that the ‘Steppe’
1184 ancestral components (Yamnaya/EHG) contributed to increased height in present-day populations
1185 (Supplementary Note 4h). This shows that the height differences in Europe between north and south
1186 may not be due to selection, as claimed in many previous studies, but may be a consequence of
1187 differential ancestry.

1188

1189 Likewise, European hunter gatherers are genetically predicted to have dark skin pigmentation and
1190 dark brown hair ^{11,20,21,79,83,168,204,205}, and indeed we see that the WHG, EHG and CHG components
1191 contributed to these phenotypes in present-day individuals whereas the Yamnaya and Anatolian
1192 farmer ancestry contributed to light brown/blonde hair pigmentation (Supplementary Note 4h).
1193 Interestingly, loci associated with overdispersed mood-related polygenic phenotypes recorded
1194 among the UK Biobank individuals (like increased anxiety, guilty feelings, and irritability) showed
1195 an overrepresentation of the Anatolian farmer ancestry component; and the WHG component
1196 showed a strikingly high contribution to traits related to diabetes. We also found that the ApoE4
1197 effect allele is preferentially found on a WHG/EHG haplotypic background, suggesting it likely was
1198 brought to western Europe by early hunter-gatherers (Supplementary Note 4h). This is in line with
1199 the present-day European distribution of this allele, which is highest in north-eastern Europe, where
1200 the proportion of these ancestries are higher than in other regions of the continent ²⁰⁶.

1201

1202 *Conclusion*

1203

1204 Our study has provided fundamental new insights into one of the most transformative periods of
1205 human biological and cultural evolution. We have demonstrated that a clear east-west division
1206 known from Stone Age material culture, extending from the Black Sea to the Baltic and persisting
1207 across several millennia, was genetically deeply rooted in populations with different ancestries. We
1208 showed that the genetic impact of the Neolithic transition was highly distinct, east and west of this
1209 boundary. We have identified a hitherto unknown source of ancestry in hunter-gatherers from the
1210 Middle Don region contributing ancestry to the Yamnaya pastoralists, and we have documented
1211 how the later spread of steppe-related ancestry into Europe was very rapid and mediated through
1212 admixture with people from the Globular Amphora Culture. Additionally, we have observed two
1213 near-complete population replacements in Denmark within just 1,000 years, concomitantly with
1214 major changes in material culture, which rules out cultural diffusion as a main driver and settles
1215 generation-long archaeological debates. Our analyses revealed that the ability to detect signatures of
1216 natural selection in modern human genomes is drastically limited by conflicting selection pressures
1217 in different ancestral populations masking the signals. Developing methods to trace selection in
1218 individual ancestry components allowed us to effectively double the number of significant selection
1219 peaks, which helped clarify the trajectories of a number of traits related to diet and lifestyle. Our
1220 results emphasise how the interplay between major ancient selection and admixture events
1221 occurring across Europe and Asia in the Stone and Bronze Ages have profoundly shaped patterns of
1222 genetic variation in modern human populations.

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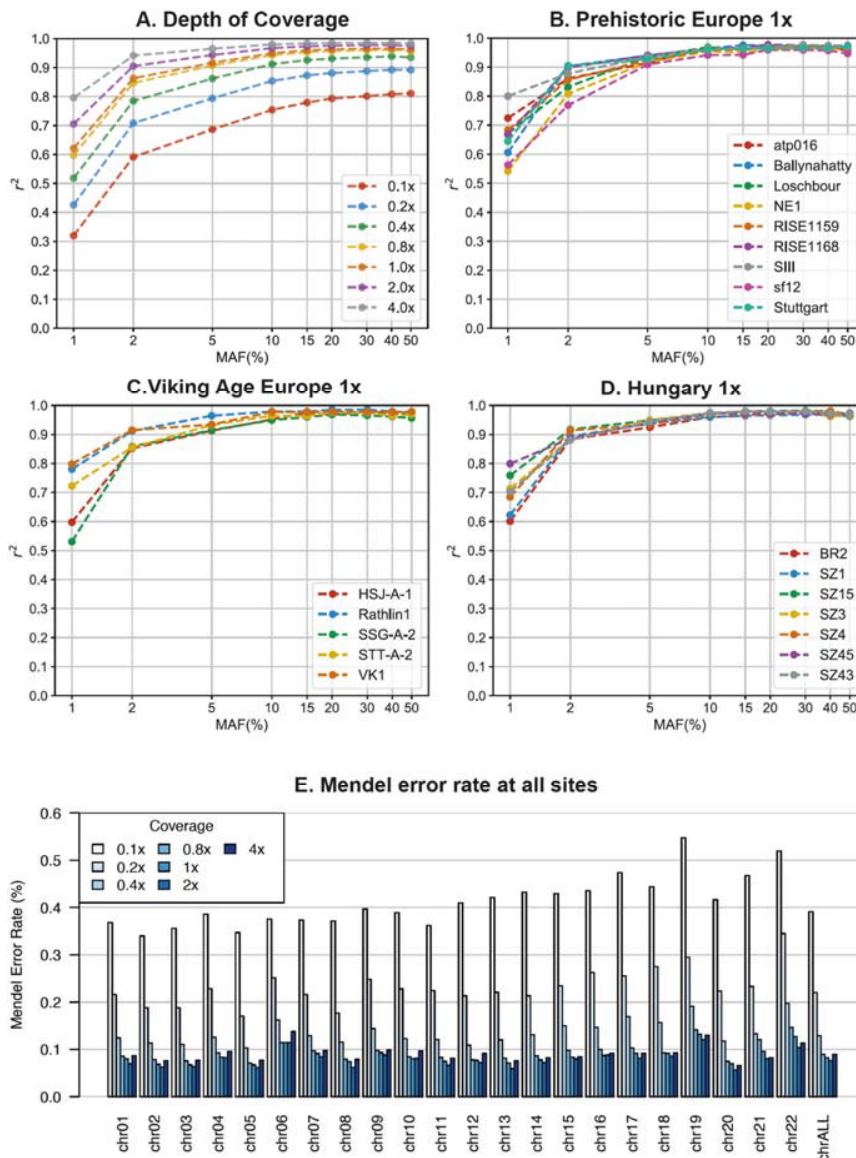
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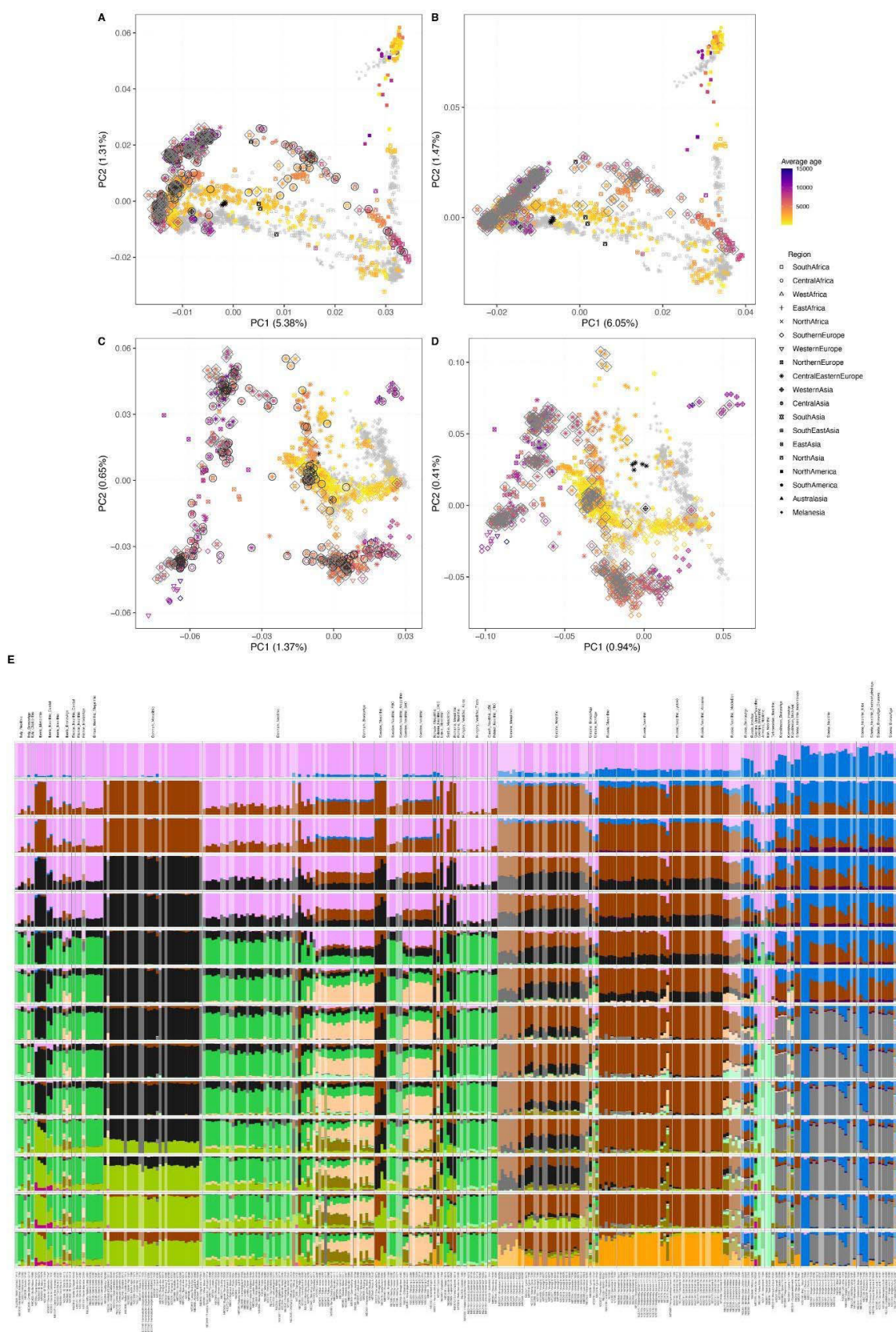
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1229 **Extended Data Figures**



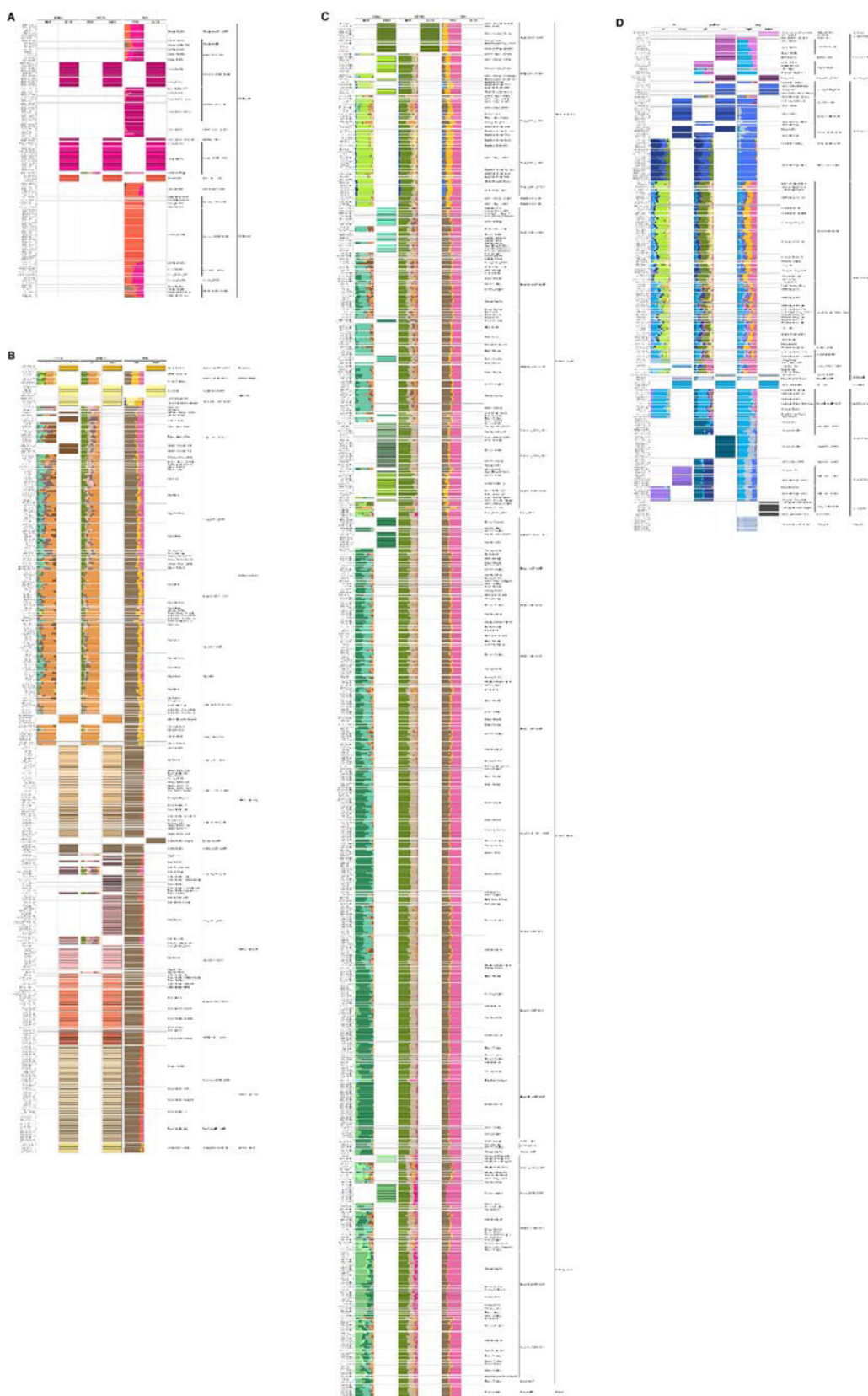
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Extended Data Fig.1. Imputation accuracy of aDNA. Panel A shows imputation accuracy across the 42 high-coverage ancient genomes when downsampled to lower depth of coverage values. Panels B-D show imputation accuracy for 1X depth of coverage across 21 high-coverage ancient European genomes. In panels A-D, imputation accuracy is shown as the squared Pearson correlation between imputed and true genotype dosages as a function of minor allele frequency of the target variant sites. Panel E shows imputation accuracy as Mendelian error rates for a re-sequenced Neolithic trio²⁷ downsampled to a range of low coverage values.

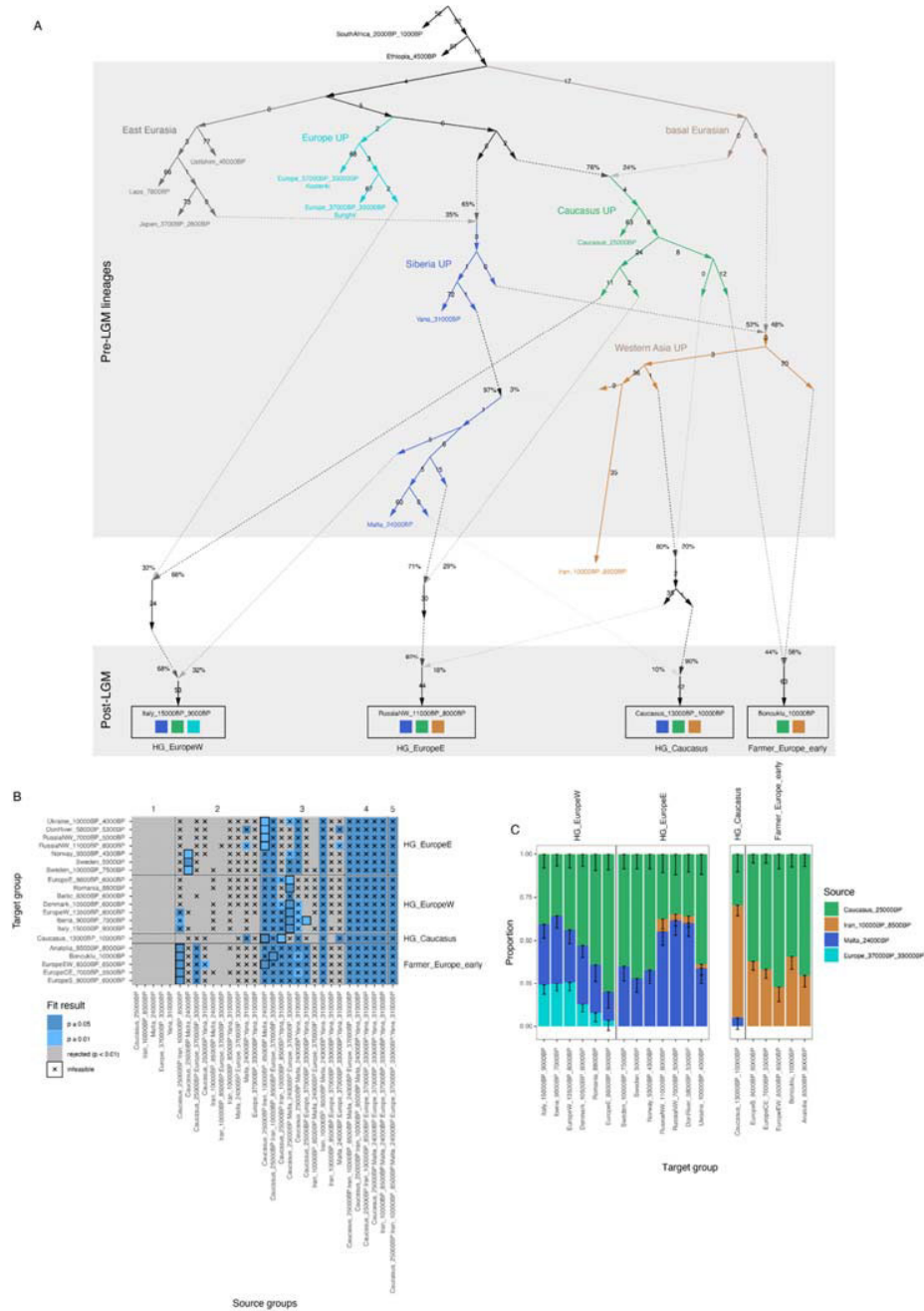


1240 **Extended Data Fig. 2. Genetic structure of the 317 herein-reported ancient genomes.** (A)-(D) Principal component
1241 analysis of 3,316 modern and ancient individuals from Eurasia, Oceania and the Americas (A, B), as well as restricted
1242 to 2,126 individuals from western Eurasia (west of Urals) (C, D). Shown are analyses with principal components
1243 inferred either using both modern and imputed ancient genomes passing all filters, and projecting low coverage ancient
1244 genomes (A, C); or only modern genomes and projecting all ancient genomes (B, D). Ancient genomes sequenced in
1245 this study are indicated either with black circles (imputed genomes) or grey diamonds (projected genomes). (E) Model-
1246 based clustering results using ADMIXTURE for 284 newly reported genomes (excluding close relatives and individuals
1247 flagged for possible contamination). Results shown are based on ADMIXTURE runs from K=2 to K=15 on 1,584
1248 ancient individuals. Low-coverage individuals represented by pseudo-haploid genotypes are indicated with alpha
1249 transparency.
1250

1252 **Extended Data Fig. 3. Genetic clustering of ancient individuals.** Genetic clusters inferred from pairwise identity-by-
1253 descent (IBD) sharing of 1,401 ancient Eurasian individuals, indicated using colored symbols throughout (A) Network
1254 graph of pairwise IBD sharing between 596 ancient Eurasians predating 3,000 BP, highlighting within- and between-
1255 cluster relationships. Each node represents an individual, and the width of edges connecting nodes indicates the fraction
1256 of the genome shared IBD between the respective pair of individuals. Network edges were restricted to the 10 highest
1257 sharing connections for each individual, and the layout was computed using the force-directed Fruchterman-Reingold
1258 algorithm. (B) Temporal distribution of clustered individuals, grouped by broad ancestry cluster. (C), (D) Geographical
1259 distribution of clustered individuals, shown for individuals predating 3,000 BP (C) and after 3,000 BP (D). (E)-(H)
1260 Fine-scale population structure among genetic clusters. Modern individuals are shown in gray, with population labels
1261 corresponding to their median coordinates. (E), (F) PCA of 3,119 Eurasian (E) or 2,126 west Eurasian (F) individuals.
1262 (G), (H) t-distributed stochastic neighbour embedding (t-SNE) using the first 12 principal components of the all
1263 Eurasian panel (E). Shown are embeddings with two different exaggeration factors ρ , emphasising local (G, $\rho=1$) or
1264 global (H, $\rho=30$) structure.
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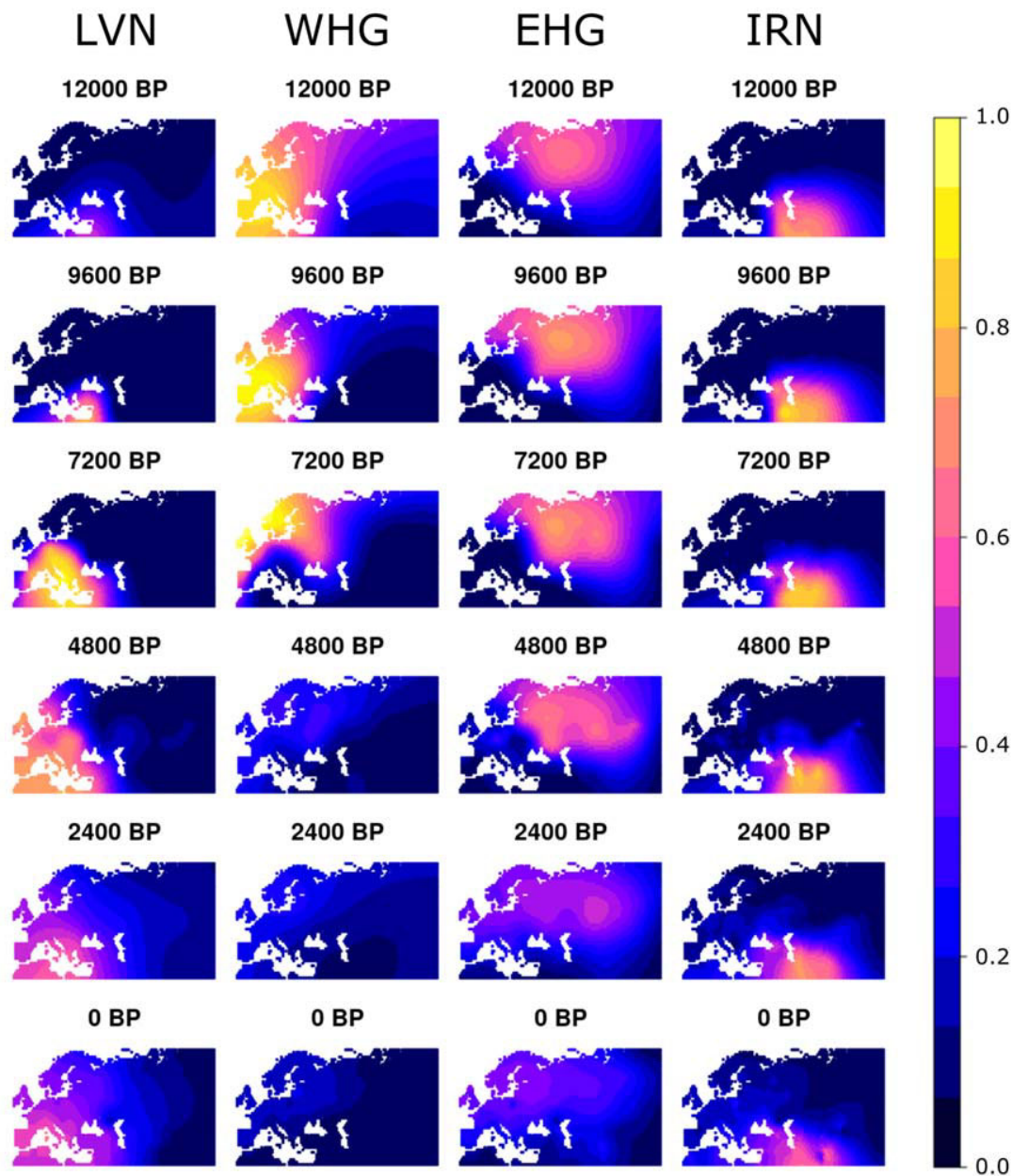
1267 **Extended Data Fig. 4. Admixture modelling.** Supervised admixture modelling using non-negative least squares on
 1268 IBD sharing profiles. Panels (A)-(D) show estimated ancestry proportions of four global Eurasian clusters,
 1269 corresponding to (A) European hunter-gatherers before 4,000 BP; (B) Individuals from Europe and Western Asia from
 1270 around 10,000 BP until historical times, including Neolithic farmers, Caucasus hunter-gatherers and recent individuals
 1271 with genetic affinity to the Levant; (C) European individuals after 5,000 BP, as well as pastoralist groups from the
 1272 Eurasian Steppe; (D) Central, East and North Asian individuals with east Eurasian genetic affinities. Column pairs show
 1273 results of modelling target individuals (left columns) using three panels of increasingly distal source groups (right
 1274 columns): “postBA”: Bronze Age and Neolithic source groups; “postNeol”, Bronze Age and later targets using Late
 1275 Neolithic/early Bronze Age and earlier source groups; “deep”, Mesolithic and later targets using deep ancestry source
 1276 groups. Note that some clusters of individuals can be either sources or targets across distinct panels.



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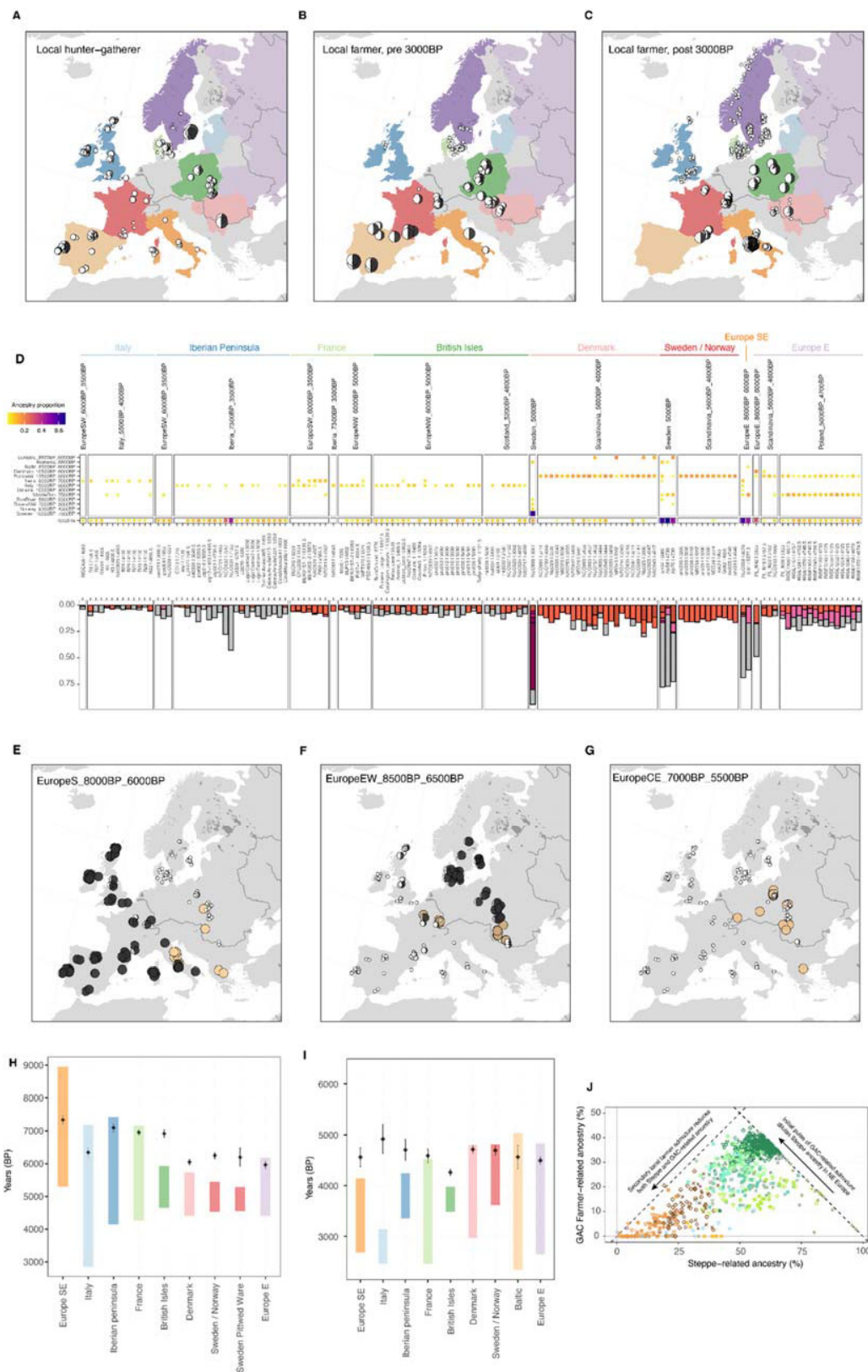
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1279 **Extended Data Fig. 5. Deep Eurasian population structure.** (A) Admixture graph fit relating deep Eurasian lineages
1280 predating the Last Glacial Maximum (LGM) to later West Eurasian ancestry clusters (worst $|Z| = 3.65$). (B) Rotating
1281 outgroup *qpAdm* analysis showing fit results for modelling post-LGM target groups as mixtures of all possible
1282 combinations involving one to five source groups. Colours of the individual matrix cells indicate the fit for a particular
1283 model, either rejected at $p < 0.01$ (grey), $0.01 \leq p < 0.05$ (light blue) or $p \geq 0.05$ (dark blue). Cells with crosses indicate
1284 infeasible models involving negative admixture proportions. (C) Estimated ancestry proportions from *qpAdm* for post-
1285 LGM target groups inferred from the model fitting with least number of source groups.



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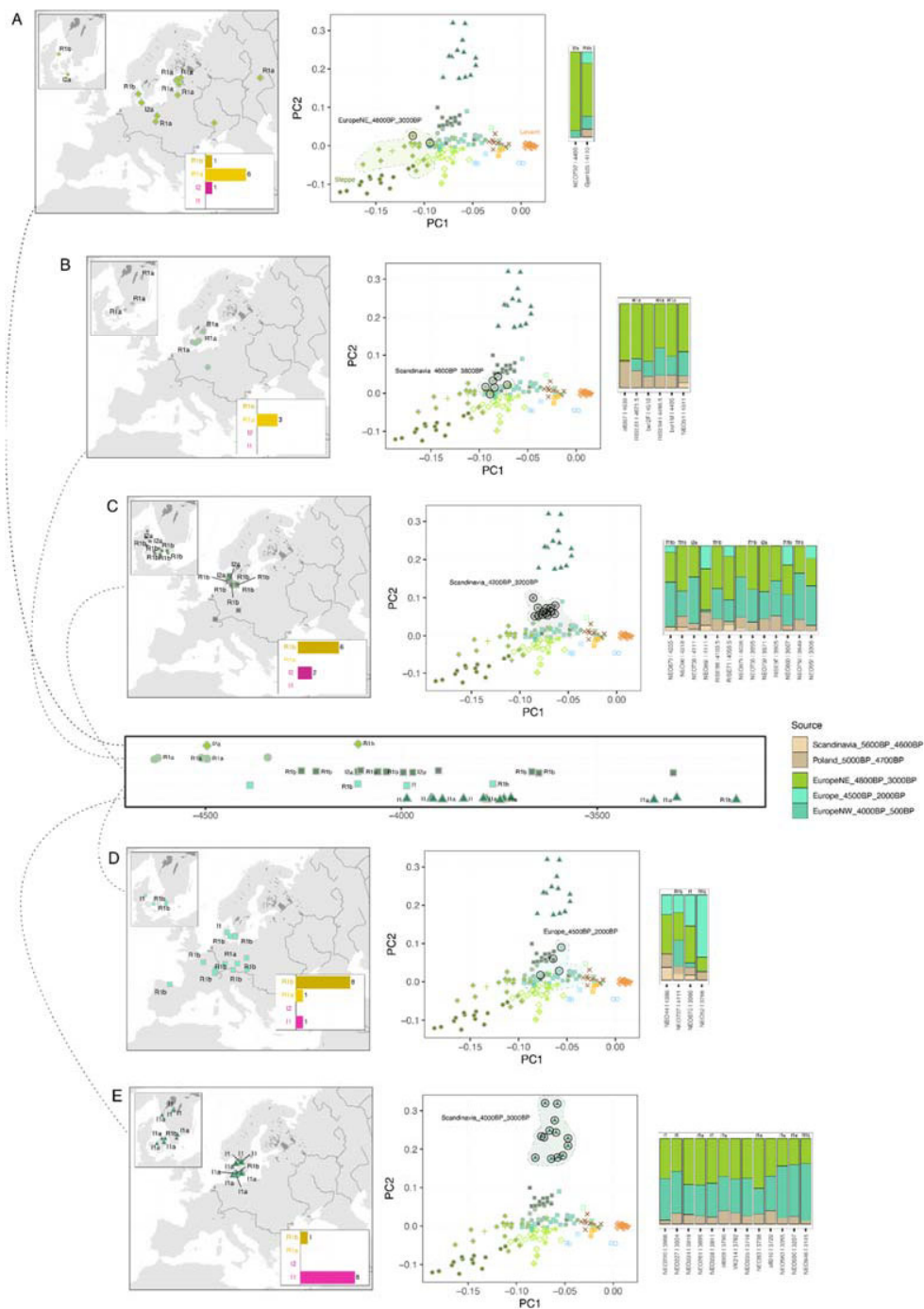
1288 **Extended Data Fig 6.** Spatiotemporal kriging of four major ancestry clusters over the last 12,000 years of human history.
1289 LVN = ancestry maximized in Anatolian farmer populations. WHG = ancestry maximized in western European hunter-
1290 gatherers. EHG = ancestry maximized in eastern European hunter-gatherers. IRN = ancestry maximized in Iranian
1291 Neolithic individuals and Caucasus hunter-gatherers.



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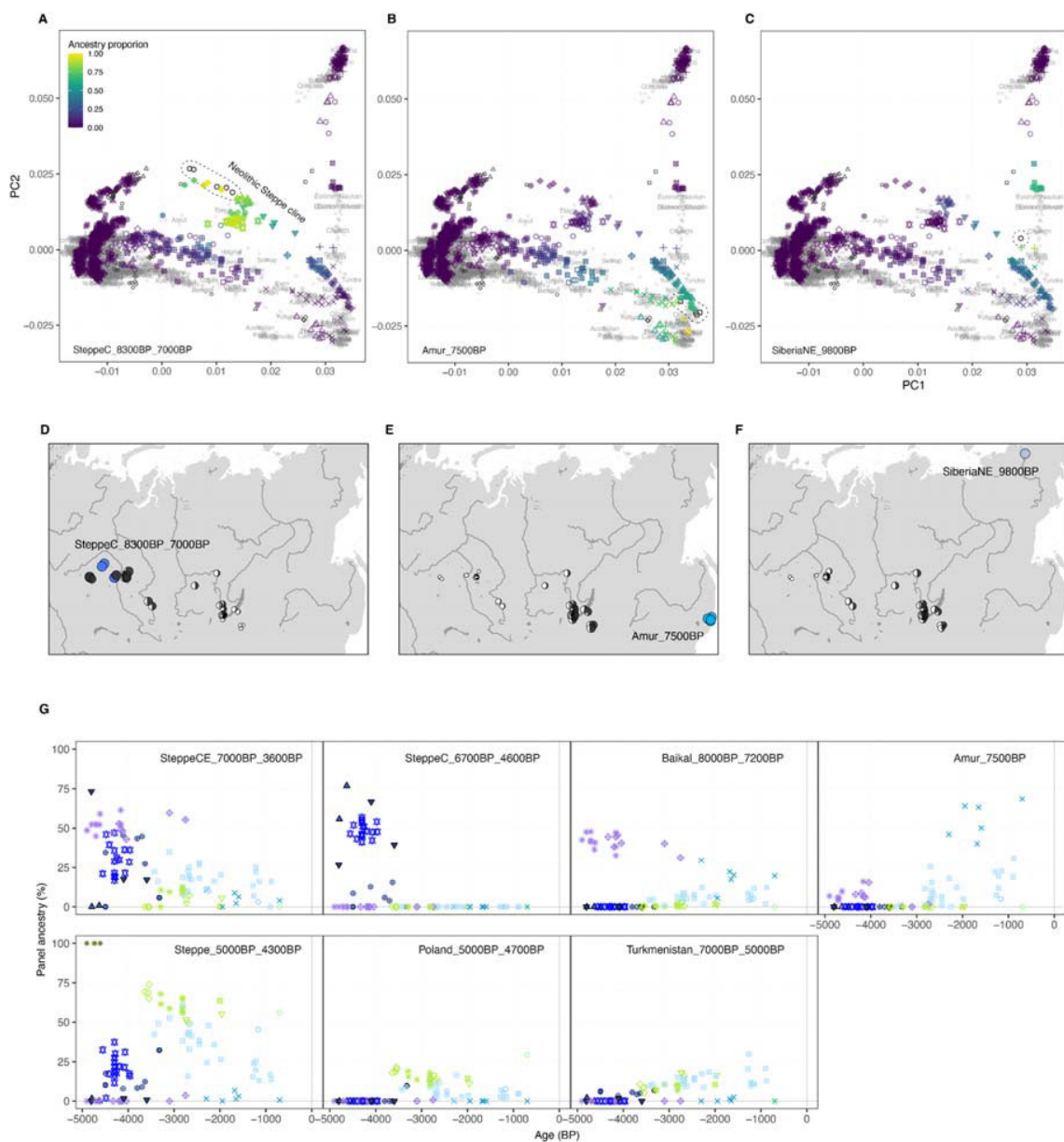
Extended Data Fig. 7. Genetic transitions in Europe. (A)-(C) Ancestry proportions contributed from preceding local groups to later individuals during the two major western Eurasian genetic transitions. (A) contribution to individuals

1295 with farmer ancestry from preceding local hunter-gatherer groups; (B,C) contribution to individuals with Steppe-related
1296 ancestry from preceding local farmer groups. Coloured areas in all maps indicate the geographic extent of individuals
1297 included in respective regions. (D) Composition of hunter-gatherer ancestry proportions from different source groups in
1298 individuals with farmer ancestry, shown as heatmap (top) and barplots (bottom). Grey bars represent contributions from
1299 local hunter-gatherers (E)-(G) Moon charts showing spatial distribution of estimated ancestry proportions of mid- to
1300 late Neolithic farmer individuals from three clusters of early Neolithic European farmers (locations indicated with
1301 coloured symbols). Estimated ancestry proportions are indicated by size and amount of fill of moon symbols. (H, I)
1302 Estimated time of admixture between (H) local hunter-gatherer groups and farmers and (I) eastern European farmers
1303 with GAC-related ancestry and Steppe pastoralist groups. Black diamonds and error bars represent point estimate and
1304 standard errors of admixture time, coloured bars show temporal range of included target individuals. The time to
1305 admixture was adjusted backwards by the average age of individuals for each region. (J) Correlation between estimated
1306 proportions of Steppe-related and GAC farmer-related ancestries, across west Eurasian target individuals. Symbol shape
1307 and colour indicate the genetic cluster of respective individuals.
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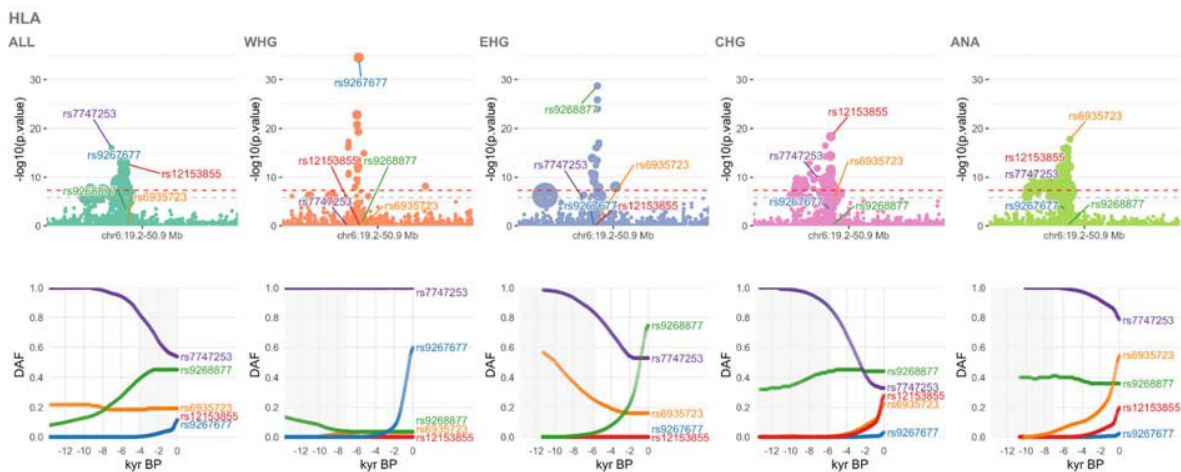
Extended Data Fig. 8. Fine-scale structure in Late Neolithic Scandinavians. (A)-(E) Geographic locations and PCA based on pairwise IBD sharing (middle) of 148 European individuals predating 3,000 BP. Geographic locations are shown for 65 individuals belonging to the five genetic clusters observed in 38 ancient Scandinavians (temporal sequence shown in timeline in centre of plot). Individual assignments and frequency distribution of major Y chromosome haplogroups are indicated in maps and timeline. Plot symbols with black circles indicate the 38 Scandinavian individuals in the PCA panels. Ancestry proportions for the 38 Scandinavian individuals estimated using proximal source groups from outside Scandinavia (“postNeolScand” source set) are shown on the right of the respective cluster results.



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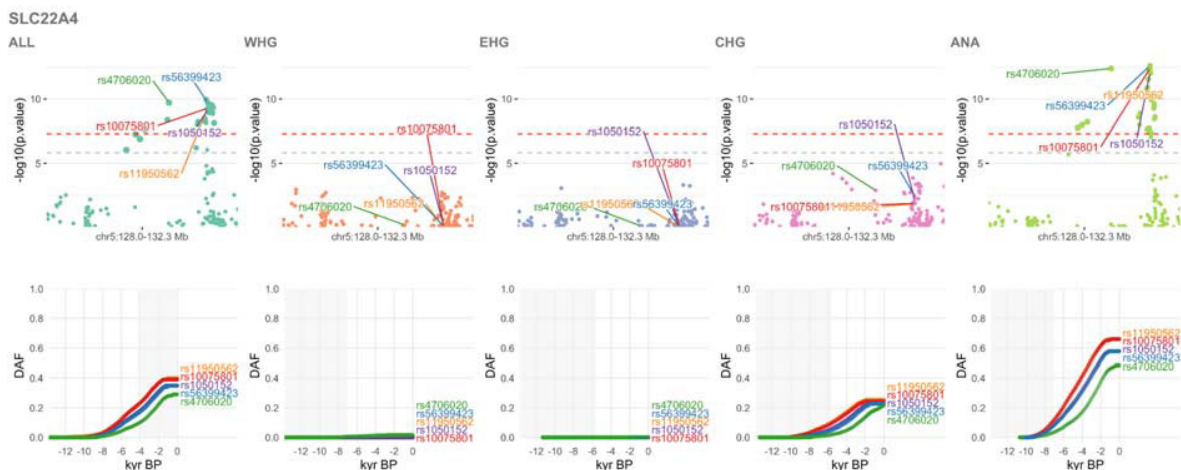
1319 **Extended Data Fig. 9. Genetic transformations across the Eurasian Steppe.** (A)–(C) Principal component analysis
 1320 of modern and ancient individuals from Eurasia, Oceania and the Americas, highlighting estimated ancestry proportions
 1321 from “deep” Siberian ancestry sources (individuals highlighted with dashed line). Present-day individuals are shown in
 1322 gray, with population labels corresponding to their median coordinates. (D)–(E) Moon charts showing spatial
 1323 distribution of estimated ancestry proportions of Siberian hunter-gatherers before 5,000 BP from “deep” Siberian
 1324 ancestry sources (names and locations indicated with coloured symbols). Estimated ancestry proportions are indicated
 1325 by size and amount of fill of moon symbols. (G) Timelines of ancestry proportions from “postNeol” sources in Central
 1326 and North Asian ancient individuals after 5,000 BP. Symbol shape and colour indicate the genetic cluster of each
 1327 individual.

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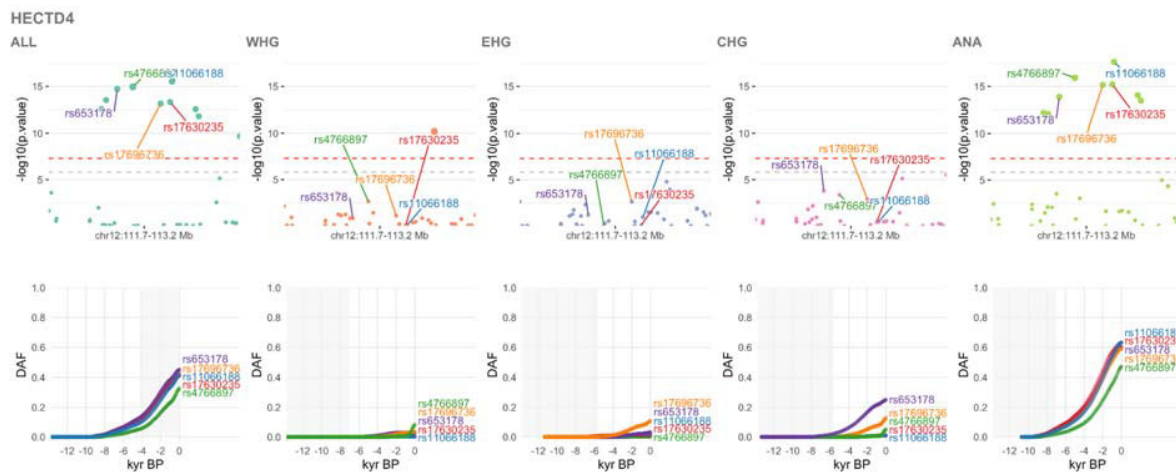
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Extended Data Fig. 10. Selection at the HLA locus. Results for the pan-ancestry analysis (ALL) plus the four marginal ancestries: Western hunter-gatherers (WHG), Eastern hunter-gatherers (EHG), Caucasus hunter-gatherers (CHG) and Anatolian farmers (ANA). Row one shows zoomed Manhattan plots of the p-values for each ancestry (significant SNPs sized by their selection coefficients), and row two shows allele trajectories for the top SNPs across all ancestries (grey shading for the marginal ancestries indicates approximate temporal extent of the pre-admixture population).



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Extended Data Fig. 11. Selective sweep at the *SLC22A4* locus. Results for the pan-ancestry analysis (ALL) plus the four marginal ancestries: Western hunter-gatherers (WHG), Eastern hunter-gatherers (EHG), Caucasus hunter-gatherers (CHG) and Anatolian farmers (ANA). Row one shows zoomed Manhattan plots of the p-values for each ancestry (significant SNPs sized by their selection coefficients), and row two shows allele trajectories for the top SNPs across all ancestries (grey shading for the marginal ancestries indicates approximate temporal extent of the pre-admixture population).



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1352 **Extended Data Fig. 12. Selective sweep at the *HECTD4* locus.** Results for the pan-ancestry analysis (ALL) plus the
 1353 four marginal ancestries: Western hunter-gatherers (WHG), Eastern hunter-gatherers (EHG), Caucasus hunter-gatherers
 1354 (CHG) and Anatolian farmers (ANA). Row one shows zoomed Manhattan plots of the p-values for each ancestry
 1355 (significant SNPs sized by their selection coefficients), and row two shows allele trajectories for the top SNPs across all
 1356 ancestries (grey shading for the marginal ancestries indicates approximate temporal extent of the pre-admixture
 1357 population).

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1359 Data availability

1360 All collapsed and paired-end sequence data for novel samples sequenced in this study will be made
 1361 publicly available on the European Nucleotide Archive, together with trimmed sequence alignment
 1362 map files, aligned using human build GRCh37. Previously published ancient genomic data used in
 1363 this study is detailed in Supplementary Table VII, and are all already publicly available.
 1364 Bioarchaeological data (including Accelerator Mass Spectrometry results) are included in the online
 1365 supplementary materials of this submission.
 1366

1367 Code availability

1368 The modified version of CLUES used in this study is available from [https://github.com/standard-](https://github.com/standard-aaron/clues)
 1369 [aaron/clues](https://github.com/standard-aaron/clues). The pipeline and conda environment necessary to replicate the analysis of allele
 1370 frequency trajectories of trait-associated variants in Supplementary Note 4a are available on Github
 1371 at https://github.com/ekirving/mesoneo_paper. The pipeline to replicate the analyses for
 1372 Supplementary Note 4c-4e can be found at <https://github.com/albarema/neo>. All other analyses
 1373 relied upon available software which has been fully referenced in the manuscript and detailed in
 1374 the relevant supplementary notes.
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1839

1840 **Author Information**

1841 These authors contributed equally: Morten E. Allentoft, Martin Sikora, Alba Refoyo-Martínez, Evan K.
1842 Irving-Pease, Anders Fischer, William Barrie & Andrés Ingason

1843

1844 These authors equally supervised research: Thorfinn Korneliussen, Richard Durbin, Rasmus Nielsen, Olivier
1845 Delaneau, Thomas Werge, Fernando Racimo, Kristian Kristiansen & Eske Willerslev

1846

1847 Affiliations

1848

1849 **Lundbeck Foundation GeoGenetics Centre, GLOBE Institute, University of Copenhagen,**
1850 **Copenhagen, Denmark**

1851 Morten E. Allentoft, Martin Sikora, Alba Refoyo-Martínez, Evan K. Irving-Pease, Andrés Ingason, Jesper
1852 Stenderup, Fabrice Demeter, Maria Novosolov, Ruairidh Macleod, Rasmus A. Henriksen, Tharsika Vimala,
1853 Hugh McColl, Lasse Vinner, Gabriele Scorrano, Abigail Ramsøe, Anders Rosengren, Anthony Ruter, Anne
1854 Birgitte Gotfredsen, Charleen Gaunitz, Fulya Eylem Yediay, Isin Altinkaya, Lei Zhao, Peter de Barros
1855 Damgaard, Kurt H. Kjær, Thorfinn Korneliussen, Rasmus Nielsen, Thomas Werge, Fernando Racimo,
1856 Kristian Kristiansen & Eske Willerslev

1857

1858 **Trace and Environmental DNA (TrEnD) Laboratory, School of Molecular and Life Sciences, Curtin**
1859 **University, Perth, Australia**

1860 Morten E. Allentoft
1861
1862 **GeoGenetics Group, Department of Zoology, University of Cambridge, Cambridge, UK**
1863 William Barrie, Alice Pearson, Ruairidh Macleod & Eske Willerslev
1864
1865 **Department of Historical Studies, University of Gothenburg, Gothenburg, Sweden**
1866 Anders Fischer, Karl-Göran Sjögren, Bettina Schulz Paulsson, Malou Blank & Kristian Kristiansen
1867
1868 **Institute of Biological Psychiatry, Mental Health Services, Copenhagen University Hospital, Roskilde,**
1869 **Denmark**
1870 Andrés Ingason, Vivek Appadurai,
1871
1872 **The National Museum of Denmark, Ny Vestergade 10, Copenhagen, Denmark**
1873 Lasse Sørensen, Poul Otto Nielsen, Morten Fischer Mortensen, Peter Rasmussen, Peter Vang Petersen,
1874
1875 **Sealand Archaeology, Gl. Roesnaesvej 27, 4400 Kalundborg, Denmark**
1876 Anders Fischer
1877
1878 **Department of Genetics, University of Cambridge, Cambridge, UK**
1879 Alice Pearson & Richard Durbin
1880
1881 **Wellcome Sanger Institute, Wellcome Genome Campus, Cambridge, UK**
1882 Richard Durbin & Eske Willerslev
1883
1884 **Department of Computational Biology, University of Lausanne, Switzerland**
1885 Bárbara Sousa da Mota & Olivier Delaneau
1886
1887 **Swiss Institute of Bioinformatics, University of Lausanne, Switzerland**
1888 Bárbara Sousa da Mota
1889
1890 **Department of Integrative Biology, University of California, Berkeley, USA**
1891 Alma S. Halgren, Peter H. Sudmant & Rasmus Nielsen
1892
1893 **Center for Computational Biology, University of California, Berkeley, USA**
1894 Andrew Vaughn, Aaron J. Stern, Peter H. Sudmant & Rasmus Nielsen
1895
1896 **Laboratory of Biological Anthropology, Department of Forensic Medicine, University of Copenhagen,**
1897 **Copenhagen, Denmark**
1898 Marie Louise Schjellerup Jørkov & Niels Lynnerup
1899
1900 **Muséum National d'Histoire Naturelle, Paris, France**
1901 Fabrice Demeter
1902
1903 **Research department of Genetics, Evolution and Environment, University College London, London,**
1904 **UK**
1905 Ruairidh Macleod
1906

1907 **Section for Evolutionary Genomics, GLOBE Institute, University of Copenhagen, Copenhagen,**
1908 **Denmark**
1909 Ashot Margaryan, Theis Zetner Trolle Jensen, Hannes Schroeder, Enrico Cappellini
1910
1911 **Centre for Evolutionary Hologenomics, University of Copenhagen, Copenhagen, Denmark**
1912 Ashot Margaryan
1913
1914 **Anthropology Department, University of Utah, USA**
1915 Melissa Illardo
1916
1917 **Department of Geology, Lund University, Lund, Sweden**
1918 Anne Birgitte Nielsen
1919
1920 **Department of Archaeology and Ancient History, Lund University, Lund, Sweden**
1921 Lars Larsson
1922
1923 **Tårnby Gymnasium og HF, Kastrup, Denmark**
1924 Mikkel Ulfeldt Hede
1925
1926 **Department of Health Technology, Section of Bioinformatics, Technical University of Denmark,**
1927 **Kongens Lyngby, Denmark**
1928 Gabriel Renaud
1929
1930 **Department of Archaeology and Heritage Studies, Aarhus University, Aarhus, Denmark**
1931 Niels N. Johannsen, Rikke Maring
1932
1933 **Institute of Biological Psychiatry, Mental Health Centre Sct Hans, Copenhagen University Hospital,**
1934 **Denmark**
1935 Andrew J. Schork, Anders Rosengren & Thomas Werge
1936
1937 **Department of Clinical Medicine, University of Copenhagen, 2200 Copenhagen N, Denmark**
1938 Thomas Werge
1939
1940 **Neurogenomics Division, The Translational Genomics Research Institute (TGEN), Phoenix, AZ, USA**
1941 Andrew J. Schork
1942
1943 **Terra Ltd., Letchik Zlobin St. 20, Voronezh, 394055, Russian Federation**
1944 Andrey Skorobogatov, Ruslan Turin
1945
1946 **Department of Archaeology, University of Exeter, Exeter, UK**
1947 Alan K. Outram & Catriona J. McKenzie
1948
1949 **Institute of Archaeology and Ethnography, Siberian Branch of the Russian Academy of Sciences,**
1950 **Novosibirsk, Russian Federation**
1951 Aleksey A. Timoshchenko, Dmitri V. Pozdnyakov, Liudmila N. Mylnikova, Marina S. Nesterova &
1952 Vyacheslav I. Molodin
1953

- 1954 **Institute of Ethnology and Anthropology, Russian Academy of Sciences, Moscow, Russian Federation**
1955 Elizaveta V. Veselovskaya, Sergey Vasilyev
1956
1957 **Centre for Egyptological studies, Russian Academy of Sciences, Moscow, Russia**
1958 Sergey Vasilyev
1959
1960 **Research Institute and Museum of Anthropology, Lomonosov Moscow State University, Mokhovaya**
1961 **str. 11, Moscow, Russian Federation**
1962 Alexandra Buzhilova, Natalia Berezina, Svetlana Borutskaya
1963
1964 **Department of Environmental Biology, Sapienza University of Rome, Rome, Italy**
1965 Alfredo Coppa, Dušan Borić
1966
1967 **Peter the Great Museum of Anthropology and Ethnography (Kunstkamera), Russian Academy of**
1968 **Sciences, Saint Petersburg, Russian Federation**
1969 Alisa Zubova & Vyacheslav Moiseyev
1970
1971 **CIAS, Department of Life Science, University of Coimbra, Coimbra, Portugal**
1972 Ana Maria Silva
1973
1974 **UNIARQ, University of Lisbon, Lisbon, Portugal**
1975 Ana Maria Silva & João Zilhão
1976
1977 **Kostanay Regional University A. Baitursynov, Kostanay, Kazakhstan**
1978 Andrey V. Logvin, Irina V. Shevnina
1979
1980 **Vesthimmerlands Museum, Søndergade 44, Aars, Denmark**
1981 Bjarne Henning Nielsen
1982
1983 **Museum Nordsjælland, Frederiksgade 9, 3400 Hillerød**
1984 Per Lotz, Søren Anker Sørensen, Thomas Jørgensen
1985
1986 **Museum Vestsjælland, Klosterstræde 18, 4300 Holbæk, Denmark**
1987 Per Lotz
1988
1989 **Vendsyssel Historiske Museum, DK-9800 Hjørring, Denmark**
1990 Per Lysdahl, Sidsel Wåhlin
1991
1992 **Moesgaard Museum, Moesgård Allé 15, Højbjerg, Denmark**
1993 Søren H. Andersen
1994
1995 **Grupo EvoAdapta, Departamento de Ciencias Históricas, Universidad de Cantabria, Santander, Spain**
1996 Borja González-Rabanal
1997
1998 **Museu de Ciències Naturals de Barcelona, Barcelona, Spain**
1999 Carles Lalueza-Fox
2000

- 2001 **Institute of Evolutionary Biology, CSIC-Universitat Pompeu Fabra, Barcelona, Spain**
2002 Carles Lalueza-Fox
2003
- 2004 **ICREA, University of Barcelona, Barcelona, Spain**
2005 João Zilhão
2006
- 2007 **Departamento de Prehistoria y Arqueología Department, Universidad Autónoma de Madrid, Madrid, Spain**
2008
2009 Concepción Blasco, Corina Liesau, Patricia Ríos
2010
- 2011 **Department of Biology, University of Rome "Tor Vergata", Rome, Italy**
2012 Cristina Martinez-Labarga, Olga Rickards
2013
- 2014 **Department of History, Humanities and Society, University of Rome "Tor Vergata", Rome, Italy**
2015 Mario Federico Rolfo
2016
- 2017 **Instituto Internacional de Investigaciones Prehistóricas de Cantabria, Universidad de Cantabria, Santander, Spain**
2018
2019 David Cuenca-Solana, Igor Gutiérrez Zugasti & Manuel González-Morales
2020
- 2021 **Centre de Recherche en Archéologie, Archeosciences, Histoire (CReAAH), UMR-6566 CNRS, Rennes, France**
2022
2023 David Cuenca-Solana
2024
- 2025 **Georgian National Museum, Tbilisi, Georgia**
2026 David O. Lordkipanidze
2027
- 2028 **Tbilisi State University, Tbilisi, Georgia**
2029 David O. Lordkipanidze
2030
- 2031 **IPND, Tyumen Scientific Centre, Siberian Branch of the Russian Academy of Sciences, Tyumen, Russian Federation**
2032
2033 Dmitri Enshin, Olga Poshekhonova, Svetlana N. Skochina
2034
- 2035 **Departament de Prehistòria, Arqueologia i Història Antiga, Universitat de València, València, Spain**
2036 Domingo C. Salazar-García, J.Emili Aura Tortosa
2037
- 2038 **Department of Geological Sciences, University of Cape Town, Cape Town, South Africa**
2039 Domingo C. Salazar-García
2040
- 2041 **Department of Anthropology, New York University, New York, USA.**
2042 Dušan Borić
2043
- 2044 **Institute of Humanities, Ivanovo State University, Ivanovo, Russian Federation**
2045 Elena Kostyleva
2046
- 2047 **Saryarka Archaeological Institute, Buketov Karaganda University, Karaganda, Kazakhstan**

2048 Emma R. Usmanova
2049
2050 **South Ural State University, Chelyabinsk, Russia**
2051 Emma R. Usmanova
2052
2053 **The Saxo Institute, University of Copenhagen, Copenhagen, Denmark**
2054 Erik Brinch Petersen, Rune Iversen
2055
2056 **Museum Østjylland, Stemannsgade 2, Randers, Denmark**
2057 Esben Kannegaard, Lutz Klassen
2058
2059 **Soprintendenza Archeologia Belle Arti e Paesaggio per la Città Metropolitana di Bari, Via Pier**
2060 **l'Eremita, 25, 70122, Bari, Italy**
2061 Francesca Radina
2062
2063 **Soprintendenza per i Beni Archeologici delle Marche, Via Birarelli 18, 60100, Ancona, Italy**
2064 Mara Silvestrini
2065
2066 **Soprintendenza Archeologia, Belle Arti e Paesaggio per la provincia di Cosenza, Cosenza, Italy**
2067 Paola Aurino
2068
2069 **UMR 5199 PACEA, CNRS, Université de Bordeaux, 33615 Pessac, France**
2070 Henri Duday, Patrice Courtaud
2071
2072 **Institute of Archaeology, National Academy of Sciences of Ukraine, Kyiv, Ukraine**
2073 Inna Potekhina
2074
2075 **National University of Kyiv-Mohyla Academy, Kyiv, Ukraine**
2076 Inna Potekhina
2077
2078 **Collège de France, 75231 Paris cedex 05, France**
2079 Jean Guilaine
2080
2081 **Odense City Museums, Overgade 48, Odense, Denmark**
2082 Jesper Hansen
2083
2084 **Museum Sydøstdanmark, Algade 97, 4760 Vordingborg, Denmark**
2085 Kristoffer Buck Pedersen
2086
2087 **Institute of Archaeology and Ethnology, Polish Academy of Sciences, Kraków, Poland**
2088 Krzysztof Tunia, Piotr Włodarczyk
2089
2090 **CNRS UMR 5608, Toulouse Jean Jaurès University, Maison de la Recherche, 5 Allées Antonio**
2091 **Machado, 31058 Toulouse, Cedex 9, France**
2092 Laure Metz & Ludovic Slimak
2093
2094 **ARGEA Consultores SL, C. de San Crispín, Madrid, Spain**

- 2095 Jorge Vega, Roberto Menduiña
2096
2097 **Institute of Molecular Biology, National Academy of Sciences, Yerevan, Armenia**
2098 Levon Yepiskoposyan
2099
2100 **Russian-Armenian University, Yerevan, Armenia**
2101 Levon Yepiskoposyan
2102
2103 **Institute of Archaeology and Ethnography, National Academy of Sciences, Yerevan, Armenia**
2104 Ruben Badalyan
2105
2106 **HistorieUdvikler, Gl. Roesnaesvej 27, DK-4400 Kalundborg, Denmark**
2107 Lisbeth Pedersen
2108
2109 **Department of history and cultural heritage, University of Siena, Siena, Italy**
2110 Lucia Sarti, Mauro Calattini
2111
2112 **Centre d'Anthropobiologie et de Génomique de Toulouse, CNRS UMR 5288, Université Paul Sabatier,**
2113 **Toulouse, France**
2114 Ludovic Orlando
2115
2116 **Västergötlands museum, Stadsträdgården, Skara, Sweden**
2117 Maria Vretemark
2118
2119 **Cabinet of Anthropology, Tomsk State University, Tomsk, Russian Federation**
2120 Marina P. Rykun
2121
2122 **Institute for Eastern Research, Adam Mickiewicz University in Poznań, Poznań, Poland**
2123 Marzena H. Szmyt
2124
2125 **Institute of Archaeology, Jagiellonian University, Ul. Gołębia 11, 31-007, Kraków, Poland**
2126 Marcin Przybyła
2127
2128 **Zoological Institute of Russian Academy of Sciences, Universitetskaya nab. 1, 199034, St. Petersburg,**
2129 **Russian Federation**
2130 Mikhail Sablin
2131
2132 **Department of Anthropology, Czech National Museum, Prague, Czech Republic**
2133 Miluše Dobisíková
2134
2135 **Department of Health and Nature, University of Greenland, Greenland**
2136 Morten Meldgaard
2137
2138 **The Viking Ship Museum, Vindeboder 12, Roskilde, Denmark**
2139 Morten Johansen, Otto Christian Uldum
2140
2141 **Archaeology Institute, University of Highlands and Islands, Scotland, UK**

2142 Nick Card
2143
2144 **Laboratory for Experimental Traceology, Institute for the History of Material Culture of the Russian**
2145 **Academy of Sciences, Dvortsovaya nab., 18, 191186, St. Petersburg, Russian Federation**
2146 Olga V. Lozovskaya
2147
2148 **Scientific Research Center “Baikal region”, Irkutsk State University; 1, K. Marx st., Irkutsk, 664003,**
2149 **Russian Federation**
2150 Nikolai A. Saveliev
2151
2152 **Paleoecology Laboratory, Institute of Plant and Animal Ecology, Ural Branch of the Russian Academy**
2153 **of Sciences, Ekaterinburg, Russian Federation**
2154 Pavel Kosintsev
2155
2156 **Department of History of the Institute of Humanities, Ural Federal University, Ekaterinburg, Russian**
2157 **Federation**
2158 Pavel Kosintsev
2159
2160 **Centre for the Study of Early Agricultural Societies, Department of Cross-Cultural and Regional**
2161 **Studies, University of Copenhagen, 2300 Copenhagen, Denmark**
2162 Peder Mortensen
2163
2164 **Museum of Cultural History, University of Oslo, P.O. Box 6762. St. Olavs Plass NO-0130 Oslo,**
2165 **Norway**
2166 Per Persson
2167
2168 **ArchaeoScience, GLOBE Institute, University of Copenhagen, Copenhagen, Denmark**
2169 Pernille Bangsgaard
2170
2171 **Department of History, University of Santiago de Compostela, Spain**
2172 Pilar Prieto Martinez
2173
2174 **Lipetsk Regional Scientific Public Organisation "Archaeological Research", Lipetsk, Russian**
2175 **Federation**
2176 Roman V. Smolyaninov
2177
2178 **Laboratory for Archaeological Chemistry, Department of Anthropology, University of Wisconsin-**
2179 **Madison, Madison, USA**
2180 T. Douglas Price
2181
2182 **Nizhny Tagil State Socio-Pedagogical Institute, Nizhny Tagil, Russia**
2183 Yuri B. Serikov
2184
2185 **Institute for History of Medicine, First Faculty of Medicine, Charles University, Prague, Czech**
2186 **Republic**
2187 Vaclav Smrcka
2188

2189 **Centre for Archaeological Research Toraighyrov University, Pavlodar, Kazakhstan**
2190 Victor Merz
2191
2192 **Malmö Museer, Malmöhusvägen 6, Malmö, Sweden**
2193 Yvonne Magnusson
2194
2195 **Institute of Statistical Sciences, School of Mathematics, University of Bristol, Bristol, UK**
2196 Daniel J. Lawson
2197
2198 **Novo Nordisk Foundation Centre for Protein Research, Faculty of Health and Medical Sciences,**
2199 **University of Copenhagen, Copenhagen N, Denmark**
2200 Simon Rasmussen
2201
2202 **MARUM, University of Bremen, Bremen, Germany**
2203 Eske Willerslev
2204
2205 Contributions
2206 M.E.A., M.S., A.R.-M., E.K.I.-P., A.F., W.B., and A.I. contributed equally to this work. M.E.A., M.S.,
2207 T.S.K., R.D., R.N., O.D., T.W., F. Racimo, K.K. and E.W. led the study. M.E.A., M.S., A.F., C.L.-F., R.N.,
2208 T.W., K.K. and E.W. conceptualised the study. M.E.A., M.S., H.S., L.O., T.S.K., R.D., R.N., O.D., T.W., F.
2209 Racimo, K.K. and E.W. supervised the research. M.E.A., L.O., R.D., R.N., T.W., K.K. and E.W. acquired
2210 funding for research. A.F., J.S., K.G.S., M.L.S.J., M.U.H., A.A.T., A.C., A.Z., A.M.S., A.J.H., A.G., A.V.L.,
2211 B.H.N., B.G.R., C.B., C.L., C.M.-L., D.V., D.C.-S., D.L., D.N., D.C.S.-G., D.B., E.K., E.V.V., E.R.U., E.
2212 Kannegaard, F. Radina, H.D., I.G.Z., I.P., I.V.S., J.G., J.H., J.E.A.T., J.Z., J.V., K.B.P., K.T., L.N., L.L.,
2213 L.M., L.Y., L.P., L. Sarti, L. Slimak, L.K., M.G.M., M. Silvestrini, M.V., M.S.N., M.P.R., M.H.S., M.P.,
2214 M.C., M. Sablin, N.C., O.P., O.R., O.V.L., P.A., P.K., P.C., P. Ríos, P. Lotz, P. Lysdahl, P.P., P.B., P.d.B.D.,
2215 P.V.P., P.P.M., P.W., R.V.S., R. Maring, R. Mendiña, R.B., R.T., S.V., S.W., S.B., S.N.S., S.A.S., S.H.A.,
2216 T.D.P., T.J., Y.B.S., V.I.M., V.S., V.M., Y.M. and N.L. were involved in sample collection. M.E.A., M.S.,
2217 A.R.-M., E.K.I.-P., W.B., A.I., J.S., A.P., B.S.d.M., M.I., L.V., A.J. Stern, C.G., F.E.Y., D.J.L., T.S.K., R.D.,
2218 R.N., O.D., F. Racimo, K.K. and E.W. were involved in developing and applying methodology. J.S., C.G.
2219 and L.V. led the DNA laboratory work research component. K.G.S. led bioarchaeological data curation.
2220 M.E.A., M.S., A.R.-M., E.K.I.-P., W.B., A.I., A.P., B.S.d.M., B.S.P., A.S.H., R.A.H., T.V., H.M., A.M.,
2221 A.V., A.B.N., P. Rasmussen, G.R., A. Ramsøe, A.S., A.J. Schork, A. Rosengren, C.J.M., I.A., L.Z.,
2222 R.Maring, V.S., V.A., P.H.S., S.R., T.S.K., O.D. and F. Racimo undertook formal analyses of data. M.E.A.,
2223 M.S., A.R.-M., E.K.I.-P., A.F., W.B., A.I., K.G.S., D.J.L., P.H.S., T.S.K., and F. Racimo drafted the main
2224 text (M.E.A. and M.S. led this). M.E.A., M.S., A.R.-M., E.K.I.-P., A.F., W.B., A.I., K.G.S., A.P., B.S.d.M.,
2225 B.S.P., A.S.H., R. Macleod, R.A.H., T.V., M.F.M., A.B.N., M.U.H., P. Rasmussen, A.J. Stern, N.N.J., H.S.,
2226 G.S., A. Ramsøe, A.S., A. Rosengren, A.K.O., A.B., A.C., A.G., A.V.L., A.B.G., C.J.M., D.C.S.-G., E.
2227 Kostyleva, E.R.U., E. Kannegaard, I.G.Z., I.P., I.V.S., J.G., J.H., J.E.A.T., L.Z., L.Y., L.P., L.K., M.B.,
2228 M.G.M., M.V., M.P.R., M.J., N.B., O.V.L., O.C.U., P.K., P. Lysdahl, P.B., P.W., R.V.S., R. Maring, R.B.,
2229 R.I., S.V., S.W., S.B., S.H.A., T.J., V.S., D.J.L., P.H.S., S.R., T.S.K., O.D. and F. Racimo drafted
2230 supplementary notes and materials. M.E.A., M.S., A.R.-M., E.K.I.-P., A.F., W.B., A.I., G.G.S., A.S.H.,
2231 M.L.S.J., F.D., R. Macleod, L. Sørensen, P.O.N., R.A.H., T.V., H.M., A.M., N.N.J., H.S., A. Ramsøe, A.S.,
2232 A.J. Schork, A. Ruter, A.K.O., B.H.N., B.G.R., D.C.-S., D.C.S.-G., I.G.Z., I.P., J.G., J.E.A.T., L.Z., L.O.,
2233 L.K., M.G.M., P.d.B.D., R.I., S.A.S., D.J.L., P.H.S., T.S.K., R.D., R.N., O.D., T.W., F. Racimo, K.K. and
2234 E.W. were involved in reviewing drafts and editing (M.E.A., A.F., K.G.S., F.D., R. Macleod, H.M. and T.V.
2235 led this). All co-authors read, commented on, and agreed upon the submitted manuscript.

2236

2237 Corresponding authors

2238

2239 Correspondence to Morten E. Allentoft (morten.allentoft@curtin.edu.au), Martin Sikora

2240 (martin.sikora@sund.ku.dk), Eske Willerslev (ew482@cam.ac.uk).

2241

2242 **Ethics declarations**

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2244 Competing interests

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2246 The authors declare no competing interests.