HUMAN ORIGINS

Shadows of early migrations

Analysis of ancient nuclear DNA, recovered from 40,000-year-old remains in the Denisova Cave, Siberia, hints at the multifaceted interaction of human populations following their migration out of Africa. SEE ARTICLE P.1053

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The new discipline of palaeogenetics is delivering increasing dividends, the latest news coming from Reich, Pääbo and colleagues on page 1053 of this issue[1]. The authors' analysis of nuclear DNA of a human-like finger bone, found in Denisova Cave in southern Siberia, points towards a complex model of migration and colonization after anatomically modern humans moved out of Africa some 50,000–60,000 years ago.

Ever since 1925, when Raymond Dart's report of the first *Australopithecus* skull in southern Africa upended Victorian views of human origins, there has been debate over whether our species arose only once and spread throughout the world, replacing all extant species of *Homo*, or whether our ancestors interbred with the other populations and subspecies. The most extreme version of the 'candelabra' model of human origins — according to which human species arose multiple times independently of our *Homo ergaster* ancestors — has been largely discounted. But it has been difficult to assess more nuanced models, such as the possibility of genetic exchange with some archaic populations, including Neanderthals, and now perhaps ancient Siberians.

Until recently, genetic data and interpretation of the fossil record seemed to favour a complete-replacement model, in which all human species trace all of their genetic ancestry to a single origin in one or more African populations of moderate size some 200,000 years ago[2–5]. However, the Denisovan nuclear genome sequence[1], along with that of *Homo neanderthalensis* published by some of the same authors[6], suggest that the out-of-Africa population history of *Homo sapiens* is probably much more intertwined than previously thought, with more intertwining in some parts of the world than others.

On the basis of their analyses of ancient DNA from the Neanderthals and Denisovans, the Reich–Pääbo team proposes that limited gene flow from archaic *Homo* species to modern humans occurred in two brief episodes (Fig. 1). One episode occurred shortly after a subset of modern humans left Africa, and the second occurred only in the ancestors of Melanesian populations in Oceania. Their inference

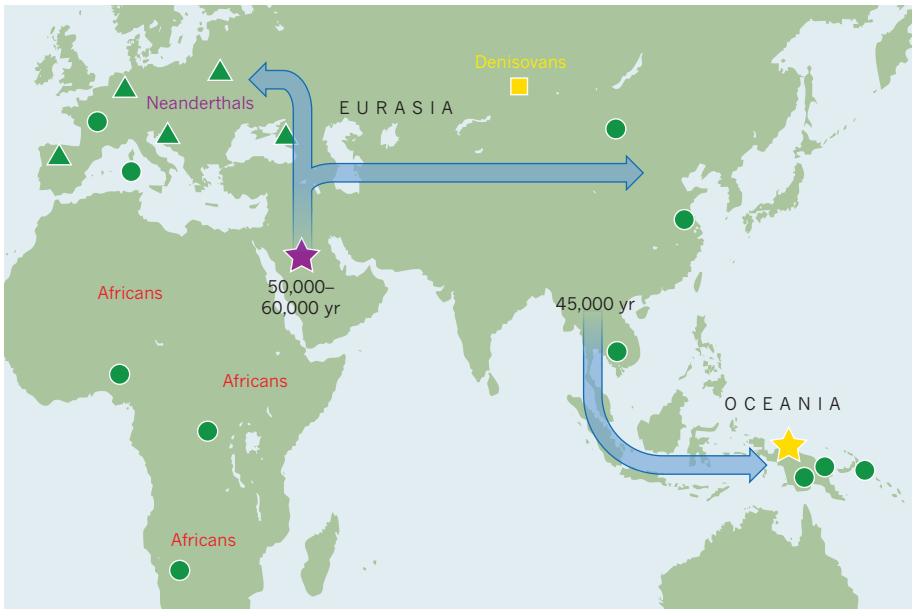

Figure 1 | New hypotheses extend the 'standard model' of modern human history. Triangles and circles respectively represent sampling locations[1,6] of Neanderthal remains and of present-day human genomes. The blue arrows indicate generally accepted major migrations of anatomically modern humans[11], following their departure from Africa 50,000–60,000 years ago. At this time, there were two primary archaic species in Eurasia, Neanderthals and *Homo erectus*; Reich, Pääbo and co-workers[1] suggest that a third group was also present, represented by the ancient Denisovan genome. From ancient DNA[1,6], they identify additional putative events involving two episodes of limited gene flow: first, genetic admixture from Neanderthals to modern humans, shortly after the exit from Africa; second, subsequent admixture with the archaic population exemplified by the nuclear DNA extracted from the Denisova finger bone. This second event seems to affect only the ancestors of present-day Melanesians, who are thought to have colonized Papua New Guinea some 45,000 years ago. African populations, both past and present, are genetically highly diverse, as indicated by the multiple labels.

of genetic admixture does not resurrect orthodox multiregional evolution, which theorizes extensive gene flow among *Homo* species across different geographical regions for hundreds of thousands of years[7]. Nailing specific details of a 'replacement plus limited gene flow' model will require much more work. But the broad outlines from sequencing ancient DNA provide a fascinating view of our genome, and present a hypothesis that can be tested when many, more diverse, human genomes (and, one hopes, more ancient ones) are available.

The new work[1] is a follow-up to an earlier paper[8], by a group led by Pääbo, on the deeply diverged mitochondrial DNA (mtDNA) genome recovered from the same finger fragment. Reich, Pääbo and colleagues[1] have now sequenced the bone's nuclear genome to approximately 2× coverage — that is, on average, they have obtained sequence from two ancient DNA fragments that cover a given base in the genome. They compare these fragments with low (1–5×) coverage data from 12 modern-human genomes, as well as with the Neanderthal genome[6] sequenced to 1.5×.

Nuclear DNA comes from the 22 pairs of autosomal chromosomes and the sex (X, Y) chromosomes. Apart from containing the vast majority of genetic information, nuclear DNA is well suited for analysis of gene flow because genetic recombination provides tens of thousands of semi-independent data points for comparing genetic relationships among present-day and ancient samples. The fragments of ancient DNA illuminate our understanding of human origins and, like the

shadows in Plato's proverbial cave, give us the broad outlines of ancient human migrations.

And what an interesting story they tell! It seems that the Denisovan was most similar genetically to Neanderthals, but not so similar as to have been sampled from the same population. The Reich–Pääbo team now demonstrates that Denisovans and Neanderthals are sister taxa, clustering, on average, slightly more often than either does with modern human samples. Compared with modern humans, the Denisovan sample clusters slightly more often (about 1–3% of time) with the present-day European or east Asian genomes as compared with the African genomes from the Yoruba, Mbuti and San. This is consistent with reported gene flow from a Neanderthal population into the ancestors of modern-day Eurasians[6], if Denisovans and Neanderthals are close sister taxa.

What is particularly fascinating, however, is that the Denisovan sample seems to share an extra genetic affinity (beyond that for European and Asian genomes) with present-day island Melanesians. This is rather unexpected, as the earliest occupation of Papua New Guinea, an island in Oceania, by modern humans occurred only about 45,000 years ago[9,10], and suggests quite a complicated picture for the ancestry of the Denisovan finger fragment.

Studying ancient molecular diversity is not without its pitfalls — the molecular shadows we perceive may well have a more complex underpinning. In their Supplementary Information, Reich, Pääbo and co-workers[1] go into exquisite detail to discount many potential sources of bias in their data, including contamination, handling of the ancient material and differences in depth-of-coverage among genomes.

Many of these problems can indeed be discounted, but some technical hurdles remain. Sequencing technology and DNA preservation may affect the interpretation of the clustering statistic for ancient genomes — for example, the finding that greater numbers of derived alleles (gene variants) are shared between Eurasians and Neanderthals than between Eurasians and Denisovans could be due to differences in sequencing technology. Nonetheless, it seems that comparison of ancient and modern genomes processed at the same time provides a consistent picture of extra allele-sharing between Denisovans and present-day Melanesians, as well as between Denisovans and Neanderthals.

Perhaps the most powerful use of ancient DNA sequencing technology is in the realm of hypothesis generation. For example, from the Denisovan remains, one can make explicit predictions about the patterns of genetic variation in modern humans who are yet to have their DNA sequenced. Specifically, if there is 5–7% extra allele-sharing in the genomes of Melanesians with an archaic *Homo* population, by sequencing modern individuals from the region, every so often we should find oddly divergent regions of the genome in some Melanesian individuals. The same idea has been proposed to test Neanderthal admixture models (namely, looking for regions of the human genome in which the highly divergent fragments of DNA sequence are non-African and potentially inherited from an ancient population).

As this work[1] illustrates, studies of human genomic variation need to expand beyond the realm of medical interest. The study of diverse human genomes (both ancient and present-day) is the most powerful tool available for understanding our common human origins and history. The success of this research depends, of course, on proper community and individual engagement of diverse peoples (including those from isolated human populations), who may possess the genomic history of ancient human migrations across the globe. Together with the palaeoanthropological record, analyses of ancient and modern DNA will help us to better understand our own creation myths, and illuminate the details of the molecular shadows in the cave. ■

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QUANTUM TECHNOLOGY

Electrons spin in the field

Nanowires are candidates for enabling the exchange of quantum information between light and matter. The rapid control of a single electron spin by solely electrical means brings this possibility closer. SEE LETTER P.1084

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The quest to develop ways to store and manipulate quantum information in condensed-matter systems is establishing a tool kit for controlling the nanoworld — one that promises far-reaching technological innovation. One example is the idea of encoding data, both classical[1] and quantum[2], in the spin orientation of a single electron (its intrinsic magnetic moment). During the past five years, this vision has largely been realized[3–7], and researchers are now turning to other goals, such as high-speed control of the spin orientation and the suppression of 'decoherence' processes that lead to a loss of quantum information. Innovative methods in quantum control[8,9] and new material systems are leading the way in tackling this next generation of challenges.

On page 1084 of this issue, Kouwenhoven and co-workers[10] report an experiment that exploits the unique material properties of an indium arsenide (InAs) semiconductor nanowire to rapidly control the quantum state of a single electron spin using only electric fields. Beyond just flipping the spin orientation of a single electron, the authors tailor the precise timing of electric-field pulses to extend the spin coherence time (during which the information encoded in the quantum state of the spin is preserved).

Controlling electron and nuclear spins is central to magnetic resonance technologies such as magnetic resonance imaging. These technologies use radio- or microwave-frequency magnetic fields to manipulate some 10^{23} spins in macroscopic volumes. On the nanometre scale, the application of spatially selective, oscillating magnetic fields is a formidable challenge, which makes controlling single spins difficult. Although proof-of-principle experiments have shown that nanometre-scale magnetic control is possible[11], the time it takes to rotate the orientation of the electron spin magnetically is long and does not allow for many rotations within a spin coherence time. This limitation inhibits the use of this technique for quantum information processing.

Kouwenhoven and colleagues' experiment[10] addresses this shortcoming by moving from magnetic to all-electric fields to achieve rapid control over the spin. Although an interaction