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## Commentary Fuyan human of 120–80 kya cannot challenge the Out-of-Africa theory for modern human dispersal

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Recently, Liu et al. reported a mass collection of human teeth found in Fuyan cave in Hunan province of southern China, dating back to 120–80 thousand years age (kya) [1]. Morphological measurement of these samples indicated that they can be unequivocally assigned to Modern Human (*Homo sapiens*). This great finding, as commented by Ewen Callaway, suggested that Modern Human had reached Asia between 80 and 120 kya [2]. This early human trekked out of Africa suggested that remains from the Skhul and Qafzeh Caves in Israel may also be successful migrants out of Africa. Also, the solid evidence of Modern Human from Fuyan Cave conflicted with the time scale given by genetics which proposed that the entire genetic lineages of eastern Eurasians can only be traced back to 55–60 kya. To explain this inconsistency, R. Dennell drew a scenario about multiple-waves of modern human's migration into different region of Eurasia [3].

This exciting discovery was widely reported by the media throughout the world. But there are deviations about the understanding of this finding in the public. Some reports considered that this finding will challenge the "Out-of-Africa" theory for dispersal of the Anatomically Modern Human (here after "AMH") or may indicate that Modern Human originated in southern China. As a traditional belief, public and/or academia in China tend to believe that modern humans in China are direct descendants of archaic humans in East Asia like Jinniushan Man (representing Archaic *Homo sapiens*), Peking Man, and even Yuanmou Man (representing *Homo erectus*). A series of physical genotypes had been analyzed to support the "continuous evolution" of human in East Asia.

Here we summarized the most advanced achievements of genetic studies about the early dispersal history of AMH. We proposed that genetics do provide time framework for 100–50 kya modern human remains outside of Africa, and hence, remains of AMH at this period in eastern Eurasia will not challenge the Outof-Africa theory for dispersal of AMH.

It is worth to explain the deviation of previous genetic dating. The public and non-genetic researchers have always been confused by the variants of time scales for human evolution estimated with varied genetic markers. Sometimes, different sets of markers may yield results in several folds [4]. This situation caused doubts about the confidence level of time estimations with genetics and further reconstructions of human history with these estimations. In previous genetic studied, age estimation using DNA sequences can be affected by the choice of mutation rates largely. In the recent years, this issue was almost resolved by using ancient DNA sequences with confident archaeological dating.

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Previous genetic studies proposed that all modern humans in eastern Eurasia can generally trace their ancestors back to about 60 kya. In this article, we used the broad sense of eastern Eurasia which including South Asia, Central Asia, North Asia, East Asia and Southeast Asia. From mitochondria perspective, the most common recent ancestor (TMCRA) of three macro-haplogroups, a.k. M, N, and R, in eastern Eurasia only lived about 55–60 kya [5]. Since the mutation rate of mtDNA had been calculated by ancient DNA, it's generally accepted that the age estimations of mtDNA in recent researches are confident and can be used to explore the history of modern populations. Full sequence of human Y-chromosome can also be used for age estimation; however, this technology was accessed only in the recent years, largely delayed by the long length (~60 M) and intense repeat structure of Y chromosome. Mutation rate of Y-chromosome full sequence had been proposed by several methods, measuring from human-chimpanzee comparisons, deep-rooting pedigrees, or founding events in human history [4].

In the recent years, ancient mtDNA and Y-chromosome extracted from remains with confident archaeological dating had been used to calibrate the mutation rate [6]. Also, scholars had also concerned about various mutation rates on different region of DNA sequence when constructing the final evolution mode of mtDNA and Y-chromosome.

According to the most advanced studies of mtDNA, TMCRA of most non-African's maternal pedigree (a.k. L3) live at about 67.3 or 71.2 kya [5]. But it's worth to notice that mtDNA haplogroup (HG) L1-L3a also contribute to a considerable portion of maternal gene pool of populations in Middle East (especially Yemen). Therefore, it's most probably that mtDNA HG L1-L3 diverted in the adjacent region of northeast Africa and Arab Peninsula. Considering the possible Yemeni origin of lineage L6, the date of "Out-of-Africa" of AMH from mtDNA perspective may be older than the age of L3'4'6'7 (a.k. 105,300 ± 24,150 years ago [5], Fig. 1a). This deduction is consistent with the age of human remains found at the Skhul and Qafzeh Caves in Israel, dating back to about 92 kya.

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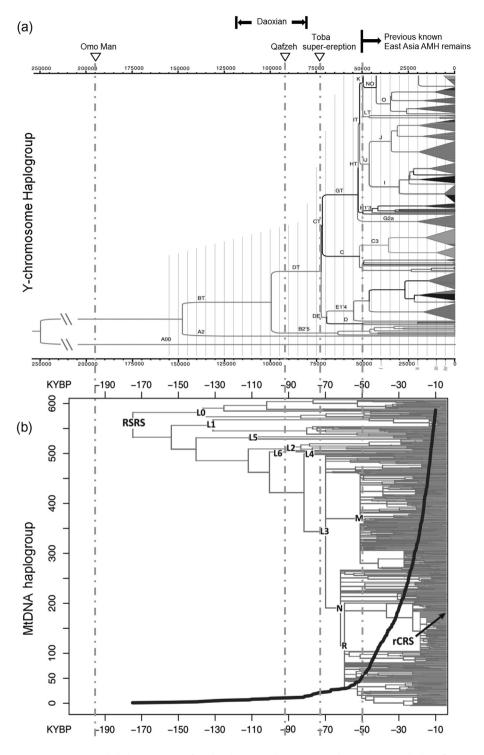


Fig. 1. Ages of several important AMH remains and phylogenetic tree of modern human Y-chromosome and mtDNA. Note: The base figures were cited from Karmin et al. 2015 [7] and Behar et al. 2012 [5].

A new scenario of early differentiation of human Y-chromosomes was revealed by several studies about full Y-Chromosome sequences of global populations [7]. When using a mutation rate calibrated by Y-chromosome sequence of 45 kya Ust'Ishim man, the splitting time of HG DT from the branch HG B was measured to be about 99.8 kya [7]. But on the contrary, TMCRA of HG DT's living descendants is only about 71.7 kya (see Fig. 1b). This means that HG DT had went through a long-term bottleneck for about 28 ky before it gave birth to HG DE and HG CT that are ancestors of all non-African males.

We can also observe rapid expansions of both mtDNA (like HG M and parts of R's sub-branches) and Y-chromosome (like HG C, D, GT and K) between 60 kya and 50 kya [7]. All major paternal lineages and most lineages of maternal lineages of non-African modern human appeared at this stage. Due to uncertain mutation rate and evolution mode, previous studies generally revealed that

ancestors of all non-African populations can only traced back to 60-50 kya. Considering that advanced achievements mentioned above, we can determine that this age (60–50 kya) is no the date of "Out-of-Africa", but the period when early human start their expansion into the inner land of Eurasia from refuges outside of Africa.

Two recent studies of human genomic diversity provided more evidences to understand the early dispersal of Modern Human. Based on high-coverage whole-genome sequence studies, Pagani et al. 2016 proposed that the presence of AMHs out of Africa is earlier than 75,000 years ago [8]. Another research published on the same issue of Nuture Journal demonstrated that the ancestors of some pairs of present-day human populations (African vs non-African) were substantially separated by 100,000 years ago and Non-Africans split from African hunter gatherers 130,000 years ago [9]. Therefore, evidences from autosome genomes also support the observation of mitochondrial DNA and Y-chromosome we described above [10].

It is also worth to notice that the lower limit of bottleneck periods of human Y-chromosome HG DT (71.7 kya), mtDNA HG L3 (67.3 or 71.2 kya), and autosome (75 kya) are extremely coincides with the date of Toba super-eruption (74 kya). This super-eruption may had cause the dramatically decrease or extinction of modern human populations in South Asia, Southeast Asia and East Asia. Hence, this major geologic event is consistent with the observation of long-term bottleneck on Y-chromosome, mtDNA, and autosome genetic structure of modern human outside of Africa at some degree.

The advanced genetic studies mentioned above may help to reveal the detailed history of early AMH dispersal. "Out-of-Africa" theory of human origin is generally comprised of two parts of content. Firstly, it is generally accepted that various kinds of *H. habilis*, H. ergaster, H. erectus, H. sapiens, and H. heidelbergensis found outside of Africa are results of continuous migration of *Homo* species which revolved from Australopithecus on Africa continent. There are few arguments about this part of content after the findings of fossils of Omo Man and *H. sapiens idaltu*. Secondly, it proposed that all non-African modern humans are descendants of ancestor who migrated from Africa at a relative recent age (about 50–60 kyr from previous researches), even though limit gene flow from other early Homo species cannot be excluded [10].

According to the most advanced calculations of human Y-Chromosome, the most common recent ancestor of modern human outside Africa should be dating back to 100 kya. This scenario is consistent with the calculations of human mtDNA and the finding of human remains in Qafzeh Cave, Israel, dating back to 92 kya. Long-term of bottleneck effects were observed on both Y-chromosome sequence and mtDNA sequence of modern human during the 100–50 kya. At about 50 kya, genealogy of human paternal Y-chromosome and maternal mtDNA differentiated gradually during this time and gave birth to most of the major lineages for all non-African [7]. Hence, we can conclude that genetic evidences of three makers systems (Y-chromosome, mtDNA, and autosome) do provide time frame for 100-50 kya modern human remains in eastern Eurasia. Remains of Homo sapiens at this period in Eastern Eurasia will not challenge the Out-of-Africa theory for dispersal of Automatically Modern Human.

Finally, analysis of ancient DNA will helps to understand the details about the great dispersal of modern human through the world and the complex genetic introgression between different kinds of *Homo* species. We hope that in the future, more remains of early modern human can be found between Middle East and Southern East Asia. Scientific excavation, accurate archaeology dating and DNA extraction from human remains are urgently needed to expand our understanding about human's history.

## **Conflict of interest**

The authors declare that they have no conflict of interest.

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