The Human Genetic History of East Asia: Weaving a Complex Tapestry

Review

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East Asia encompasses a wide variety of environments, peoples, cultures and languages. Although this review focuses on East Asia, no geographic region can be considered in isolation in terms of human population history, and migrations to and from East Asia have had a major impact. Here, we review the following topics: the initial colonization of East Asia, the direction of migrations between southeast Asia and northern Asia, the genetic relationships of East Asian hunter-gatherers and the genetic impact of various social practices on East Asian populations. By necessity we focus on insights derived from mitochondrial DNA and/or Y-chromosome data; ongoing and future studies of genome-wide SNP or multi-locus re-sequencing data, combined with the use of simulation, model-based methods to infer demographic parameters, will undoubtedly provide additional insights into the population history of East Asia.

Introduction

East Asia is defined here as the geographic region bordered by the Ural Mountains in the west, by the Himalayan Plateau in the southwest, by the Bering Strait in the northeast, and extending into island southeast Asia. A vast area, East Asia encompasses a wide range of environments, from permafrost tundra to tropical rainforest. The geography of the region also ranges from high mountain ranges to sea-level areas, with various bodies of water surrounding and flowing into inter-island regions. However, the only significant geographic barrier to human dispersal in the region would appear to be the Himalayan Plateau. Despite the apparent lack of dispersal barriers, there is extensive diversity among the peoples, cultures and languages of East Asia. Understanding the genetic history of East Asia is therefore of interest for illuminating how this extensive diversity arose.

Although the earliest presence of members of the genus *Homo*, *Homo erectus*, in East Asia dates back to at least 1.6 million years [1], all modern human populations in East Asia (and elsewhere in the world) are descended from one or more migrations of anatomically modern humans from Africa some 50–70 thousand years ago (kya). While the focus of this review is on the genetic history of East Asia, no geographic region can be considered in complete isolation; moreover, migrations to and from East Asia have played an important role in human population history. Briefly, these migrations include: initial colonization some 50–60 kya by modern humans coming from Africa by southern or northern routes (discussed in more detail below); more recent migrations to and from western Eurasia (e.g., via the Silk Road) [2,3]; a probable expansion from

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southern Siberia into eastern Europe about 12–14 kya [4]; expansion of Sino-Tibetan speakers into northeastern India [5,6]; the colonization of the New World via the Bering Strait around 15 kya [7,8] (see accompanying review on the Americas); and the Austronesian expansion, beginning around 6 kya from Taiwan through the Philippines and Indonesia, eventually reaching island and coastal Melanesia, Micronesia, Polynesia, and even Madagascar [9-11] (see accompanying review on Oceania). We will concentrate on the following topics: the initial settlement of East Asia, the subsequent north-to-south and south-to-north migrations, the genetic relationships of East Asian hunter-gatherers, and the impact of various social practices on patterns of genetic variation in East Asian populations. The genetic evidence we discuss consists mainly of mitochondrial DNA (mtDNA) (Figure 1) and non-recombining Y chromosome (NRY) data (Figure 2), because the relevant autosomal DNA data for addressing Asian population history are still relatively scarce. However, the situation is changing rapidly, especially with the recent publication of the results of the Pan-Asian SNP consortium [12], which analyzed approximately 50,000 SNPs in 1808 individuals from 73 Asian populations, and we refer to these and other autosomal DNA data where appropriate.

Initial Settlement of East Asia

Once it became generally accepted that modern humans arose recently in Africa, attention was focused on the number and timing of dispersals of modern humans from Africa. Based on archaeological data, patterns of cranial variation and the limited genetic evidence then available, it was suggested [13,14] that there were two major dispersal events: first, an early dispersal some 50–100 kya, via a southern route across Saudi Arabia and along the coast of India and southeast Asia, eventually reaching Sahul, the combined Australia–New Guinea landmass; second, a later dispersal between 15–50 kya that went north of the Himalayas (see also the accompanying South Asia review). According to the 'early southern dispersal' hypothesis, subsequent migrations, partly driven by agricultural expansions, would have largely erased the genetic evidence of this early dispersal, with the possible exception of certain 'refugia' populations, such as southeast Asian hunter-gatherers (e.g., Malaysian Semang and Filipino Negrito groups), Andamanese and indigenous Australians.

Indeed, subsequent mtDNA and NRY studies of these (and other) populations have identified what is commonly interpreted as the signature of an early southern dispersal. All human mtDNA haplogroups fall into three main clades, designated L, M, and N; L is restricted to Africa or recent migrants from Africa, whereas almost all non-African haplogroups belong to M or N, both of which arose from African haplogroup L3 [15]. Both M and N show a rapid radiation of basal mtDNA lineages, many of which are restricted to the above refugia populations, that have been dated to around 50–60 kya [16–18]. Similarly, NRY haplogroups C-M130 and D-M174 have been suggested to support an early southern dispersal route [19,20]. C-M130 is found sporadically in India

Figure 1. Map depicting the distribution of major mtDNA haplogroups in East Asia.

Abbreviations and references are: sCh, southern China [19,61]; nCh, northern China [19,61]; Tib, Tibet [19,56,62–64]; Mon, Mongolia [62,64,65]; wEv, western Evens [66]; cEv, central Evens [66]; eEv, eastern Evens [66]; STE, Stony Tunguska Evenk [66]; Ien, Iengra [66]; Nyu, Nyukzha [66]; YSE, Yakut-speaking Evenks [66]; Yak, Yakuts [66]; Yuk, Yukaghirs [66]; Krk, Koryaks [66]; Tuv, Tuvans [66]; Kor, Korea [19,62]; Jap, Japan [62,67]; Tai, Taiwan [19,68]; Vie, Vietnam [62]; Tha, Thailand [19,62]; Mal, Malaysia [10,69]; Sum, Sumatra [68]; Jav, Java [68]; Bor, Borneo [68]; Ten, Tengarras [68]; Mol, Moluccas [68]; Phi, Philippines [68].
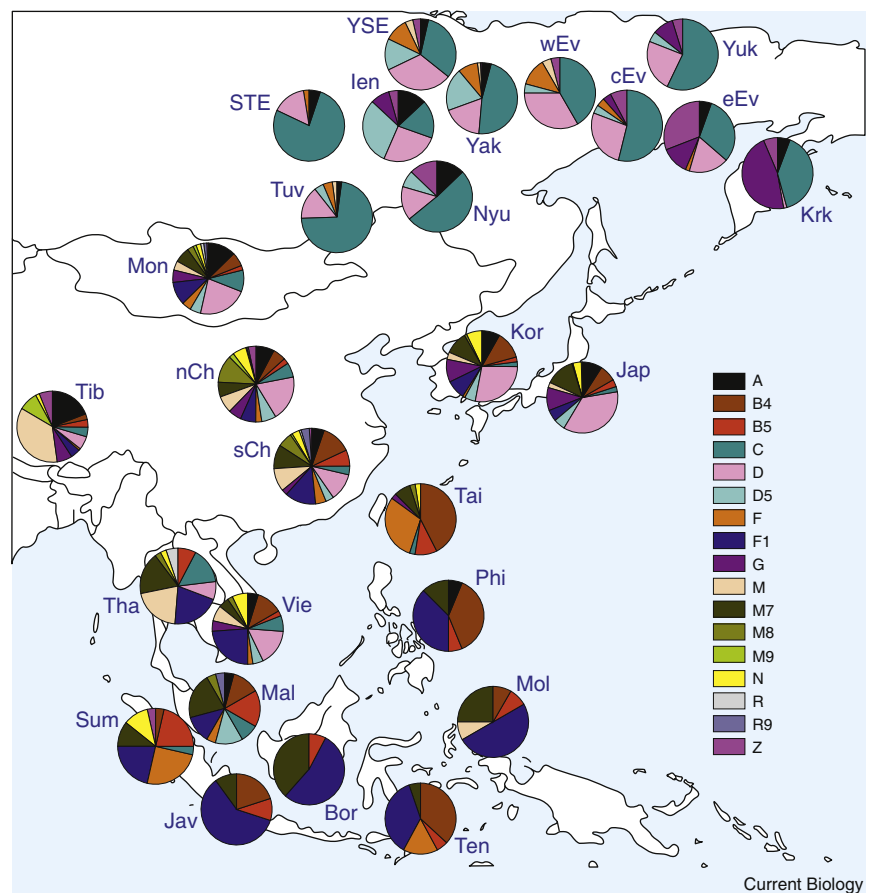
and southeast Asia, and reaches its highest frequencies in eastern Indonesia [21] and some Filipino Negrito groups (F. Delfin, M. Stoneking, and M.C.A. DeUngria, unpublished data). C-M130 also gave rise to two other NRY haplogroups, C-M38 and C-M217, which are at their highest frequencies in Oceania and northeastern Asia, respectively [20]. D-M174 is derived from African haplogroup DE-M1 (Yap+), is found at highest frequency in Andamanese, Tibetans and Japanese, and only sporadically elsewhere, and has been dated to about 60 kya [19]. The ages and distributions of haplogroups C-M130 and D-M174 are thus consistent with an early southern dispersal. Taken together, the genetic support for an early southern dispersal route is viewed as quite strong [15,22] (see also the South Asia review).

However, some caveats are in order. The dating of the radiation of mtDNA haplogroups M and N to 50–60 kya relies on the 'rho' method [23], which has recently been shown in a simulation study to give unreliable results, especially when the demographic history of a population departs from the standard model of constant population size [24]. The dispersal events inferred from dating mtDNA haplogroups, and from dating NRY haplogroups via the rho method, could thus be considerably younger than 50–60 kya. Another major concern in dating both mtDNA and NRY haplogroups is deciding which rate estimate to use [25,26]. Furthermore, while the early southern dispersal has been largely argued for on the basis of the age and phylogeographic distribution of the relevant mtDNA and NRY haplogroups, no attempt has been made to model actual population demographic history and dispersal events using simulation-based approaches [27–29]. Such approaches could determine if an early southern dispersal is indeed the best explanation for the data, and, if so, to what extent alternative scenarios can be ruled out. These caveats aside, it is our view that an early southern dispersal remains so far the best explanation for the genetic data, and we would like to emphasize that with more accurate dating of mtDNA and NRY haplogroups, additional autosomal DNA data, and with the simulation-based modeling approach

advocated here, the early southern dispersal route may be expected to be supported and illuminated further, rather than contradicted. Indeed, the recent Pan-Asian SNP study found strong support for a largely southern origin of extant southeast and east Asian populations [12].

Northern *versus* Southern Expansions in East Asia

A question that has received considerable attention is the extent to which there have been north-to-south *versus* south-to-north migrations in East Asia. Early mtDNA studies suggested a distinction between northeastern and southeastern Asian groups, with greater diversity in southeastern groups, suggesting a southern origin of the northeastern groups [30,31]. More detailed phylogeographic studies of mtDNA variation have supported this north–south division with overall greater genetic diversity in southern groups [32–34], and attempts have been made to link the expansion of specific mtDNA haplogroups with particular climatic events, most notably the end of the Last Glacial Maximum [15,35]. Studies of NRY haplogroups also tend to support south-to-north migrations [36–38], although some haplogroups are suggested to have arisen in the north and then spread to the south [39]. North–south clines have also been observed in some studies of autosomal SNPs [40,41], but no directionality of spread could be inferred. Other studies have argued against a simple north–south division in favor of isolation-by-distance [42] or multi-directional gene flow [43]; it has also been suggested that there is a strong north–south boundary in the distribution of mtDNA lineages but not NRY lineages, which may
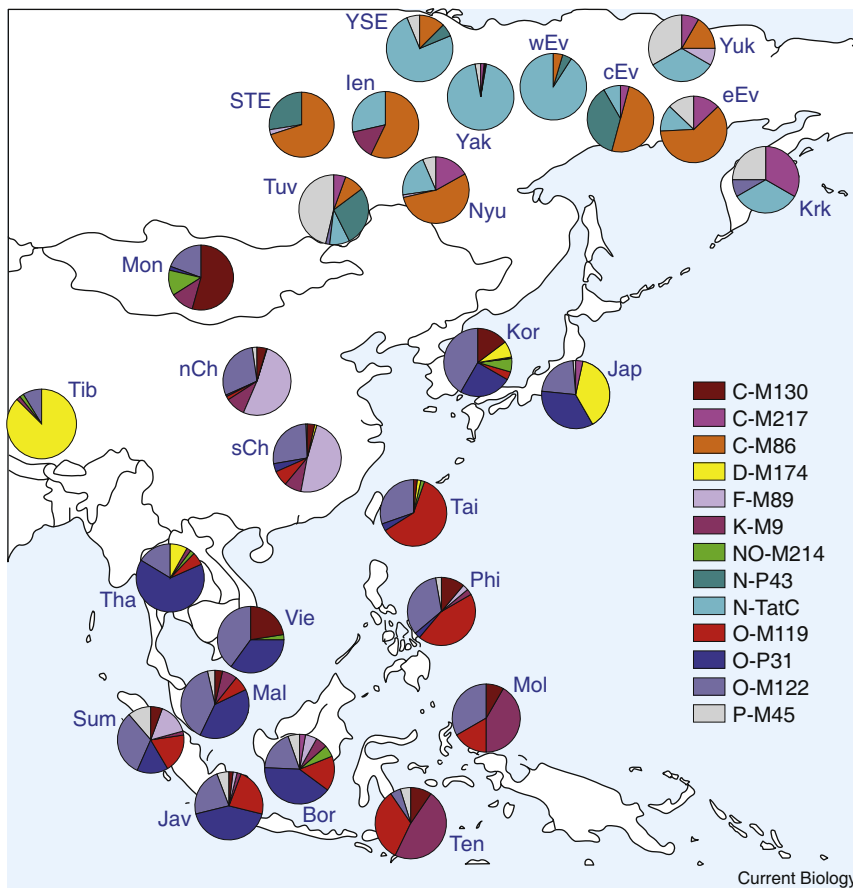
Figure 2. Map depicting the distribution of major NRY haplogroups in East Asia.

Abbreviations and references are: sCh, southern China [19,61]; nCh, northern China [19,61]; Tib, Tibet [19,56,62–64]; Mon, Mongolia [62,64,65]; wEv, western Evens [66]; cEv, central Evens [66]; eEv, eastern Evens [66]; STE, Stony Tunguska Evenk [66]; Ien, Iengra [66]; Nyu, Nyukzha [66]; YSE, Yakut-speaking Evenks [66]; Yak, Yakuts [66]; Yuk, Yukaghirs [66]; Krk, Koryaks [66]; Tuv, Tuvans [66]; Kor, Korea [19,62]; Jap, Japan [62,67]; Tai, Taiwan [19,68]; Vie, Vietnam [62]; Tha, Thailand [19,62]; Mal, Malaysia [10,69]; Sum, Sumatra [68]; Jav, Java [68]; Bor, Borneo [68]; Ten, Tengarras [68]; Mol, Moluccas [68]; Phi, Philippines [68].

MtDNA and NRY analyses suggest a significant proportion of unique haplotypes in East Asian hunter-gatherers. Analyses of the Semang, for example, indicate a high frequency of unique mtDNA lineages, in particular M21 [17], which diverged early in the radiation of haplogroup M. The dates associated with M21 and other basal mtDNA lineages found in southeast Asia of 50–60 kya [47,48] must be viewed with caution, as the dating method may not be reliable [24]. However, the position of these lineages in the mtDNA phylogeny clearly indicates an early divergence, suggesting that their presence in southeast Asia reflects an early migration of modern humans from Africa [17]. Similarly, there are unique, basal haplogroup N mtDNA lineages in the Mamanwa, a Negrito group from Mindanao in the Philippines, that are absent from neighboring groups (E. Gunnarsdottir and M. Stoneking, unpublished data). Some Negrito groups also exhibit high frequencies of Y-STR haplotypes on the background of NRY haplogroups C-M130 and K-M9 that are not found elsewhere in southeast Asia but are associated with Y-STR haplotypes found in aboriginal Australians (F. Delfin, M. Stoneking, and M.C.A. DeUngria, unpublished data).

The above limited genetic data available for Semang and Negrito groups does suggest a different history for these hunter-gatherer groups than for other East Asian groups. However, the recent Pan-Asian SNP study [12] arrives at a different conclusion. Negrito groups from Malaysia do not show any close genetic relationship with Negrito groups from the Philippines; instead, Negrito groups from both Malaysia and the Philippines tend to genetically resemble their non-Negrito geographic neighbors. The authors of the Pan-Asian SNP study [12] conclude that their results "… *point toward a history that unites the Negrito and non-Negrito populations of Southeast and East Asia via a single primary wave of entry of humans into the continent.*" A possible reconciliation of the genome-wide SNP results with the above mtDNA and NRY results for Negrito groups is a scenario involving early isolation followed by recent admixture. We suggest that the ancestors of the Negritos either represent an earlier migration, or they were isolated from other Asian groups early after entering Asia in the

reflect more substantial male than female migration in recent times [44].

However, strong support for a south-to-north direction of migration in east Asia is provided by the Pan-Asian SNP study [12]. This study found a strong and highly significant correlation between haplotype diversity and latitude, with higher diversity in the south and lower diversity in the north. Such a pattern, coupled with a maximum-likelihood analysis of population relationships that also indicates a south-to-north direction of population spread, provides compelling evidence for a primary south-to-north direction for the colonization of east Asia. However, some movement from north-to-south cannot be ruled out.

Hunter-gatherers in East Asia

Hunter-gatherer groups have long been of interest to anthropologists because they are generally assumed to maintain a lifestyle that characterized all human populations up until about 10 kya, when agriculture was developed. Groups in East Asia that either are currently hunter-gatherers or were until recent times include the Ainu of northern Japan, the Semang of Malaysia, the Mlabri from Thailand, 'Negrito' groups from the Philippines, southeast Asian 'sea nomads' from the coast of Thailand and Myanmar, various groups from Borneo subsumed under the generic term 'Punan', as well as various Siberian groups [45]. There is, thus, a greater diversity of hunter-gatherer groups in East Asia than in Africa; however, African hunter-gatherer groups (such as Pygmies, San, and Hadza) have been much more intensively studied genetically than those from East Asia [46].

same migration as the ancestors of non-Negrito groups, to account for the distinctive mtDNA and NRY lineages in Negrito groups. The Negrito groups subsequently experienced high levels of migration in recent times from neighboring groups, which is observed in the autosomal DNA data at a level that would account for the genetic similarities between Negrito groups and their non-Negrito neighbors [12], as well as in the mtDNA and NRY data mentioned above. Further analyses of the Pan-Asian SNP data, which incorporate similar data from relevant Oceanic populations (such as those from Australia and New Guinea), should shed additional light on this question.

It seems probable that the present-day Semang and Negrito groups have maintained their hunting-gathering lifestyle since their ancestors arrived in East Asia. However, the same cannot be said for all other hunter-gatherer groups in East Asia. In particular, genetic and linguistic analyses of the Mlabri, an elusive hunting-gathering group from northern Thailand that was first described as late as 1938, indicate that they probably originated from an agricultural group some 500–800 years ago, and subsequently reverted to hunting and gathering [49]. Interestingly, the Pan-Asian SNP study [12] found that the Mlabri stand out as a population isolate, and moreover are most similar genetically to the H'Tin, precisely as suggested by linguistic analyses and by oral tradition [49]. Similarly, it has been suggested that the Punan of Borneo and the sea nomads may also represent 'respecialized' hunter-gatherers from an original agricultural lifestyle, rather than continuous hunter-gatherers [50]. In any event, it cannot be automatically assumed that any contemporary hunter-gatherer group reflects a pre-agricultural lifestyle, and genetic analyses can contribute to discerning their history.

The Impact of Social Practices on Genetic Variation
Human social practices, such as residence patterns and subsistence strategies, can influence the patterns of genetic variation. Studies of East Asian populations have played an important role in documenting such influences. For example, the first comparative study of human mtDNA and NRY variation found significantly larger genetic differences between populations for NRY markers than for mtDNA, and suggested that this disparity reflects a higher female migration rate due to patrilocality [51]. Patrilocality is the practice of females moving to the residence of their husbands after marriage, and about 70% of human societies are patrilocal [52]. An obvious test of the hypothesis that patrilocality is indeed responsible for the larger genetic differences between NRY and mtDNA markers would be to examine NRY and mtDNA variation in matrilocal groups. Indeed, a study of NRY and mtDNA variation in matrilocal and patrilocal groups among the hill tribes of northern Thailand [53] found strong support for the hypothesis as mtDNA variation was lower within matrilocal groups and genetic differences were bigger between matrilocal groups than patrilocal groups. The opposite pattern — lower variation within and bigger differences between patrilocal groups than matrilocal groups — was found for NRY markers [53]. A follow-up study [54] that estimated male and female migration rates from these data confirmed the overall pattern, but found interesting differences in that female migration into matrilocal groups was only slightly lower than male migration, whereas there was essentially no male migration into patrilocal groups. The genetic studies of the Thailand hill tribes thus

provide novel insights into the impact that matrilocality and patrilocality can have on patterns of genetic variation.

Population expansions, often associated with or driven by agriculture, can be inferred from genetic data. Such expansions, which are also often associated with specific language families, have been hypothesized for East Asia, including the Austro-Asiatic, Tai, Sino-Tibetan and Austronesian language families [55]. Assessing the genetic impact of such expansions can help differentiate between purely cultural mechanisms as opposed to demic diffusion (i.e., actual population migration) for the spread of cultural traits, as for example has been intensively studied with regard to the spread of agriculture from the Near East to Europe (see the review on Europe). Early mtDNA studies found an overall homogeneity in East Asian groups that was attributed to agricultural expansions [31]. Genetic evidence does suggest a north-to-south spread from China to southeast Asia of Tibeto-Burman speaking groups [56] that ultimately also reached northern India [5]. This expansion is more evident in the NRY markers than in mtDNA, suggesting male-biased migration or admixture. Genetic evidence also supports an origin for the Austronesian expansion in Taiwan [9,10], and indicate demic expansions associated with Austro-Asiatic and Daic (Tai-Kadai) speaking groups [33,57]. In addition, not all population expansions that can be inferred from genetic data are related to agriculture; for example, genetic evidence indicates a population expansion associated with the recent spread of the Han culture from northern to southern China [44].

Another social practice, for which there is evidence of a genetic impact in East Asia, is social selection: increased reproductive fitness that is transmitted socially from generation to generation. Usually associated with males who by reason of social prestige enjoy enhanced reproductive success, social selection results in high male fertility associated with one paternal lineage, which can potentially have a large impact on the Y-chromosomal gene pool. One example is an NRY lineage that is at unusually high frequency across Asia (~8% in Asia, and estimated to account for ~0.5% of worldwide NRY lineages) and appears to have originated in Mongolia about 1 kya [58]. This NRY lineage is attributed to Genghis Khan and his patrilineal descendants. Another NRY lineage occuring at a high frequency in northeastern China and Mongolia (~3.3%) is estimated to have arisen about 600 years ago, and is attributed to Qing Dynasty nobility [59]. Although one can question the specific historical assignments of these lineages, it is nonetheless clear that these two NRY lineages have increased dramatically in frequency, and social selection remains the most probable explanation.

Conclusions and Future Directions
In conclusion, the current genetic evidence tends to support an early migration of modern humans from Africa along a southern route to East Asia. Many studies find genetic differences between southern and northern East Asian populations, and while the Pan-Asian SNP study [12] conclusively shows a strong signature of a south-to-north migration, some migration in the reverse direction cannot be ruled out. Some hunter-gatherer groups do show distinctive genetic signatures, suggesting that they have maintained their hunting-gathering lifestyle since pre-agricultural times, while other hunter-gatherer groups may have reverted recently from an agricultural lifestyle. Genetic analyses of East Asian groups have also demonstrated an important

impact of human cultural practices — in particular, residence pattern, social selection and agriculture-related population expansions — on genetic variation.

However, current knowledge of the genetic history of East Asia is limited in two important ways. The first is that most of our knowledge is based on patterns of mtDNA and NRY variation. While extraordinarily informative, mtDNA and NRY are just two genetic loci, and hence are inherently limited in the inferences that can be drawn regarding population history. The good news is that recent technical advances have greatly facilitated studies of autosomal DNA variation, based on either genome-wide SNP analyses or multi-locus re-sequencing, and we can soon expect more large-scale studies of autosomal DNA variation in East Asian populations, as exemplified by the Pan-Asian SNP study [12].

The second limitation is that most studies of mtDNA and NRY variation adopt a phylogeographic framework, which involves studying the geographic distribution and estimating the age of particular mtDNA or NRY haplogroups of interest. The problem with this is that while the phylogeographic approach does indeed provide a very detailed picture of the history of a particular haplogroup, it is not at all clear how to use this information to make inferences about the history of a particular population. Ages of haplogroups, even if they are estimated accurately, which currently is much in doubt [24], do not equate to ages of populations; a haplogroup which arose 50 kya may have only been contributed to a population yesterday. We would argue that the way forward is to incorporate computational approaches using model-based methods to make inferences about population size changes, times of divergence, and migration rates [27–29]. Such methods have the advantage of not only providing information as to which scenario concerning population history is most strongly supported by the data, but also as to which alternative scenarios are NOT rejected by the data. A recent example of just such an approach is the inference of regional changes in population size through time, estimated from mtDNA coding-region sequences, that indicates that most of the ancestors of current worldwide human populations resided in southern Asia between 20–45 kya [60]. The availability of large-scale, genome-wide data from East Asian populations, combined with model-based approaches for inferring demographic history, will likely render this review obsolete — a development we happily anticipate.

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