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Evolution and demography of the great apes

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CrossMark

The great apes are the closest living relatives of humans.
Chimpanzees and bonobos group together with humans, while
gorillas and orangutans are more divergent from humans. Here,
we review insights into their evolution pertaining to the topology
of species and subspecies and the reconstruction of their
demography based on genome-wide variation. These
advances have only become possible recently through next-
generation sequencing technologies. Given the close
relationship to humans, they provide an important evolutionary
context for human genetics.

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The great apes are the closest living relatives of humans.
However, the topology of the great ape clade was not
resolved until a few decades ago. Analyses of mitochon-
drial DNA and single nuclear loci [1,2] grouped chim-
panzees and bonobos together with humans. Gorillas
diverged from their common ancestor, while orangutans
have the largest phylogenetic distance to humans.
Multiple efforts have been undertaken to reconstruct
the demographic history among the great apes [3–5]. In
the last years, deep sequencing technologies provided
a more detailed picture from whole-genome data

[6,7•,8•,9•]. Furthermore, genome-wide variation among
subspecies has been assessed, which resulted in novel
applications for conservation genetics [10,11•].

The study of great apes is highly relevant to the under-
standing of human evolution. Because of our joint evolu-
tionary history over the past few million years, humans
share a significantly higher proportion of genetic material
with great apes than with any other living organism. Thus,
great apes provide a unique resource to study the extent
at which humans differ from other primates. More com-
plete catalogues of primate variation allow to understand
what makes humans human, particularly to interpret the
functional significance of the variation observed in
humans compared to other great apes [6]. Furthermore,
analyses on the evolution of structural variation [12], the
emergence of novel human-specific genes [13] and gene
loss [14], as well as inferences of positive selection [15]
are augmented by a clear picture of great ape variation.
Also, investigating great ape genomics yields a compara-
tive background which could improve biomedicine [16].

In this review, we will summarize the latest findings about
the diversity in population dynamics, demography and
genome-wide variation within great apes, especially in
the light of the recent developments in whole genome
sequencing (as summarized in Figure 1).

The *Pan* clade: common chimpanzees and bonobos

Chimpanzees (*Pan troglodytes*) and bonobos (*Pan paniscus*)
have the highest similarities to our genomes. Thus,
studying the evolution and biology of *Pan* populations
is of enduring interest to highlight features that are
particular to our own species. Sequencing of chimpanzee
[17••] and bonobo [8•] genomes revealed high identities
to the human genome in orthologous sequences
(~98.7%), although there is still some uncertainty about
the total genome differences, partly because of the un-
equal quality of the reference genomes. Still, there is
ample evidence that mechanisms differentiating humans
from *Pan* might not only be based on raw variation in
sequences, but also on differences in regulation of gene
expression and epigenetic mechanisms [18–22]. The
coalescence time between *Pan* and *Homo* is still debated.
Values range from 5 to 6 Mya [9•,23••,24] to 10–13 Mya
[25,26] based on sequence divergence. However, this
depends on the methodology used but most importantly
on the still unresolved mutation rate and its variation

Figure 1
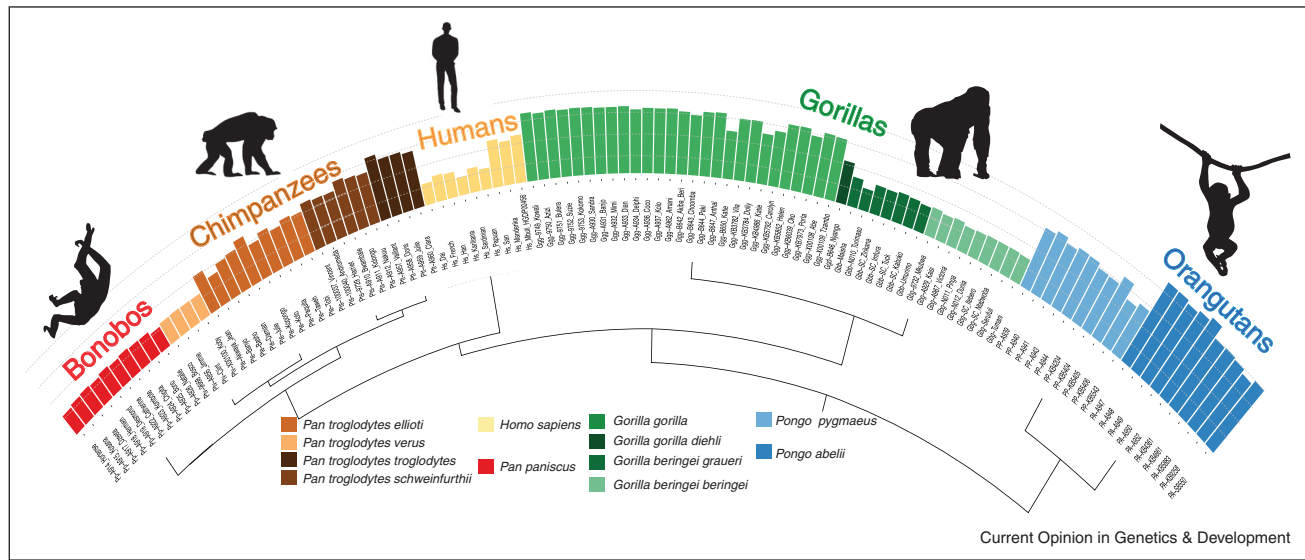
Phylogenetic relationships and variation of genetic diversity among the great apes. The height of the bars represents genome-wide diversity. *Source*: Data from Locke *et al*. (2012), Prado-Martinez *et al*. (2013), and Xue *et al*. (2015) were re-analysed based on sequence read mapping to their respective species reference genomes.

across the phylogeny [27]. Chimpanzee and bonobo coalescence estimates suggest that these species diverged 1–2 Mya [8•].

The chimpanzee taxonomy has been highly debated and is today divided into two monophyletic clades, each consisting of two different subspecies [23••]. Central and Eastern chimpanzees are the genetically closest subspecies, consistent with recent divergence times [23••,28]. Nigeria-Cameroon, the latest recognized chimpanzee subspecies [29,30], and Western chimpanzees form a second monophyletic group, showing older divergence time and higher genetic differentiation [31]. Gene flow among the ancestral populations of these two populations was estimated to have ceased at ∼700 kya [23••]. Population genetic studies based on mitochondrial DNA [32,33], microsatellite data [28,34], nuclear fragments [35•,36], and whole-genome sequences [23••] suggest a complex evolutionary history of the *Pan* lineage. Analyses of historical effective population sizes (N_e) revealed that the ancestral *Pan* lineage probably had a large N_e around 3 Mya, and suffered from a dramatic decline afterwards. The initial split of bonobos and the common chimpanzee ancestors ∼1.5 Mya was followed by a subsequent increase of N_e in almost all chimpanzee subspecies to different degrees [23••]. Present-day population estimates show the highest N_e in Central chimpanzees, followed by Eastern, Nigeria-Cameroon and Western chimpanzees, with patterns of genetic diversity decreasing accordingly [23••] (Figure 1).

The diversity of chimpanzee populations has also been influenced by multiple events of admixture, potentially reducing divergence times between populations. Previous studies based on coalescent modelling approaches have detected evidences of recent gene flow between the neighboring Central and Eastern populations [23••]. More ancient admixture between the ancestor of Central and Eastern chimpanzees and Nigeria-Cameroons has also been described [28], as well as between Eastern and Western chimpanzees [37]. Hence, the distribution of chimpanzee subspecies seems to have changed during certain periods in the past, and individuals from some populations must have migrated into different populations. Population structure within bonobos has been little explored, although mitochondrial sequences revealed substantial population differentiation strongly determined by the Congo River and its numerous tributaries [38,39].

The *Gorilla* clade: Western and Eastern gorillas

Gorillas are the first outgroup of the human-chimpanzee clade. Their genome was first sequenced in 2012 [9•], but has been re-sequenced recently to very high quality [40•], showing at which extent incomplete lineage sorting has complicated the study of these two sequential speciation processes. The divergence of the gorilla species to either human or chimpanzees and bonobos occurred, dependent on mutation rate and generation time, between 8 and 19 Mya [23••,26,41].

Taxonomically, two gorilla species have been recognized with two subspecies each: Western gorillas (*Gorilla gorilla*) and Eastern gorillas (*Gorilla beringei*), whose divergence time is still debated. Estimates range from ~100 kya to more than 1 Mya [23[••],42,43], dependent on the extent of estimated gene flow and the time at which it is inferred. More recent estimates set the divergence time at ~261 kya [44[•]]. The maternally inherited mitochondrial genome has been sequenced from Western [45] and Eastern gorillas [46], suggesting a deeper split of mitochondrial lineages than for the rest of the genome, as well as sex-specific migration patterns, particularly more limited female dispersal compared to male migrations. The separation of the two gorilla species has been shaped by Pleistocene refugia and rivers [47], continuing in profound population substructure also in recent times [48,49].

Western lowland gorillas have a ten-fold higher effective population size ($N_e \sim 20\,000$) than Eastern lowland gorillas ($N_e < 2000$) [23[••]], which is comparable to the difference between modern humans in Africa and Neandertals [50]. Cross river gorillas, which split from Western lowland gorillas ~68 kya [44[•]], and Mountain gorillas, which split from the Eastern gorillas ~150 kya, have smaller effective population sizes than the other subspecies of the genus [11[•],23[••]]. Mountain gorillas and Eastern lowland gorillas experienced a long-lasting population decline, resulting in a low genetic diversity and high burden of deleterious mutations [11[•]]. Eastern gorillas also suffered from inbreeding, at some extent comparable to the Altai Neandertal [51]. The effect of inbreeding is even stronger in Mountain gorillas, having led to a purging of loss-of-function mutations as a result of the sustained reduced effective population size [11[•]]. Only Western lowland gorillas exhibit relatively high genetic diversity and low levels of inbreeding in the wild, while Cross river gorillas suffered from a severe population decline only in recent times, which could be determined from historical samples [52]. However, ongoing habitat loss may also increase the occurrence of inbreeding in Western lowland gorillas, as observed in an individual with an albino phenotype [10].

The *Pongo* clade: Bornean and Sumatran orangutans

Due to their largest phylogenetic distance to humans, orangutans (genus: *Pongo*), the only Asian great apes, are of special interest when investigating the evolutionary relationships among the *Hominidae*. The orang-utan genome was published in 2011 [7], revealing a strikingly slower rate of structural genome evolution in the *Pongo* lineage. Assuming uniform mutation rates and generation times within *Hominidae*, the most recent common ancestor of orangutans and the other great apes is thought to have occurred somewhere between 15 and 21 Mya [23[••],53–55]. Within the genus *Pongo*, clear morphological distinctions [53] and genetic differentiation [7[•],56,57[•]]

delineate two species, *P. abelii* on Sumatra and *P. pygmaeus* on Borneo with different subspecies [53]. No subspecies have been proposed for *P. abelii*, despite profound population structure and coalescence times among Sumatran populations being much older compared to Borneo [57[•],58,59].

Orangutans experienced a complex evolutionary history, driven by an idiosyncrasy of their biology, that is, their extremely pronounced female philopatry and male-biased dispersal [60–63], as well as the highly dynamic environmental conditions on the Sunda archipelago. Orangutans were once widely distributed throughout mainland Southeast Asia and most of the Sundaland islands [63–66]. Autosomal and mitochondrial data point to a colonization of Sundaland in the Pliocene from the Southeast Asian mainland to what is now central Sumatra [57[•],67[•]]. From there, expansion took place to the north of present-day Lake Toba on northern Sumatra. The extensive recurring activity of the Toba volcano [68] during the Pleistocene caused a deep separation of orang-utan populations to the south and to the north of it [57[•],59,67[•]]. The split across Lake Toba is the oldest in the evolutionary history of orangutans on Sundaland [67[•]], with a coalescence time in the mtDNA phylogeny of ~3.5–4.0 Mya [57[•],59]. Because of its location and degree of genetic distinctiveness [69], the only extant population south of Lake Toba, Batang Toru, is thought to be a representative of this ancestral gene pool.

Demographic modelling revealed that Borneo was likely colonized in the early to middle Pleistocene from southern/central Sumatra [67[•]]. This is also supported by the sister position of the Batang Toru mtDNA lineage to that of all extant Bornean orangutans with a coalescence time ~2.0–2.5 Mya [57[•],59]. The ensuing speciation of Bornean and Sumatran orangutans was a gradual process with gene flow between the islands occurring over several hundred thousand years after the initial split [42,67[•]]. Studies using full genome data estimated a speciation time of 0.4–1.2 Mya [7[•],23[••],42,67[•]], comparable to what has been found in chimpanzees and bonobos. In line with these findings, a recent comparison of Y-chromosomal data [59] revealed a much more recent coalescence of Y-chromosomal lineages (~430 kya) compared to the species split time estimated from autosomal genomes (800 kya to 1.1 Mya). This indicates that male-mediated gene flow had still continued after the initial separation, facilitated by fluctuating sea-levels during this period that periodically reconnected both islands.

Following their divergence, Bornean and Sumatran orangutans experienced very different population histories. Demographic modelling revealed a steady population decline in Bornean orangutans over the past ~300 000 years, resulting in very low effective population sizes ($N_e = 5000–10\,000$) in the more recent past

[7[•],23[••],67[•]]. Moreover, several studies point towards a strong bottleneck and common refugium during the penultimate glacial period 130–190 kya [59,67[•],70]. In contrast, Sumatran orangutans showed a steady increase in N_e during the Middle Pleistocene [23[••],59] until around 70 kya, at which time their N_e crashed by more than an order of magnitude. This crash coincided with the Toba supereruption ~73 kya, which has been the largest volcanic eruption of the Quaternary [68], and in combination with more recent anthropogenic factors resulted in very low current N_e of ~5000 [23[••],59,67[•]].

Conclusions

Here, we reviewed the latest efforts to characterize genomic diversity in great apes and understand their population dynamics. Most scenarios project extinction of several great ape subspecies within the next 30–50 years [71]. While reservoirs of genetic diversity exist in captivity, these are, in general, poor surrogates for understanding natural standing genetic variation [23[••]]. Millions of humans have now been genotyped and, scientifically, there is no impediment to procuring a similar barcode catalogue of variation from some of the most endangered primates in the world — a catalogue which is crucial in understanding the origins of our species. The reconciliation of taxonomic and genetic data needs to be made highest priority, especially with regards to conservation biology. We believe that this information will lay the groundwork for future research in conservation genetics in order to preserve the natural populations of our closest relatives.

Acknowledgments

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