

Natural hybridization in primates and what “-omics” contributed to primate taxonomy and systematics

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„Nothing in biology makes sense except in the light of evolution“ (Theodosius Dobzhansky 1973)

„Without taxonomy to give shape to the bricks, and systematics to tell us how to put them together, the house of biological science is a meaningless jumble“ (Robert M. May 1990)

These two often cited sentences clearly reflect the fact that the modern evolutionary synthesis is the overall basis of biology. Both, taxonomy (the science of identifying, naming and classifying organisms) and systematics (the science of reconstructing phylogenetic relationships), are essential for evolutionary and biodiversity research (Edwards & Cavalli-Sforza 1964; Harvey et al. 1996; Wiley et al. 1991) as well as for many other biological disciplines. This includes the determination of evolutionary units (EUs), which can be identified and diagnosed due to their distinct genetic make-up and/or independent demographic history (Avice 2005). This is of great importance when issues related to conservation are tackled, since much of the total genetic diversity within a species is often partitioned among sets of geographic populations (demes) (Avice 2005). Likewise, phylogenetic research is the framework for testing hypotheses concerning the evolution of traits, e.g. physiology, morphology, behaviour, diseases, or co-evolutionary processes. In particular, for comparative analyses of adaptive processes, and for the discrimination between ancestral and derived states, taxonomy and systematics, i.e. a robust phylogeny are inevitable (Bjork et al. 2011; Rohland et al. 2007; Shultz et al. 2011; Switzer et al. 2005; Zinner et al. 2009, 2011). Consequently, any change in a specific character can be tracked back into the past (Losos 2011).

Non-human primates are our closest living relatives and due to their similar anatomy, physiology and genetic make-up, various non-human primate species are used as model organisms in biomedical research, in particular in preclinical studies, virology, toxicology and neuroscience. Similarly, non-human primates are appropriate model species to study the roots of human behaviour and sociality, and to trace back and understand human evolution and genomics (Enard & Pääbo 2004; Goodman et al. 2005; Strum 2012). Finally, nearly half of all primate species are threatened and some are even close to extinction (IUCN 2012), so that immediate conservation actions are required. For all these biological and medical disciplines and for conservation purposes, knowledge about the taxonomic/genetic diversity of primates and their evolutionary history is an essential cornerstone.

For example, rhesus (*Macaca mulatta*) and long-tailed macaques (*M. fascicularis*), the two most commonly used non-human primate model species in biomedical research, have wide distributions in Asia. They exhibit extreme intra-specific genetic diversity, which most likely impact susceptibility and resistance to various diseases. Actually, local populations of rhesus macaques carry different MHC alleles, which are known to affect the survival time of experimentally SIV infected animals (Saueremann et al. 2008) and accordingly influence SIV experiments. Consequently, genome-wide markers are urgently required to select appropriate individuals for respective experiments.

Likewise, the question: “What makes us human?” can only be answered by comparative analyses of data derived from the genome and transcriptome of humans and chimpanzees. Humans and chimpanzees differ in less than 2% of their genomes, but analyses on RNA level have shown that both species show species-specific gene expression patterns, with main differences particularly pronounced in the brain (Enard et al. 2002).

Molecular work similarly contributed to a better understanding of primate diversity. In the last two decades, the number of primate species increased dramatically from 230 in 1996 (Rowe 1996) to 480 in 2013 (Mittermeier & Wilson 2013), primarily as a result of applying the Phylogenetic Species Concept (Cracraft 1983) instead of the Biological Species Concept (Dobzhansky 1937; Mayr 1942), but also due to the discovery of numerous cryptic species by applying molecular methods. This is particularly true for nocturnal primates, because morphological differences are small and often not diagnostic, and only molecular studies revealed that these taxa are more diverse than previously believed. Likewise, molecular studies expanded our knowledge about distributional ranges of taxa, allowing better and more efficient conservation measurements.

Surprisingly, in course of many molecular studies on primate diversity and phylogeny, numerous cases of natural hybridization were uncovered. In fact, it is now estimated that natural hybridization occurs in more than 10% of all primate species and it was observed in all major radiations (Zinner et al. 2011). Hybridization, as the admixture of previously isolated gene pools, was not expected at such a magnitude, because as in other animal species, inter-specific hybridization was regarded as an evolutionary dead end, since hybrid offspring often show limited vitality or were sterile, as for instance in mules (horse x donkey). In some cases, however, the exchange of genes between species may have accelerated adaptation and may have led to the formation of new lineages. Thus, hybridization can be regarded as one important evolutionary mechanism driving speciation processes. Hybridization can be a recent and ongoing process that can be also detected by intermediate morphotypes, e.g., in baboons, or it occurred in the past, which left only traces of genetic exchange in the genome, e.g., in some Asian langur genera. Recent and ancient hybridization events occur/occurred mainly between subspecies and species, but they have also been detected between primate genera and even in the human lineage (Zinner et al. 2011). Besides bidirectional hybridization, where males and females of both parent taxa contribute to hybridization, also unidirectional hybridization can occur, where only one sex of one parent taxon contributes, but not the other. Such an introgression normally results in mitochondrial or Y chromosomal capture, or nuclear swamping, depending on the contributing sex. In any case, one can expect to find indications for mosaic genomes either in the hybrids or the introgressed taxon.

Ancient hybridization events are normally not detectable when analysing morphological traits. Such events are only revealed by molecular studies including various differently inherited molecular markers. Sometimes traces of hybridization in genomes are so minimal that they can only be detected by comparing many different loci and even whole genomes are sometimes required. A prominent example therefore is the gene flow among modern humans, Neanderthals and Denisovans (Figure 1) (Green et al. 2010; Meyer et al. 2012). Respective studies have shown that Neanderthals have contributed ~2% to non-African modern humans and that ~6% of the genomes of Papuans derived from Denisovans, a human species whose fossils have been found in the Denisova Cave in Siberia.

The various cases of natural hybridization events among primate taxa suggest that the Biological Species Concept might be not applicable and outdated at least for primates. Numerous other species

concepts are available, but all of them have their drawbacks. The Phylogenetic Species Concept might be best practical for primates (Groves 2012). However, a general problem in taxonomy remains: the classification of hybrid taxa. Recognizing them all as distinct taxa or at least distinct evolutionary units might be a possible solution. This, however, would increase the number of taxa (species) dramatically.

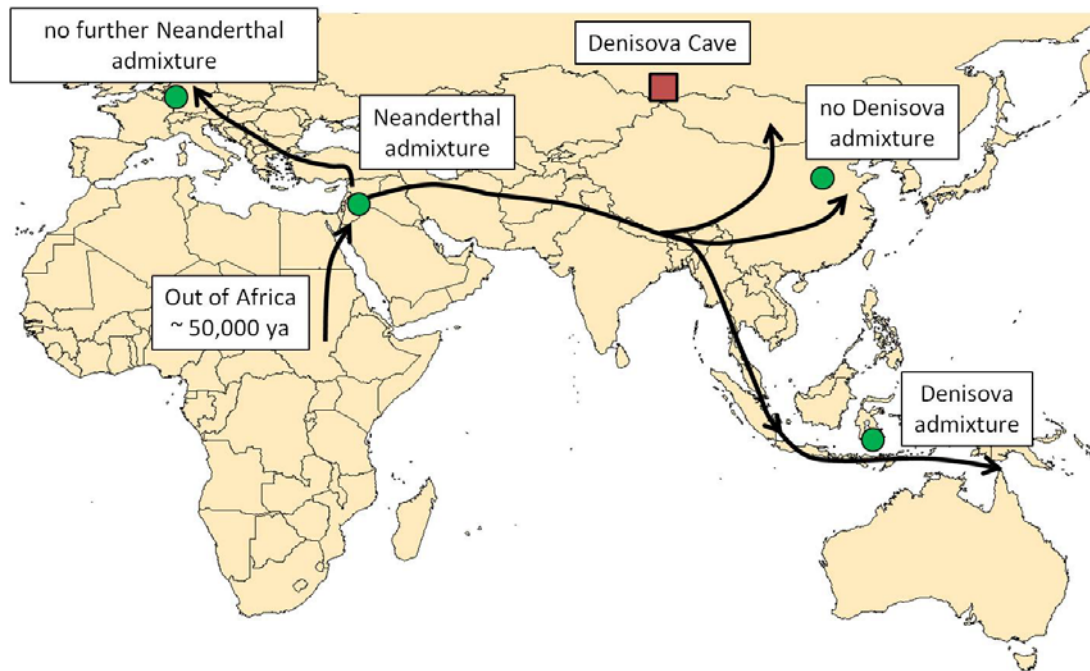


Figure 1: Dispersal of modern humans from Africa. A map illustrating the dispersal of modern humans from Africa about 50,000 years ago, followed by admixture with Neanderthals in the ancestry of all non-Africans, followed by admixture with Denisovans in the ancestry of New Guineans (adapted from Stoneking & Krause 2011).

Main challenges/Relevance to society

1. Research on primate taxonomy and systematics is important for many biological (and medical) research disciplines, because primates are our closest living relatives and accordingly widely used in biomedical research and as model to study human evolution.
2. Only comparative analyses of human and non-human primate genomes, transcriptomes and proteomes will provide the necessary information what makes us human. It will help us to understand the evolution, discovery and interpretation of the genetic underpinnings of human adaptation and diseases.
3. Since Darwin, understanding speciation processes is one of the most important research interests of evolutionary biologists. The many cases of natural hybridization in primates provide good models to test for natural selection and adaptation, and how species evolve.
4. Due to the large intra-specific genetic diversity of biomedical model species, e.g. rhesus and long-tailed macaques, genomic tools are required to select individuals for experiments. This will dramatically reduce the number of individuals in experiments.
5. Many new primate species were discovered in recent years by molecular studies and it can be expected that the full genetic/taxonomic diversity of primates is not fully assessed yet.

6. Nearly 50% of all primate species are threatened and some are even close to extinction, so that immediate conservation actions are required. Genetic methods can help to define distributional ranges and to select appropriate areas for protection.
7. For most if not all these reasons, data from a few genomic loci is not sufficient and complete genome sequences are required, because they allow deep insights into genome evolution and provide the necessary information to address the topics above. The application of high-throughput next-generation sequencing methods will be an efficient, economical and fast way to do so.
8. Analysing the amount of sequence data will be a major challenge and skilled bioinformaticians are required. Taxonomic knowledge is becoming more and more rare. Assign specimens to taxa is the basis of taxonomic research and thus skilled taxonomists are necessary.

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