*Proc. Natl. Acad. Sci. USA*
Vol. 85, pp. 7627–7631, October 1988
Evolution

# Molecular systematics of higher primates: Genealogical relations and classification

(DNA sequences/rhesus macaque/human evolution/phylogeny/globin gene region)

MICHAEL M. MIYAMOTO*†, BEN F. KOOP‡, JERRY L. SLIGHTOM§¶, MORRIS GOODMAN¶, AND MICHELE R. TENNANT||

*Department of Zoology, University of Florida, Gainesville, FL 32611; Departments of ‡Molecular Biology and Genetics and ¶Anatomy and Cell Biology, Wayne State University School of Medicine, Detroit, MI 48201; §Division of Molecular Biology, The Upjohn Company, Kalamazoo, MI 49001; and ||Department of Biological Sciences, Wayne State University, Detroit, MI 48202

*Communicated by Charles G. Sibley, June 20, 1988 (received for review April 7, 1988)*

**ABSTRACT** **We obtained 5′ and 3′ flanking sequences (5.4 kilobase pairs) from the $\psi\eta$-globin gene region of the rhesus macaque (*Macaca mulatta*) and combined them with available nucleotide data. The completed sequence, representing 10.8 kilobase pairs of contiguous noncoding DNA, was compared to the same orthologous regions available for human (*Homo sapiens*, as represented by five different alleles), common chimpanzee (*Pan troglodytes*), gorilla (*Gorilla gorilla*), and orangutan (*Pongo pygmaeus*). The nucleotide sequence for *Macaca mulatta* provided the outgroup perspective needed to evaluate better the relationships of humans and great apes. Pairwise comparisons and parsimony analysis of these orthologues clearly demonstrated (*i*) that humans and great apes share a high degree of genetic similarity and (*ii*) that humans, chimpanzees, and gorillas form a natural monophyletic group. These conclusions strongly favor a genealogical classification for higher primates consisting of a single family (Hominidae) with two subfamilies (Homininae for *Homo, Pan,* and *Gorilla* and Ponginae for *Pongo*).**

Huxley (1) and Darwin (2) were the first to suggest that African apes [represented then by the common chimpanzee (*Pan troglodytes*) and the gorilla (*Gorilla gorilla*) and more recently as well by the pygmy chimpanzee (*Pan paniscus*)] are the closest living relatives of humans (*Homo sapiens*). The taxonomic importance of these observations was not addressed by Huxley (1), as humans were assigned by him to their own suborder of Primates. In contrast, Darwin (2) proposed that, from a genealogical perspective, humans should not occupy more than a unique subfamily or family. In the last century, most classifications for higher primates recognized separate families for humans and great apes: Hominidae for humans and Pongidae for the African apes and orangutan (*Pongo pygmaeus*) of southeast Asia (i.e., refs. 3 and 4). In these schemes, gibbons (*Hylobates* and *Symphalangus*) were assigned to either their own family (Hylobatidae) or to that for the great apes (Pongidae). In the latter case, little doubt exists that the family Pongidae is rendered unnatural [paraphyletic or polyphyletic (5)] by the inclusion of these hominoid genera (6–8). Greater dispute surrounds the genealogical affinities of the great apes themselves, and as such, the monophyly of their family (Pongidae, restricted hereafter to African and Asian apes). The morphological studies of Schultz (9) and Kluge (10) support the existence of a great ape clade (and therefore the monophyly of Pongidae). In contrast, Schwartz (11, 12), using anatomical data, argues for separate human/orangutan and chimpanzee/gorilla lineages, whereas molecular data and other morphological evidence clearly favor a human/African ape arrangement (and not a monophyletic Pongidae). At present, the human/African ape grouping remains the most widely accepted hypothesis, as it is heavily supported by both DNA·DNA hybridization (13, 14) and nucleotide sequence (15) data.

The $\beta$-globin gene family in catarrhine primates [humans, great apes, and Old World monkeys (family Cercopithecidae)] has been well characterized in terms of its evolution, structure, and function (16). In catarrhines, this cluster consists of six $\beta$-related globin genes linked 5′ to 3′: $\varepsilon$ (embryonic)–$\gamma^1$–$\gamma^2$ (fetal)–$\psi\eta$ (inactive pseudogene)–$\delta$–$\beta$(adult) (17). In this study, upstream and downstream flanking sequences of the $\psi\eta$-globin locus [an additional 5.4 kilobase pairs (kbp)] were determined for the rhesus macaque (*Macaca mulatta*, family Cercopithecidae).** These sequences were combined with published nucleotide data (15, 18) and then compared to orthologous regions available for human (*Homo sapiens*, as represented by five alleles), common chimpanzee (*Pan troglodytes*), gorilla (*Gorilla gorilla*), and orangutan (*Pongo pygmaeus*). These orthologues, covering nearly 10.8 kbp, represented the longest contiguous stretch of noncoding DNA known for humans and other higher primates (19). The completed sequence for rhesus macaque provided the outgroup perspective needed to evaluate further the phylogenetic relationships and taxonomic affinities of higher primates (6–8). With this sequence, extensive molecular evidence was obtained in favor of a genealogical classification for humans and great apes (20, 21).

## MATERIALS AND METHODS

**Nucleotide Sequences.** Nucleotide sequence data from the $\psi\eta$-globin gene region of *Macaca mulatta* were obtained from the same pBR322 clone (pMmul4.7-R10.0) used by Koop *et al.* (15) and Slightom *et al.* (22). The same 5′ and 3′ flanking sequences obtained by Miyamoto *et al.* (19) were determined for this clone by the chemical sequencing method (23). The data obtained (5.4 kbp) were then combined with published $\psi\eta$-gene sequences for rhesus macaque (15), thereby completing the same orthologous region (7.6 kbp) available for human, common chimpanzee, gorilla, and orangutan (19). Adjacent sequences from further downstream [an additional 3.2 kbp of 3′ flanking DNA (18)] were added to these 7.6-kbp orthologues, thereby completing the 10.8-kbp alignment of continuous noncoding DNA used in our analysis.

The nucleotide data base for humans consisted of five partial sequences representing different alleles of the 10.8-kbp region. In all, two upstream and three downstream alleles

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. §1734 solely to indicate this fact.

†To whom reprint requests should be addressed.
**The sequence reported in this paper is being deposited in the EMBL/GenBank data base (IntelliGenetics, Mountain View, CA, and Eur. Mol. Biol. Lab., Heidelberg) (accession no. J03818).

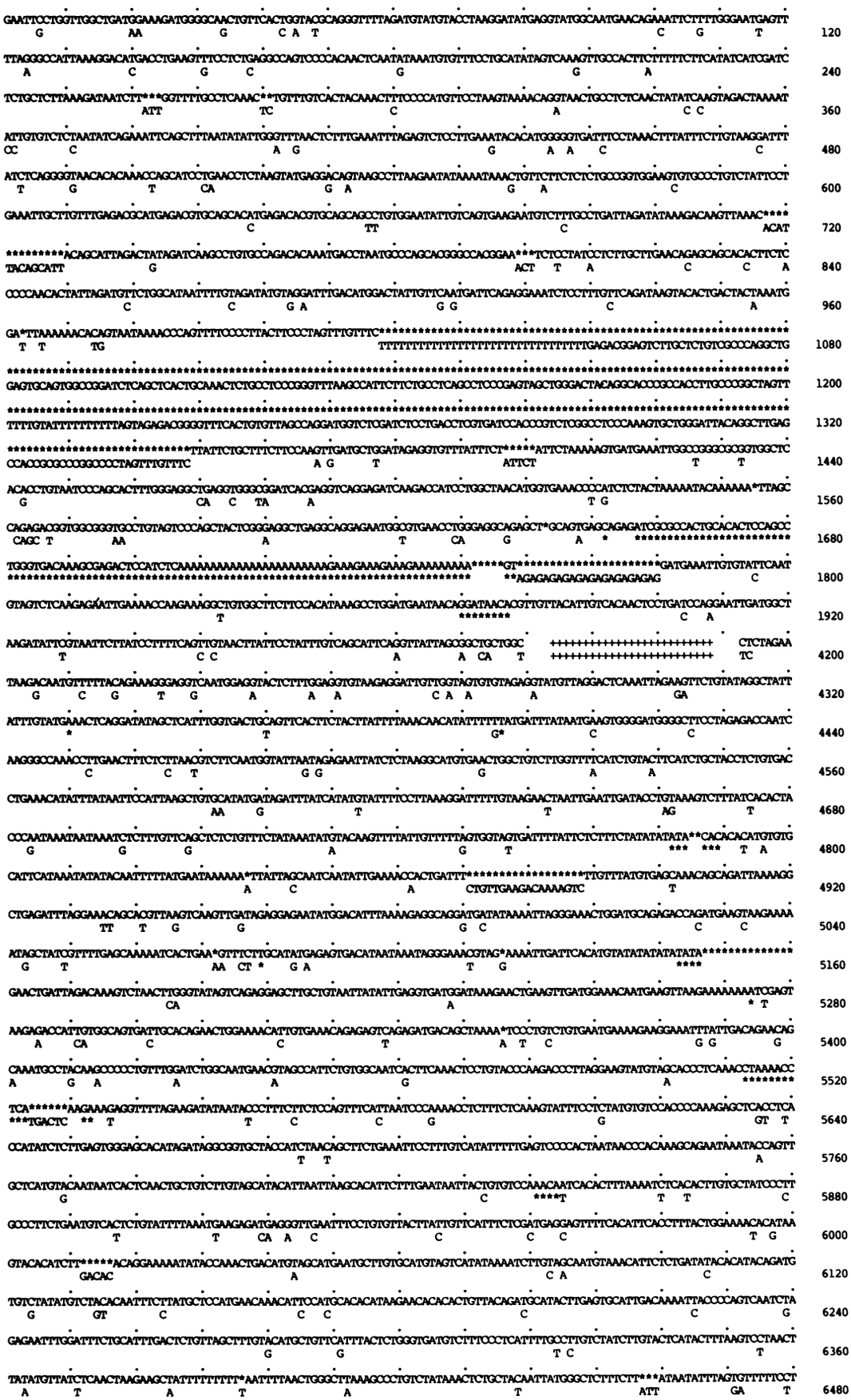

FIG. 1. (*Figure continues on the opposite page.*)

FIG. 1. Aligned DNA sequences of the $\psi\eta$-globin flanking regions for *Homo sapiens* and *Macaca mulatta* (upper and lower lines, respectively). Only nucleotides at variable sites for rhesus macaque and only regions corresponding to sequence obtained in this study are shown. The location of the Koop *et al.* (15) sequences is represented by the double row of + beginning after position 1999. The entire 10.8-kbp alignment is divided into upstream (positions 1–7556) and downstream (7551–10760) regions by the *Eco*RI site (7551–7556) signifying the start of the Maeda *et al.* (18) sequences. The human orthologue represented here is that of Collins and Weissman [CW (16)], as corrected by Miyamoto *et al.* (19). The nucleotide alignments of Koop *et al.* (15), Maeda *et al.* (18), and Miyamoto *et al.* (19) are followed in this study. To preserve the entire 10.8-kbp alignment, gaps (asterisks) are sometimes retained between human and rhesus macaque even in the absence of polymorphism (i.e., position 1555). All five species share an *Alu* repeat element with a downstream orientation at positions 1424–1756 (27). In contrast, a unique *Alu* repeat with an upstream orientation is exhibited by rhesus macaque at sites 1018–1334.

are known from Collins and Weissman [CW (16), as corrected by Miyamoto *et al.* (19)], Chang and Slightom [CS (24)], Maeda *et al.* [R and T (18)], and Poncz *et al.* [PONCZ (25)], respectively. By including all five alleles, a better representation of sequence variation (polymorphism) in humans was incorporated in our analysis of higher primate relationships.

**Evolutionary Analysis.** Estimates of sequence divergence were calculated first from pairwise comparisons of the five catarrhine primates and then from pairs of the five human alleles. In the former analysis, two combined sequences for human (alleles CW + R and CW + T) were used in the interspecific comparisons of the catarrhine species (Table 1). Averaged percent divergences were then calculated from these combined sequences. The CW, R, and T alleles were chosen for these comparisons because they collectively covered the entire 10.8-kbp region under consideration.

Genealogical reconstructions for the nine sequences (five human alleles and four other catarrhine orthologues) were accomplished with the Phylogenetic Analysis Using Parsimony (PAUP) program (26), as described by Miyamoto *et al.* (19).

Table 1. Pairwise divergences among the $\psi\eta$-globin sequences of *Homo sapiens* (HSA), *Pan troglodytes* (PTR), *Gorilla gorilla* (GGO), *Pongo pygmaeus* (PPY), and *Macaca mulatta* (MMU)

| Species compared | BP | Substitutions | | | Gaps | % divergence |
|---|---|---|---|---|---|---|
| | | TS | TV | TS/TV | | |
| HSA/PTR | 10,121 | 98.5 | 44.5 | 2.21 | 20.5 | 1.61 |
| HSA/GGO | 10,131 | 112.5 | 35.5 | 3.17 | 27 | 1.72 |
| HSA/PPY | 10,059.5 | 199.5 | 95.5 | 2.09 | 47.5 | 3.39 |
| HSA/MMU | 9,911.5 | 457 | 212 | 2.16 | 72.5 | 7.43 |
| PTR/GGO | 10,172 | 121 | 43 | 2.81 | 24 | 1.84 |
| PTR/PPY | 10,081 | 205 | 104 | 1.97 | 47 | 3.52 |
| PTR/MMU | 9,933 | 466 | 222 | 2.10 | 71 | 7.59 |
| GGO/PPY | 10,102 | 220 | 90 | 2.44 | 42 | 3.47 |
| GGO/MMU | 9,955 | 464 | 207 | 2.24 | 69 | 7.38 |
| PPY/MMU | 9,943 | 459 | 218 | 2.11 | 67 | 7.43 |

The pairwise comparisons between *Homo sapiens* and the other species were based on averages between hybrid combinations of the upstream sequence of Collins and Weissman (16) and the downstream alleles (R and T) of Maeda *et al.* (18). BP, base positions under comparison; TS, transitions; TV, transversions; TS/TV, transition-to-transversion ratio; and Gaps, insertions and deletions. Percent divergence is equal to [(TS + TV + Gaps)/(BP + Gaps) × 100%], in which gaps are counted as single events regardless of their length.

## RESULTS

**Pairwise Comparisons.** Estimates of percent divergence revealed that the $\psi\eta$-globin orthologues of higher primates (Fig. 1) shared a high degree of sequence identity (Table 1). On average, the most divergent representative of higher primates (orangutan) differed from the other three (humans and the African apes) by 3.46% (range: 3.39–3.52%). Humans and common chimpanzees shared the fewest differences (1.61%), whereas *Pan* and *Gorilla* differed the most among these three (1.84%). On average, higher primates varied from the outgroup (rhesus macaque) by 7.46% (range: 7.38–7.59%).

Only minor sequence differences were detected among the five human alleles (Table 2). The two upstream alleles (CS and CW) varied by three gap differences in homonucleotide runs and direct contiguous repeats (19). In the downstream region, R, T, and PONCZ differed on average by less than 0.50% (range: 0.16–0.67%). Clearly, the T orthologue exhibited the greatest differences among the downstream alleles.

**Higher Primate Phylogenies.** Parsimony scores were calculated for all possible dichotomous arrangements of the study group (four higher primates) and outgroup (rhesus macaque). For each of the 15 interspecific possibilities, three

Table 2. Pairwise comparisons between the two upstream sequences (CS and CW) and among the three downstream alleles (PONCZ, R, and T) of *Homo sapiens*

| Alleles compared | Sites | BP | Substitutions | | TS/TV | Gaps | % divergence |
|---|---|---|---|---|---|---|---|
| | | | TS | TV | | | |
| CS/CW | 2000–4192 | 2129 | 0 | 0 | 0.00 | 3 | 0.14 |
| R/T | 7551–10760 | 3157 | 9 | 7 | 1.29 | 2 | 0.57 |
| R/PONCZ | 7579–10760 | 3133 | 0 | 4 | 0.00 | 1 | 0.16 |
| T/PONCZ | 7579–10760 | 3129 | 9 | 10 | 0.90 | 2 | 0.67 |

Abbreviations and calculations for percent divergence follow those described for Table 1. "Sites" refers to those positions of the overall alignment (Fig. 1) considered in each comparison.

alternative arrangements for the downstream alleles of human (R, T, and PONCZ) were simultaneously considered as well. The single most-parsimonious genealogy identified in this fashion (Fig. 2) was associated with 1140 total mutations (base substitutions and gap events). A human/African ape clade was supported by this solution, as was a close relationship between *Homo* and *Pan* (13–15, 18, 19, 28). Furthermore, a direct relationship between the R and PONCZ alleles was favored by this phylogeny.

The evidence in favor of the most-parsimonious results was quite strong (Fig. 2). The human/African ape grouping in the most-parsimonious solution was supported by 82 unequivocal synapomorphies [unique mutations (5)] representing 51 transitions, 23 transversions, and 8 gap events (Table 3). Minimally, 74 extra mutations relative to the most-parsimonious score were needed to replace this arrangement with an alternative one for humans and the African apes (Fig. 2). Even greater numbers of additional mutations were required (87 and 88, respectively) by the great ape hypothesis of Schultz (9) and Kluge (10) and by the human/orangutan versus African ape arrangement of Schwartz (11, 12). Clearly, these parsimony results provided strong evidence for a human/African ape grouping (13–15).

In a similar fashion, the *Homo/Pan* clade was supported by 10 unequivocal synapomorphies representing 4 transitions, 3 transversions, and 3 gap events (Table 3). In this case, 7 additional mutations relative to the most-parsimonious score were needed to replace this arrangement by the chimpanzee/gorilla or human/gorilla alternatives (Fig. 2).

## DISCUSSION

**Genetic Identities.** The percent divergence estimates calculated for higher primates clearly support the contention that humans and great apes share a very high degree of sequence identity (Table 1). Overall, higher primates differ by 1.61–3.52% according to our results. These measurements conform closely to the divergence estimates calculated from DNA·DNA hybridization (13, 14) and from sequence comparisons of other noncoding genomic regions (27, 29). The extensive genetic similarities among higher primates become even greater when coding regions are considered instead [e.g., divergences decrease to <1.00–1.50% (27, 30, 31)]. Thus, an extensive body of molecular evidence exists in support of the widely held view that the nuclear genomes of higher primates are very similar.

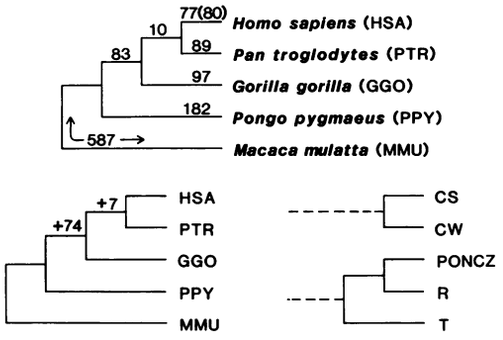


FIG. 2. (*Upper*) Most-parsimonious solution for *Homo sapiens* [as represented by five alleles (see below)], *Pan troglodytes, Gorilla gorilla, Pongo pygmaeus,* and *Macaca mulatta*. Branch lengths, in terms of number of mutations, are indicated next to internodes. Internode lengths for human are based on combinations of the CW + R and CW + T alleles (first and parenthetical values, respectively). Ambiguous changes (those with more than one parsimonious placement) are assigned to terminal branches rather than to internal internodes (19). Such resolutions limit the total numbers of synapomorphies to only those that provide unequivocal support for the clusters. (*Lower Left*) Minimum numbers of extra mutations needed to replace the *Homo/Pan* and human/African ape clades with other groupings. (*Lower Right*) Parsimonious arrangement of the five human alleles. The relationships between upstream and downstream alleles remain unresolved (as reflected by broken lines) due to the lack of sequence overlap.

Table 3. Putative synapomorphies [listed by base position(s)] in support of the *Homo/Pan* and human/African ape clades (Fig. 2)

| Clade | Substitutions | | | | | Gaps |
|---|---|---|---|---|---|---|
| | TS | TS | TS | TV | TV | |
| HSA/PTR | 1694 | **1472** | | 563 | 7428 | *D (1491-1494)* |
| | 4902 | **2635** | | 5912 | | *I (1739)** |
| | | | | | | **D (127-132)** |
| HSA/PTR/ GGO | 533 | 7129 | **285** | 1565 | *2214* | D (280-281) |
| | 743 | *121* | **375** | 4229 | **223** | I (4396)* |
| | 805 | *300* | **386** | 4862 | **229** | I (5513-5523) |
| | 909 | *326* | **646** | 4935 | **358** | D (5524-5529) |
| | 975 | *422* | **969** | 5965 | **746** | *I (1385-1391)* |
| | 1426 | *631* | **1448** | 6124 | **1011** | *D (1879)* |
| | 1532 | *750* | **1482** | 6363 | **2773** | I (970) |
| | 1567 | *1185* | **1546** | 7148 | **2783** | I (2933)* |
| | 1578 | *1263* | **1620** | 7250 | **2802** | |
| | 1629 | *1307* | **2024** | *654* | **2834** | |
| | 1795 | *1381* | **2028** | *1214* | **3125** | |
| | 4360 | *1467* | **2091** | *1840* | | |
| | 4941 | *1484* | **2155** | | | |
| | 4946 | *1592* | **2552** | | | |
| | 5086 | *1677* | **2612** | | | |
| | 5461 | **80** | **2714** | | | |
| | 5577 | **244** | **2874** | | | |

Base positions in italics and boldface correspond respectively to the nucleotide numbering systems of Koop *et al.* (15) and Maeda *et al.* (18), whereas all other sites refer to the sequence alignment in Fig. 1. Gap events [insertions (I) and deletions (D)] involving homonucleotide repeats are denoted with asterisks (19). Abbreviations follow those used in Table 1.

The smallest interspecific divergence (1.61% for *Homo* and *Pan*) is approximately 2.5 times as great as the largest value found among the human alleles (0.67% in the T and PONCZ comparison). This observation implies that intraspecific variation in humans contributes relatively little to the interspecific differences among higher primates. Nevertheless, the closely spaced branching points for human, common chimpanzee, and gorilla must be viewed with caution, as they remain particularly vulnerable to errors caused by polymorphisms [(19, 32) and see below].

**Genealogical Relationships.** A close genealogical relationship among humans and African apes is strongly supported by the $\psi\eta$-globin sequences (Fig. 2 and Table 3). This arrangement for higher primates is heavily corroborated by an extensive body of independent evidence from both molecular and morphological sources (see refs. 6–8 and 21 for reviews). In contrast, very little evidence (indeed, virtually none from molecular sources) exists in favor of the hypotheses adopted by Schultz (9), Kluge (10), and Schwartz (11, 12). Great apes do not form a monophyletic unit nor are humans closely related to orangutans according to our results and those of others (13–15). Rather, the evidence remains overwhelmingly in favor of a human/African ape clade (6–8, 21).

A close relationship between human and chimpanzee is clearly favored by the $\psi\eta$-globin sequences (Fig. 2 and Table 3). As such, the *Homo/Pan* clade is retained as our best estimate of human and African ape relationships (13, 14, 19, 21, 28). Nevertheless, the question of branching error due to intraspecific variation remains despite our use of multiple human alleles (30). In this respect, new sequences from different individuals of great apes will be important for the

determination of polymorphic patterns in higher primates and their relationship to polymorphisms in humans (19). A better understanding of intraspecific polymorphism and its importance in reconstructing phylogeny is expected to emerge once these sequences are provided (32).

**Evolutionary Rates and Divergence Times.** The time of divergence for the initial separation of orangutan from human and the African apes is usually placed somewhere between 10 and 15 million years (Myr) ago (33, 34). Rates of $\psi\eta$-globin evolution, as calculated with these dates and the branch lengths in Fig. 2, are quite similar among human ($1.12–1.68 \times 10^{-9}$ mutations per site per year), common chimpanzee ($1.19–1.78 \times 10^{-9}$), gorilla ($1.17–1.76 \times 10^{-9}$), and orangutan ($1.19–1.78 \times 10^{-9}$). When these figures are taken alone, the slightly slower rates for human must be viewed as insignificant. However, a general trend in support of a rate slowdown in human is starting to emerge from studies of both nuclear and mitochondrial DNA (35), and within this broader context, the $\psi\eta$-globin data can be viewed as additional evidence in favor of this hypothesis. Nevertheless, this trend must be viewed with caution, as different stretches in the $\psi\eta$-globin region are known to evolve at different rates (18, 19, 28).

Molecular clock calculations using the same dates and branch lengths as above indicate that the initial divergence of human, chimpanzee, and gorilla occurred sometime between 5.3 and 8.0 Myr ago (7). These calculations, furthermore, place the separation of human and chimpanzee somewhere between 4.7 and 7.1 Myr ago. These times of divergence for humans and African apes closely agree with the estimates of others as synthesized from both molecular and paleontological information (13, 14, 36, 37).

**Taxonomic Conclusions.** The current body of molecular and morphological data provides convincing support for the following conclusions: (*i*) that humans and African apes form a natural monophyletic group; and (*ii*) that higher primates (*Homo, Pan, Gorilla,* and *Pongo*) share a high degree of genetic identity. The close relationship among humans and African apes documents that the family Pongidae (*Pan, Gorilla,* and *Pongo*) is not monophyletic. Furthermore, the extensive genetic similarities shared by higher primates demonstrate that a separate family for *Homo* (Hominidae) is not warranted. In short, the widely adopted classifications for higher primates are in need of taxonomic revision (7, 20, 21). Humans and great apes can be placed into a single family (Hominidae) with two subfamilies (Homininae for *Homo, Pan,* and *Gorilla* and Ponginae for *Pongo*) as proposed previously by Goodman and Moore (20) and Groves (21). By adopting these recommendations, a genealogical classification (in the sense of ref. 5) is supported that more fully reflects both the relationships and the genetic similarities of its members (38).

In conclusion, the following genealogical classification [based on phyletic sequencing (38) and the taxonomic schemes of Goodman and Moore (20) and Groves (21)] is strongly recommended:

Family Hominidae Gray, 1825 (emended)
- Subfamily Homininae Gray, 1825 (emended)
  - *Gorilla* I. Geoffroy St. Hilaire, 1852 (1 species)
  - *Homo* Linnaeus, 1758 (1 species)
  - *Pan* Oken, 1816 (2 species)
- Subfamily Ponginae Elliot, 1913 (emended, new rank)
  - *Pongo* Lacepede, 1799 (1 species).

We thank N. Maeda and C.-I. Wu for access to their sequences before publication; S. M. Boyle for use of his computer programs; and D. H. A. Fitch and C. G. Sibley for their useful comments and suggestions on the manuscript. This research was supported by funds from the Alfred P. Sloan Foundation, the Gershenson Foundation, and the National Science Foundation (BSR-8607202) to M.G. and the National Institutes of Health (RO1 HL33940) to M.G. and J.L.S. and by grants from the National Science Foundation (BSR-8857264) and the Interdisciplinary Center for Biotechnology Research (University of Florida) to M.M.M.

1. Huxley, T. H. (1863) *Man's Place in Nature* (Appleton, New York).
2. Darwin, C. R. (1871) *The Descent of Man* (Murray, London), Vol. 1.
3. Simpson, G. G. (1945) *Bull. Am. Mus. Nat. Hist.* **85,** xvi–350.
4. Thorington, R. W., Jr., & Anderson, S. (1984) in *Orders and Families of Recent Mammals of the World,* eds. Anderson, S. & Jones, J. K., Jr. (Wiley, New York), pp. 187–217.
5. Hennig, W. (1966) *Phylogenetic Systematics* (Univ. Chicago Press, Urbana, IL).
6. Andrews, P. (1986) in *Major Topics in Primate and Human Evolution,* eds. Wood, B. A., Martin, L. & Andrews, P. (Cambridge Univ. Press, Cambridge, U.K.), pp. 107–129.
7. Goodman, M. (1986) in *Evolutionary Perspectives and the New Genetics,* eds. Gershowitz, H., Rucknagel, D. L. & Tashian, R. E. (Liss, New York), pp. 121–132.
8. Andrews, P. (1987) in *Molecules and Morphology in Evolution: Conflict or Compromise?,* ed. Patterson, C. (Cambridge Univ. Press, Cambridge, U.K.), pp. 23–53.
9. Schultz, A. H. (1963) in *Classification and Human Evolution,* ed. Washburn, S. L. (Aldine, Chicago), pp. 85–115.
10. Kluge, A. G. (1983) in *New Interpretations of Ape and Human Ancestry,* eds. Ciochon, R. L. & Corruccini, R. S. (Plenum, New York), pp. 151–177.
11. Schwartz, J. H. (1984) *Nature (London)* **380,** 501–505.
12. Schwartz, J. H. (1987) *The Red Ape—Orang-utans and Human Origins* (Houghton Mifflin, Boston).
13. Sibley, C. G. & Ahlquist, J. E. (1984) *J. Mol. Evol.* **20,** 2–15.
14. Sibley, C. G. & Ahlquist, J. E. (1987) *J. Mol. Evol.* **26,** 99–121.
15. Koop, B. F., Goodman, M., Xu, P., Chan, K. & Slightom, J. L. (1986) *Nature (London)* **319,** 234–238.
16. Collins, F. S. & Weissman, S. M. (1984) *Prog. Nucleic Acid Res. Mol. Biol.* **31,** 315–462.
17. Goodman, M., Koop, B. F., Czelusniak, J., Weiss, M. L. & Slightom, J. L. (1984) *J. Mol. Biol.* **180,** 803–823.
18. Maeda, N., Wu, C.-I., Bliska, J. & Reneke, J. (1988) *Mol. Biol. Evol.* **5,** 1–20.
19. Miyamoto, M. M., Slightom, J. L. & Goodman, M. (1987) *Science* **238,** 369–373.
20. Goodman, M. & Moore, G. W. (1971) *Syst. Zool.* **20,** 19–62.
21. Groves, C. P. (1986) in *Comparative Primate Biology,* eds. Swindler, D. R. & Erwin, J. (Liss, New York), Vol. 1, pp. 187–217.
22. Slightom, J. L., Koop, B. F., Xu, P.-L. & Goodman, M. (1988) *J. Biol. Chem.,* in press.
23. Maxam, A. M. & Gilbert, W. (1980) *Methods Enzymol.* **65,** 499–560.
24. Chang, L.-Y. E. & Slightom, J. L. (1984) *J. Mol. Biol.* **180,** 767–783.
25. Poncz, M., Schwartz, E., Ballantine, M. & Surrey, S. (1983) *J. Biol. Chem.* **258,** 11599–11609.
26. Swofford, D. L. (1985) *PAUP: Phylogenetic Analysis Using Parsimony* (Illinois Natural History Survey, Urbana, IL).
27. Koop, B. F., Miyamoto, M. M., Embury, J. E., Goodman, M., Czelusniak, J. & Slightom, J. L. (1986) *J. Mol. Evol.* **24,** 94–102.
28. Holmquist, R., Miyamoto, M. M. & Goodman, M. (1988) *Mol. Biol. Evol.* **5,** 217–236.
29. Savatier, P., Trabuchet, G., Cheboune, Y., Faure, C., Verdier, G. & Nigon, V. M. (1987) *J. Mol. Evol.* **24,** 297–308.
30. Savatier, P., Trabuchet, G., Cheboune, Y., Faure, C., Verdier, G. & Nigon, V. M. (1987) *J. Mol. Evol.* **24,** 309–318.
31. Slightom, J. L., Theisen, T. W., Koop, B. F. & Goodman, M. (1987) *J. Biol. Chem.* **262,** 7472–7483.
32. Nei, M. (1986) in *Evolutionary Perspectives and the New Genetics,* eds. Gershowitz, H., Rucknagel, D. L. & Tashian, R. E. (Liss, New York), pp. 133–147.
33. Andrews, P. & Cronin, J. (1982) *Nature (London)* **297,** 541–546.
34. Delson, E. (1985) *Nature (London)* **313,** 532–533.
35. Li, W.-H. & Tanimura, M. (1987) *Nature (London)* **326,** 93–96.
36. Sarich, V. M. & Wilson, A. C. (1967) *Science* **158,** 1200–1203.
37. Pilbeam, D. (1986) *Am. Anthropol.* **88,** 295–312.
38. Wiley, E. O. (1981) *Phylogenetics. The Theory and Practice of Phylogenetic Systematics* (Wiley, New York).