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Review article

Evolution of the Simiiformes and the phylogeny of human chromosomes

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Summary. This paper is based on the results of Primate chromosome studies obtained using high resolution techniques in our and other laboratories. We discuss the origin and the evolution of the chromosomes in the human karyotype and the time in evolution of the Simiiformes when they acquired their present morphology. Our results indicate that the chromosomes that underwent a higher number of reorganizations during the evolution of the Simiiformes coincide with the chromosomes most often implicated in human chromosome pathology. We describe the main reorganizations that took place during Primate evolution. Centromere activation and inactivation and heterochromatin changes are discussed as mechanisms of chromosome evolution.

Introduction

In the early 70s, de Grouchy et al. (1972), Dutrillaux et al. (1973), and Egozcue et al. (1973a, b) demonstrated that the chromosomes of man show a high degree of homeology with those of other primate species, such as the chimpanzee and the gorilla. Since then, many authors have carried out studies comparing the chromosomes of different genera from the same family (Lejeune et al. 1973; Dutrillaux et al. 1975, 1978, 1979a, b, 1980a, 1986a; García et al. 1976; Estop et al. 1978a; Finaz et al. 1978; Caballín et al. 1980; Ponsà et al. 1980, 1981; Ponsà and Egozcue 1981; Dutrillaux and Couturier 1981, 1986; Yunis and Prakash 1982; Stanyon et al. 1983, 1986; Viegas-Péquignot et al. 1985; Seuánez 1987; Muleris et al. 1986; Sineo et al. 1986), or even different families among them (Dutrillaux 1979a; Dutrillaux and Rumpler 1980; Dutrillaux et al. 1980b, 1982a, 1986b; Estop et al. 1983; Ponsà et al. 1983, 1986; Miró et al. 1986; Clemente et al. 1987, 1990; de Grouchy 1987). Although banding methods are still less precise than desired, the data obtained so far have allowed a hypothesis to be established on the chromosomal changes that have taken place during primate evolution.

The study of primate evolution is based not only on cytogenetic techniques, but also on molecular studies such as gene mapping (Cronin and Sarich 1976; Groves 1978; Estop et al. 1978b; Garver et al. 1978; Pearson et al. 1978, 1979, 1982; Creau-Golberg et al. 1980, 1981; Cochet et al. 1982; Ma et al. 1982; Ma 1983; Ma and Kurnit 1984; Lalley et al. 1987), DNA hybridization (Templeton 1983a, b, 1985; Sibley and Ahlquist 1984), mitochondrial DNA analyses (Ferris et al. 1981; Brown et al. 1982), and nucleotide or amino acid sequencing (Hewett-Emmett et al. 1976; Lucotte 1979; Lucotte and Jouventin 1980; Lucotte and Lefebvre 1980a, b; Goodman et al. 1982a, b, 1983; Goodman 1986; Koop et al. 1986).

According to Seuánez (1987), the cytogenetic and molecular evolutionary events may have been independent. So far, the cytogenetic homeologies confirmed by gene mapping affect only structural genes, but other mutations may have taken place that are not detected by cytogenetic techniques. Cytogenetic studies have allowed the banding patterns of human chromosomes, the different types of polymorphisms existing in human populations, and the reorganizations found in different types of human pathology to be characterized with considerable precision (Paris Conference 1971, 1975; JSCN 1978; Kaiser 1984; Berger et al. 1985a, b; Fryns et al. 1986). The results obtained so far indicate that for reasons still unknown, some human chromosomes are more prone than others to undergo pathological reorganizations.

In this paper, we describe the parsimonious phylogenetic tree of human chromosomes using the out-group method (Watrous and Wheeler 1981; Maddison et al.

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1984) for each and every one of the chromosome pairs now present in the human karyotype, taking into account gene-mapping data (Pearson et al. 1979, 1982; Lalley et al. 1987) in those cases in which more than one possibility exists; however, gene mapping has not always been useful to resolve these questions. Finally, we try to determine whether a correlation exists between stable chromosomes in the human karyotype and stable chromosomes in primate evolution.

Material and methods

Data on the following species are included in this study:

- Family Cebidae: *Cebus apella* (CAP), *Cebus albifrons* (CAL), *Lagothrix lagothricha* (LLA) (Clemente et al. 1987)

- Family Cercopithecidae: *Papio sphynx* (PSP), *Erythrocebus patas* (EPA), *Miopithecus talapoin* (MTA), *Cercopithecus nigroviridis* (CNI), *Cercopithecus mona campbelli* (CMC), *Cercopithecus petaurista* (CPE), *Cercopithecus cephus* (CCE) (Clemente et al. 1990); *Cercopithecus aethiops* (CAE), *Cercopithecus cynosurus* (CYN), *Cercopithecus sabaeus* (CSA) (Sineo et al. 1986); *Macaca mulatta* (MMU) (Small et al. 1985)

- Family Hominidae: *Pan troglodytes* (PTR), *Gorilla gorilla* (GGO), *Pongo pygmaeus* (PPY) (Yunis and Prakash 1982); *Pan paniscus* (PPA), *Pan troglodytes* (PTR) (Stanyon et al. 1986); *Homo sapiens* (HSA) (from our laboratory and Yunis and Prakash 1982)

Chromosome preparations were obtained using equivalent high resolution techniques (Yunis 1976; Viegas-Péquignot and Dutrillaux 1978; Camargo and Cervenka 1980; Small et al. 1985; Antich and Gean, unpublished). In the latter method, cells were cultured as described in Clemente et al. (1987). G- (Gallimore and Richardson 1973), C- (Sumner 1972), and NOR- (Bloom and Goodpasture 1976) banded karyotypes were used in this study.

Results

HSA 1

In the Cebidae, human chromosome 1 corresponds to two chromosomes with different morphologies and different patterns of heterochromatin depending on the species studied (Clemente et al. 1987). In the Cercopithecidae, HSA 1 may correspond to two chromosomes or to a single chromosome that differs from that present in *Pan, Gorilla,* and *Pongo* by a pericentric inversion, by the presence of terminal heterochromatin in the Pongidae, and also by a small paracentric inversion in the long arms of chromosome 1 of Gorilla. Yunis and Prakash (1982) have established that chromosome 1 of PTR and PPY corresponds to the ancestral form for the Hominidae and that HSA 1 would have originated by means of a pericentric inversion and the addition of juxtacentromeric heterochromatin, giving rise to the secondary constriction now present in HSA 1.

According to these data, it is possible that in the common ancestor of the Cercopithecidae and the Hominidae, the chromosome that originated HSA 1 would have been produced by centric fusion of two acrocentrics with a morphology corresponding to the equivalent chromosomes now found in CAP, which would also correspond to the ancestral chromosomes for all the Platyrrhini. According to Dutrillaux (1979b), this chromosome would be similar to that found now in PSP, CNI, and EPA. Later on in the evolution of the Cercopithecini, it would have undergone a fission, affecting the same region where the previous fusion had taken place. While the characteristics of HSA 1p are very similar in all species studied, HSA 1q has probably undergone several reorganizations (Fig. 1a, b).

HSA 2

Human chromosome 2 is the result of telomeric fusion of two chromosomes present in all species studied in the Cebidae, Cercopithecidae, and Hominidae. The evolution of the short (HSA 2p) and long (HSA 2q) arms of chromosome 2 will be analyzed separately.

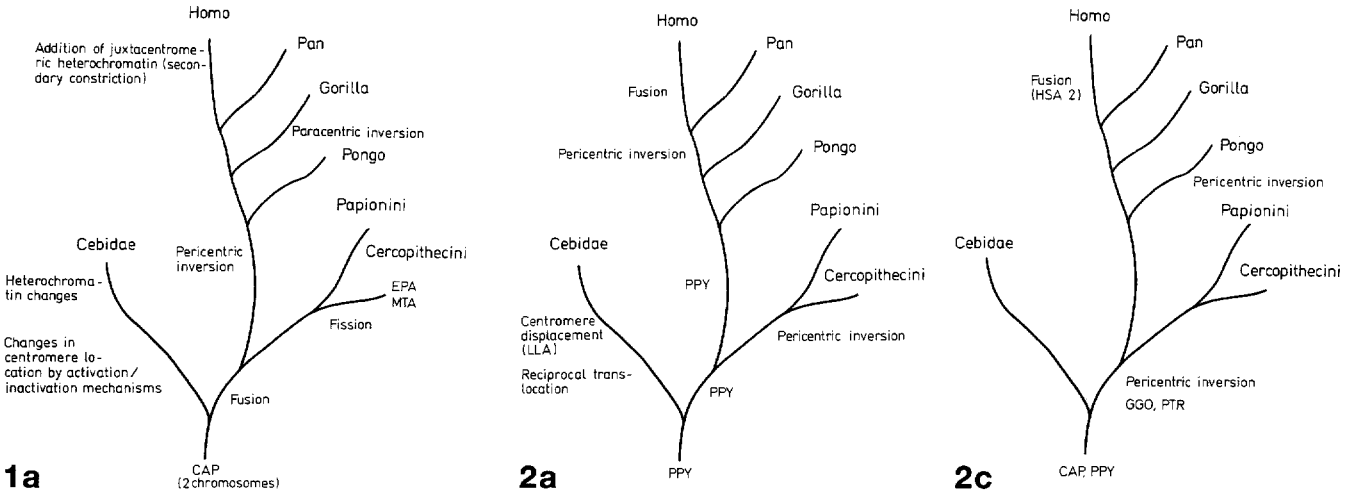
HSA 2p

According to Yunis and Prakash (1982) the ancestral morphology of the short arms of human chromsome 2 corresponds to that found in PPY and GGO. PTR 2p would have originated by pericentric inversion of the ancestral chromosome.

A homeologue to HSA 2p is found in all Cebidae and Cercopithecidae species studied, although with different morphologies. In the Cercopithecidae, this chromosome has the same morphology observed in PTR, while in the Cebidae it has the same morphology now found in PPY and GGO, showing heterochromatic regions not present in HSA 2 (Fig. 2a, b). According to these data, the ancestral chromosome of the Simiiformes would have the same morphology as that in PPY and CAP (Watrous and Wheeler 1981; Maddison et al. 1984); it would have fused with another chromosome in the branch that originated the Platyrrhini and would have been maintained without changes in the Catarrhini. Later on, and during the evolution of the Hominidae, it would have undergone a pericentric inversion in the ancestor of *Pan* and *Homo*. The same pericentric inversion can be observed in the Cercopithecidae (Fig. 2a, b).

HSA 2q

According to Yunis and Prakash (1982) the ancestral morphology of this chromosome would correspond to that found now in PTR and GGO. The corresponding homeologue found in PPY would have originated by pericentric inversion of the ancestral chromosome. In the Cercopithecidae, this chromosome shows the same morphology as in PTR and GGO, while in the Cebidae it is comparable to the chromosome of PPY, following in both families the same pattern described for HSA 2p. Our results seem to indicate that the ancestral chromosome for the Simiiformes would be the acrocentric type now found in the Cebidae and in PPY, which would have undergone an evolutionary process similar to that described for HSA 2p (Fig. 2b, c).



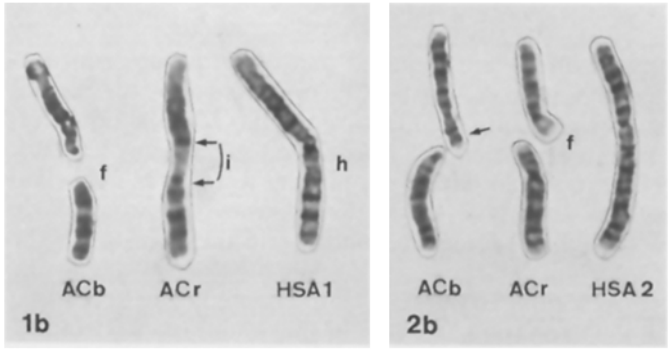


Fig. 1. **a** Evolution of HSA 1 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree. **b** Reorganizations that took place during the evolution of HSA 1 from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA). *f* Centric fusion, *i* inversion, *h* heterochromatin

Fig. 2. **a** Evolution of HSA 2p in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree. **b** Reorganizations that took place during the evolution of HSA 2 from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA). → Breakpoint, *f* centric fusion. **c** Evolution of HSA 2q in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree

HSA 3

In the Platyrrhini, HSA 3 corresponds to at least two different chromosomes that have undergone complex reorganizations. As a result, clear homeologies cannot be established (Dutrillaux 1979a, b). In the Cercopithecidae, HSA 3 corresponds to two chromosomes in the Cercopithecini and to a single chromosome in the Papionini. In the Hominidae, HSA 3 shows the same morphology in *Homo*, *Pan*, and *Gorilla*. According to Yunis and Prakash (1982) this morphology differs by two pericentric inversions from that found in the Sumatran orangutan *(Pongo pygmaeus abelii)*. Seuánez (1979) proposed that the acrocentric morphology observed in the orangutan from Borneo (*Pongo pygmaeus pygmaeus)* would be the ancestral form for the Hominidae. A pericentric inversion would have produced the chromosome now found in the Sumatran orangutan, and another inversion would have given rise to the morphology now present in *Homo, Pan,* and *Gorilla.*

According to our results, chromosome 3 of the orangutan from Borneo only differs by pericentric inversion from that found in the Papionini. Thus, in the common ancestor of the Catarrhini, the homeology to human chromosome 3 would have been produced by the fusion of at least two chromosomes that would also be present in the Platyrrhini; the chromosome would have been maintained unchanged in the Papionini and would have undergone a centric fission in the Cercopithecini. In the Hominidae, this chromosome would have suffered the pericentric inversions indicated above (Fig. 3).

HSA 4

In this chromosome, several pericentric inversions have been detected in the different species of the family

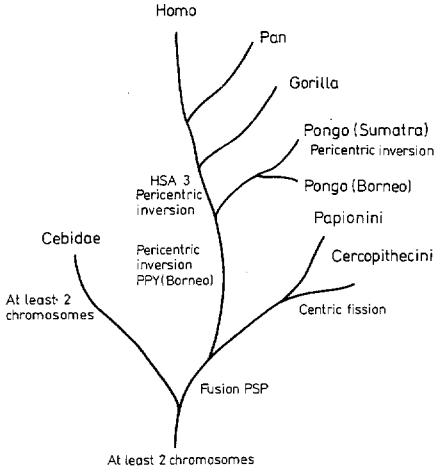


Fig. 3. Evolution of HSA 3 in Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree

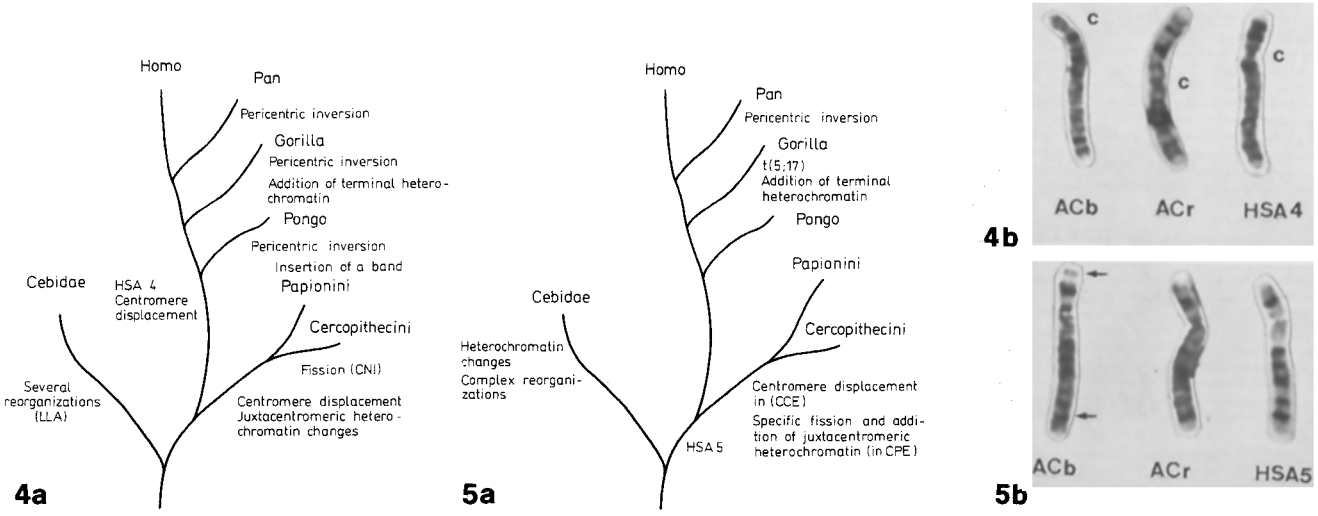


Fig. 4. **a** Evolution of HSA 4 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree. **b** Reorganizations that took place during the evolution of HSA 4 from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA). *c* Centromere

Fig. 5. **a** Evolution of HSA 5 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree. **b** Reorganizations that took place during the evolution of HSA 5 from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA). → Breakpoint

Hominidae. According to Yunis and Prakash (1982) and Dutrillaux and Couturier (1986) the morphology of HSA 4 would correspond to the ancestral form for these four genera (*Homo, Pan, Gorilla,* and *Pongo).* In the Cebidae and the Cercopithecidae, the G-banding pattern of the corresponding chromosome is maintained, although with different locations of the centromere. These differences do not seem to be due to pericentric inversion mechanisms, but to activation/inactivation of centromeres. These data are in agreement with the hypothesis of Yunis and Prakash (1982) and Dutrillaux and Couturier (1986) according to which HSA 4 would be the most primitive chromosome in the Hominidae from a morphological point of view.

Our results support the interpretation of Dutrillaux et al. (1982b) using high resolution R bands, but not those of Estop et al. (1978a, b) and Ponsà et al. (1986). Gene-mapping data (Lalley et al. 1987) are also contradictory, so that the homeologies of HSA 4 cannot be established. During its evolution, HSA 4 also shows changes in the amount of terminal, centromeric, and juxtacentromeric heterochromatin (Fig. 4a, b).

HSA 5

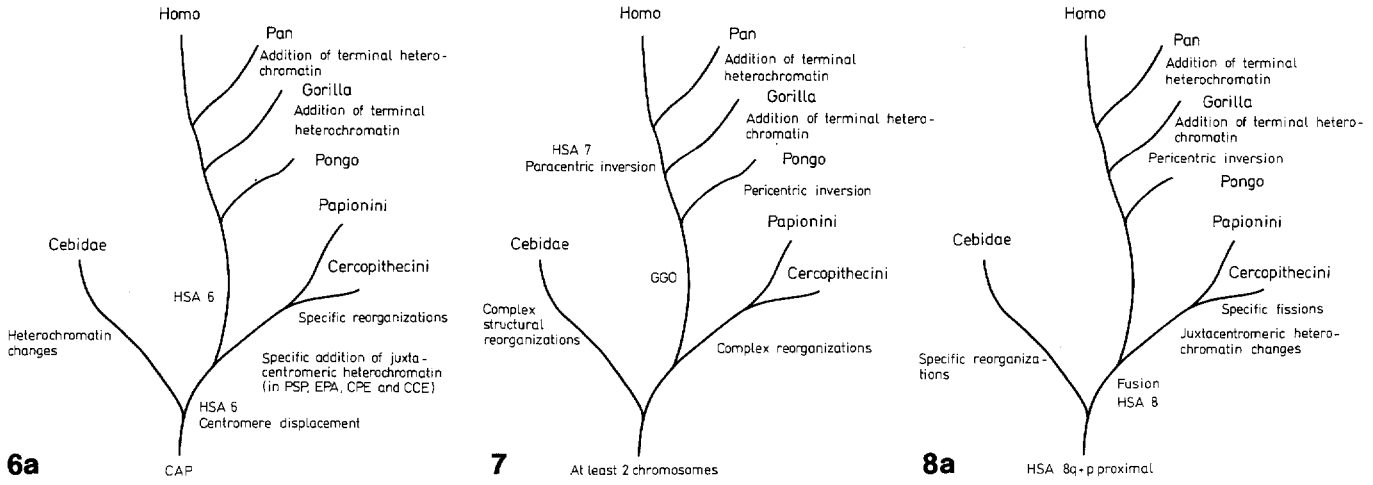
This chromosome shows homeology with the corresponding chromosomes in the Cebidae, although complex reorganizations are required to explain its present morphology in man. In the Cercopithecidae, some species show a chromosome identical to HSA 5, while others require reorganizations. According to Dutrillaux (1979b), HSA 5q would have been present as early as in the ancestral karyotype of the Simiiformes and would have acquired its present morphology in the ancestor to the Catarrhini.

According to our results, the homeologue to HSA 5q in the ancestral karyotype of the Simiiformes (Cebidae) shows an extra G(+) and an extra G(−) band in its distal end when compared with HSA 5 (Fig. 5a, b). Furthermore, changes in the amount and location of constitutive heterochromatin can be observed in the evolution of this chromosome. In CPE it shows juxtacentromeric heterochromatin, and in GGO, terminal heterochromatin (Fig. 5a, b).

HSA 6

Our results indicate that HSA 6 maintained a very conservative banding pattern during the evolution of the Simiiformes. A chromosome in the Cebidae shows the same banding patterns as HSA 6, although with a different location of the centromere. Dutrillaux (1979a, b) has explained this difference by a pericentric inversion, but it might be due to the activation/inactivation of different centromeres. In the Papionini and in some Cercopithecini species, this chromosome is identical to HSA 6, while in other Cercopithecini species the chromosome shows different reorganizations.

This would indicate that HSA 6 maintained a constant banding pattern ever since the ancestral karyotype of the Simiiformes. Later on, and in the common ancestor to the Catarrhini, this chromosome would have undergone a displacement of its active centromere. It is also possible to detect changes in the presence or absence and in the localization of heterochromatic regions during the evolution of this chromosome. These would correspond to the observation of telomeric heterochromatin in CAP, CAL, LLA, PTR, and GGO and of



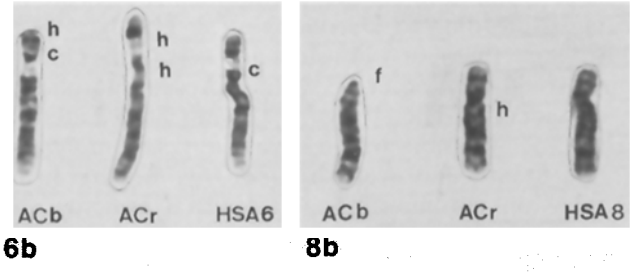


Fig. 6. **a** Evolution of HSA 6 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree. **b** Reorganizations that took place during the evolution of HSA 6 from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA). *c* Centromere, *h* heterochromatin

Fig. 7. Evolution of HSA 7 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree

Fig. 8. **a** Evolution of HSA 8 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree. **b** Reorganizations that took place during the evolution of HSA 8 from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA). *f* Fusion, *h* heterochromatin

juxtacentromeric heterochromatin in PSP, EPA, CPE, and CCE (Fig. 6a, b).

HSA 7

Human chromosome 7 shows homeologies within the three Cebidae species studied. However, these homeologies require complex structural reorganizations (Dutrillaux and Couturier 1981; Clemente et al. 1987). In the Cercopithecidae, no homeologies for this chromosome have been observed (Ponsà et al. 1986; Clemente et al. 1990), although Dutrillaux et al. (1980b) have described a single homeology that requires extremely complex reorganizations.

Our results also suggest that many reorganizations took place during the evolution of HSA 7. According to other authors (Yunis and Prakash 1982; Dutrillaux et al. 1982b; Dutrillaux 1985) the present morphology of this chromosome originated after the Cercopithecidae and the Hominidae diverged, and as indicated by Yunis and Prakash (1982), probably in the common ancestor to the genera *Pan* and *Homo* (Fig. 7).

HSA 8

Some of the published data indicate that human chromosome 8 occurred with its present morphology in the common ancestor of the Hominidae (Seuánez 1979; Yunis and Prakash 1982; Dutrillaux 1985), while others suggest that it would have occurred even earlier, in the ancestor of the Catarrhini (Ponsà et al. 1986; Clemente et al. 1990), because this chromosome, with some small changes in the amount of its juxtacentromeric heterochromatin, can be found in all Cercopithecidae species studied so far. Dutrillaux et al. (1980b) believe that this chromosome would have undergone a fission process in some Cercopithecini species. In the Cebidae, HSA 8 maintains a constant morphology, except perhaps for the distal regions of HSA 8p (Clemente et al. 1987) (Fig. 8a, b).

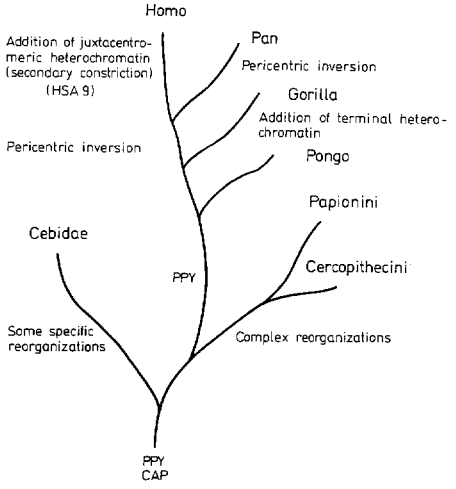


Fig. 9. Evolution of HSA 9 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree

HSA 9

This chromosome shows homeologies with all Cebidae species studied, and its morphology is equivalent to that found in *Pongo*, which according to Yunis and Prakash (1982) and Dutrillaux (1985) would correspond to that present in the ancestor of the Hominidae. Thus, this chromosome would have been present in the common ancestor of the Platyrrhini. No homeologies for HSA 9 have been found in the Cercopithecidae (Ponsà et al. 1986; Clemente et al. 1990), although some authors have suggested the existence of homeologies through extremely complex reorganizations (Dutrillaux 1979a; Dutrillaux et al. 1980a). The morphology of HSA 9 as such is only found in *Homo sapiens* (Fig. 9).

HSA 10

To find homeologies to HSA 10 in the Cebidae, different reorganizations such as pericentric inversions or centromere displacements are required. According to Dutrillaux (1979a, b) the long arm of the corresponding chromosome in the genus *Cebus* would be equivalent to that present in the ancestral karyotype of the Simiiformes, because it shows the same morphology as that observed in *Pongo*, a genus with a chromosome 10 differing from HSA 10 only by a pericentric inversion.

In our opinion, the equivalent long arms of the chromosomes of *Cebus* and *Pongo* do not show the same banding pattern, and if CAP 5q shows a paracentric inversion, it would be different from that present in PPY and would give rise to a banding pattern quite similar to that now found in HSA 10. According to Dutrillaux (1979a), Estop et al. (1978b; 1983), and Ponsà et al. (1986), in the Cercopithecidae this chromosome would show the same morphology as in *Pongo*, which as suggested by Yunis and Prakash (1982) and Dutrillaux (1985), would correspond to the ancestral morphology of that of the Hominidae. Thus, the present morphology of HSA 10 would have originated after the divergence of the orangutan. During its evolution, this chromosome would have undergone changes in the amount and localization of its terminal (LLA, PTR, GGO), interstitial (CAP, CAL), and juxtacentromeric heterochromatin (CPE and CCE) (Fig. 10a, b).

HSA 11

HSA 11 is found in all species of the family Cercopithecidae studied so far, with the single exception of CCE. This homeology, in agreement with that proposed by Ponsà et al. (1986), requires a pericentric inversion (Fig. 11a, b). Yunis and Prakash (1982) have suggested that the metacentric type found in the Cercopithecidae would correspond to the morphology present in the common ancestor of the Cercopithecidae and the Hominidae. Our results are in agreement with this hypothesis and also indicate that later on a pericentric inversion would have produced the submetacentric type now found in the Hominidae.

The homeologues to HSA 11 found in the Cebidae require specific reorganizations. The ancestral morphology in the Cebidae corresponds to an acrocentric chromosome, which would have originated the metacentric type found in the Cercopithecidae by a displacement of the centromere. The present morphology of HSA 11 would have originated before the divergence of the orangutan, as proposed by Yunis and Prakash (1982). Other than these structural changes, other changes would also have taken place affecting the presence or absence and the location of heterochromatin, because CAP and LLA show an interstitial heterochromatic region, while PTR and GGO have terminal heterochromatic bands.

HSA 12

HSA 12 is found in all Cercopithecidae species studied so far. According to Dutrillaux et al. (1980a, 1982b), Dutrillaux (1985), and Ponsà et al. (1986), this chromosome would have occurred with its present morphology in the common ancestor of the Catarrhini. Later on, pericentric inversions would have taken place in *Pan* and *Gorilla* (Yunis and Prakash 1982) (Fig. 12a, b). In the Cebidae, this chromosome corresponds to an acrocentric or to a submetacentric depending on the species studied. The results of Dutrillaux and Couturier (1981) indicate that the acrocentric type found in the genus *Cebus* is also present in the prosimian *Microcebus murinus* (MIM). This acrocentric chromosome probably corresponds to the type that occurred in the common ancestor to all Primates, while in the common ancestor to the Simiiformes it would have probably acquired a submetacentric morphology (Fig. 12a, b). Later on, different reorganizations would have taken place, as well as changes in the amount and localization of interstitial (CAP, CAL) juxtacentromeric (EPA, CCE), or terminal heterochromatin (PTR, GGO).

HSA 13

This chromosome is found in some Cebidae and Cercopithecidae species, indicating that it was probably present in the common ancestor to the Simiiformes. According to Dutrillaux and Couturier (1981, 1983) and Dutrillaux (1985), the morphology of HSA 13 is also identifiable in other mammalian species.

HSA 14

This chromosome is found in some Cebidae and Cercopithecidae species (CAP, CAL, PSP, CNI) as the long arm of a submetacentric chromosome. In other species of these two groups, the short arm of this submetacentric shows some differences that may be due to deletions or reciprocal translocations. According to Dutrillaux (1979a), HSA 14 as an independent acrocentric chromosome would have originated by centric fission in the common ancestor to the Hominidae, and later on it would have undergone a pericentric inversion in *Gorilla* (Yunis and Prakash 1982) (Fig. 13a, b).

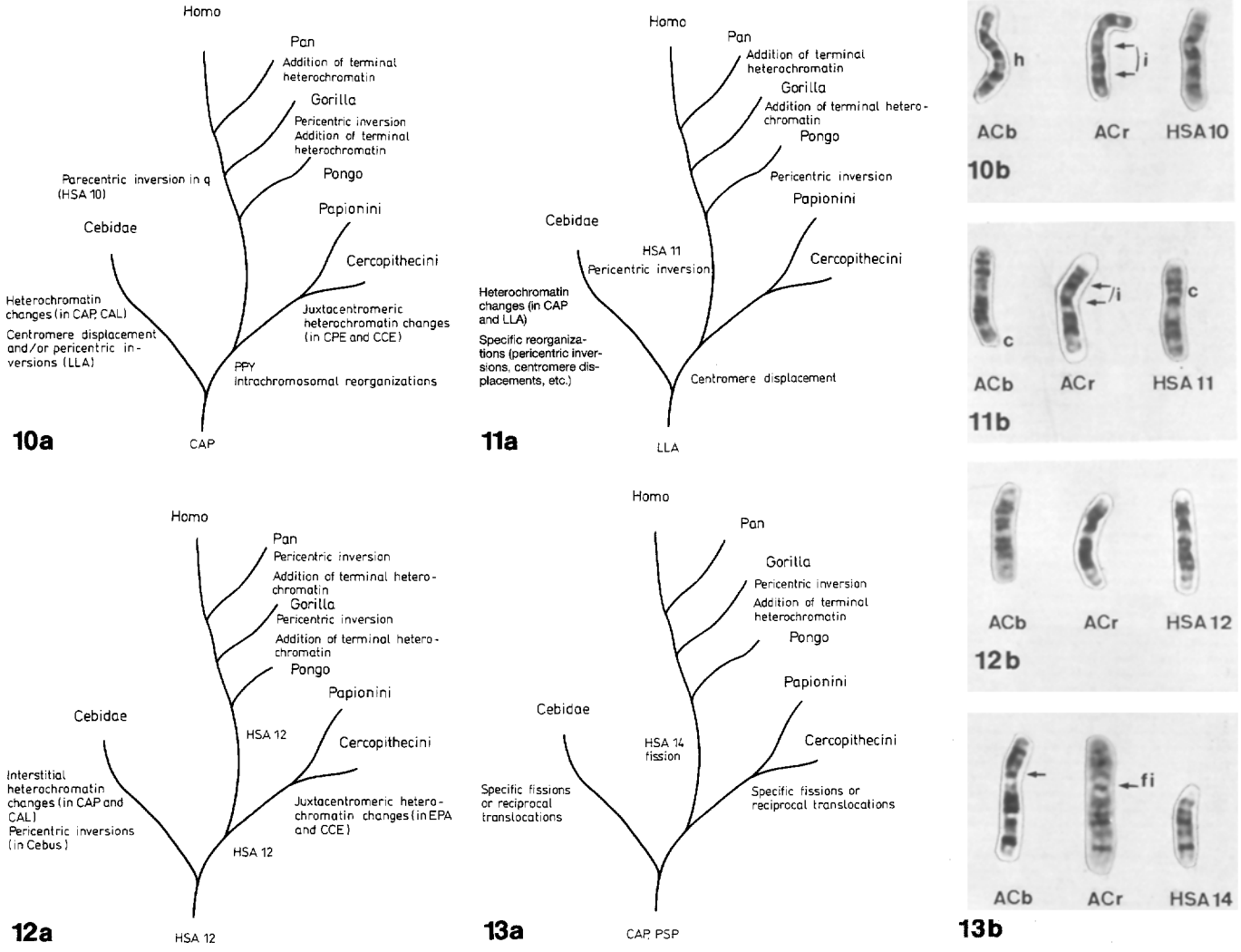


Fig. 10. **a** Evolution of HSA 10 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree. **b** Reorganizations that took place during the evolution of HSA 10 from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA). → Breakpoint, *i* inversion, *h* heterochromatin

Fig. 11. **a** Evolution of HSA 11 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree. **b** Reorganizations that took place during the evolution of HSA 11 from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA). *c* Centromere, → breakpoint, *i* inversion

Fig. 12. **a** Evolution of HSA 12 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree. **b** Reorganizations that took place during the evolution of HSA 12 from the common ancestor of Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA)

Fig. 13. **a** Evolution of HSA 14 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree. **b** Reorganizations that took place during the evolution of HSA 14 from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA). → Breakpoint, *fi* fission

HSA 15

No homeologies for this chromosome have been found in the Cebidae species studied so far. In the Cercopithecidae, it can be identified as an acrocentric in some Cercopithecini, and as the long arm of the marked (NOR) chromosome in the Papionini. This chromosome probably originated in the common ancestor to the Catarrhini and later on underwent different reorganizations.

HSA 16

This chromosome has probably suffered many different reorganizations during the evolution of the Simiiformes. No homeologies for HSA 16 have been observed in the Cebidae or in the Cercopithecidae. In the Hominidae, this chromosome shows reorganizations in the four genera of the family. Results relative to the proposed ancestral form for the Hominidae are conflictive. Seuánez (1979) proposed that the ancestral morphology would be the one now found in *Pan*, while Yunis and Prakash

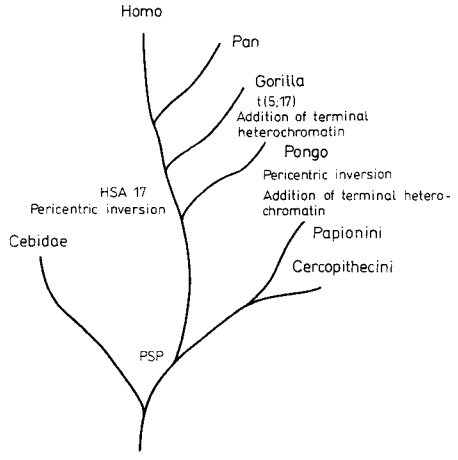


Fig. 14. Evolution of HSA 17 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree

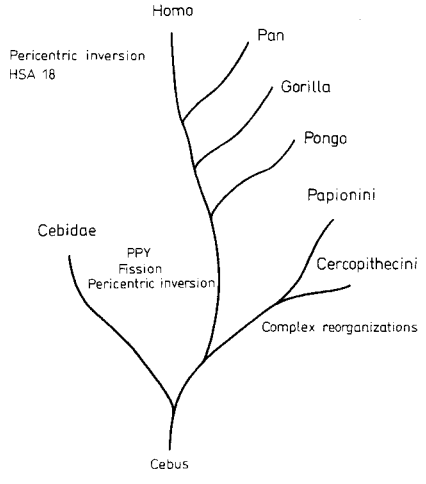


Fig. 15. Evolution of HSA 18 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree

(1982), Dutrillaux (1985), and Dutrillaux and Couturier (1986) considered that it would correspond to the type observed in *Pongo* and *Homo*.

HSA 17

No homeologies to this chromosome have been found in the Cebidae. In the Cercopithecidae, a chromosome is found that only differs from that now present in the orangutan by a pericentric inversion. According to Yunis and Prakash (1982) the ancestral chromosome of the Catarrhini would be of the type now found in the Cercopithecidae. This chromosome, by means of a pericentric inversion, would have produced the corresponding chromosome of the orangutan, and by means of a paracentric inversion, the morphology now found in *Homo*. In the remaining species of the F. Hominidae, other types of reorganization would be involved (Yunis and Prakash 1982) (Fig. 14).

HSA 18

HSA 18 shows homeologies within all Cebidae species studied, in which it is part of a longer chromosome. Although Dutrillaux et al. (1980a) and Ponsà et al. (1986) have described homeologies for this chromosome in the Cercopithecidae, we have not been able to confirm their results. With its present morphology, HSA 18 is found only in *Homo sapiens*. According to Dutrillaux and Couturier (1986), this type would correspond to the ancestral chromosome of the Hominidae. However, Seuánez (1979) and Yunis and Prakash (1982) believe that HSA 18 originated from the type now found in *Pan, Gorilla,* and *Pongo* (Fig. 15).

HSA 19

This chromosome is found in all Cebidae and Cercopithecidae species studied. As indicated by other authors (Dutrillaux et al. 1982), it would have remained unchanged since the ancestral karyotype of the Simiiformes, except for the addition of terminal heterochromatin in PTR and GGO (Fig. 16).

HSA 20

This chromosome is found with the same morphology in most Cebidae species and with a pericentric inversion in LLA. In the Cercopithecidae, no homeologies for this chromosome have been observed. Probably HSA 20 was present in the ancestral karyotype of the Simiiformes, underwent complex reorganizations in the Cercopithecidae, and was maintained unchanged in *Homo, Pan,* and *Gorilla.*

HSA 21

In the Cebidae species studied, this chromosome shows interstitial (LLA) or terminal (CAP and CAL) heterochromatic regions. No homeologies for this chromosome have been found in the Cercopithecidae. According to other authors (Seuánez 1979; Yunis and Prakash 1982; Dutrillaux 1985), this chromosome would have been found unchanged in the ancestral karyotype of the Simiiformes and would have undergone complex reorganizations in the Cercopithecidae and changes in the amount and localization of heterochromatin in the Hominidae, with terminal heterochromatic regions in PTR and GGO.

HSA 22

Unlike Dutrillaux (1979a), we have not found any homeologies for this chromosome in the Cebidae. In the Cercopithecidae it would correspond to the short arms of the marked chromosome found in the Papionini and to the long arm of the marked chromosome of the Cercopithecini. This chromosome was probably present in the ancestral karyotype of the Catarrhini, and would have been maintained unchanged in the evolutionary line that gave rise to the Hominidae, while in the Cercopithecidae it would have undergone fusions with other

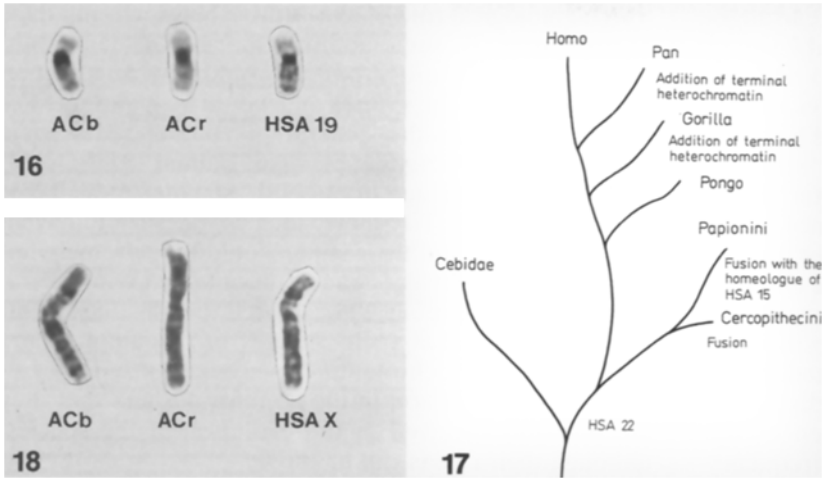


Fig. 16. Homeologies observed during the evolution of HSA 19 from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA)

Fig. 17. Evolution of HSA 22 in the Simiiformes. The main reorganizations that took place are indicated in the phylogenetic tree

Fig. 18. Homeologies observed during the evolution of HSA X from the common ancestor of the Cebidae (ACb) and the Cercopithecidae (ACr) to its present morphology in *Homo sapiens* (HSA)

chromosomes, which are different in the Papionini and the Cercopithecini (Fig. 17).

HSA X

Although it has undergone some intrachromosomal rearrangements in all Cebidae and Cercopithecidae species studied, the X chromosome has been maintained unchanged (with respect to its G-banding pattern). According to some authors (Estop et al. 1983; Dutrillaux et al. 1982a; Dutrillaux 1985; Ponsà et al. 1986), this chromosome would have been present in the ancestral karyotype of the Simiiformes and later on would have undergone changes in the amount and localization of heterochromatin (Fig. 18).

Discussion

When our results are compared with those previously published (Dutrillaux 1979b, 1985; Dutrillaux et al. 1982a, b; Dutrillaux and Couturier 1986; Seuánez 1987), three types of homeologies become evident:

1. Homeologies that coincide in all papers published so far, for both the chromosomes identified and the type(s) of reorganization(s) described. For instance, HSA X is a chromosome that has been "protected" from changes during the evolution of the Simiiformes, except for some simple intrachromosomal reorganizations (García et al. 1978; Freitas 1982). Thus, no differences exist in the interpretation of the evolution of HSA X in the studies published so far.

2. Homeologies that coincide in the assignment of the chromosomes involved, but not regarding the reorganization(s) that have taken place and that are needed to establish a correspondence between the banding patterns present in different species. For instance, the homeology proposed in this paper between HSA 6 and CAP 3 coincides with that proposed by Dutrillaux (1979a) for CCA 3. However, the differences in the location of the centromeres in these chromosomes are interpreted by Dutrillaux (1979a, b) as resulting from a pericentric inversion, while we consider that they are the result of a displacement due to a centromere activation/inactivation phenomenon.

3. Homeologies in which the chromosome assignments, of the different authors do not coincide, or others in which some authors find homeologies, while others do not. Thus, Estop et al. (1978a, b) and Ponsà et al. (1986) consider that HSA 4 corresponds to MMU 6, while Dutrillaux et al. (1982a) and ourselves, having used high resolution banding techniques, believe that HSA 4 really corresponds to MMU 4 (PSP 4). Gene-mapping studies (Pearson et al. 1982; Lalley et al. 1987) have not helped to solve the problem in this case.

During the evolution of the Simiiformes, some chromosomes seem to have been protected from structural rearrangements and are extremely similar morphologically in all species studied (HSA 19 and HSA X; Fig. 19) while

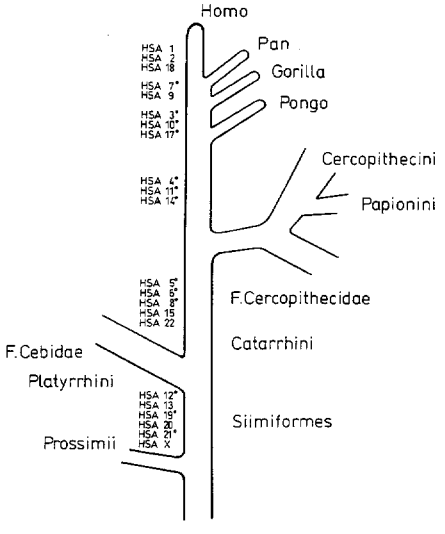


Fig. 19. Phylogeny of human chromosomes. The time in evolution where the present morphology was acquired is indicated. • Changes in the amount and/or location of heterochromatin

others have undergone multiple and variable rearrangements. Our results indicate that HSA 1, 3, and 7 would be among the chromosomes that have suffered relatively many reorganizations during the evolution of the Simiiformes. These three chromosomes would have acquired their present morphology in a later stage of evolution: HSA 3 would have originated after divergence of the orangutan; HSA 7, after divergence of the *Gorilla*; and HSA 1, during the process of speciation that gave rise to *Homo sapiens*. Furthermore, these chromosomes have also undergone many reorganizations during the evolution of the Cebidae and the Cercopithecidae (Fig. 19). Dutrillaux et al. (1980a) have indicated that in the evolution of the Cercopithecini, four-fifths of the chromosomal reorganizations affect just seven of the chromosomes, which by decreasing order of frequency correspond to HSA 1, 7, 3, 6, 4, 14, and 20.

On the other hand, it is interesting to note that the chromosomes that have undergone more rearrangements in the evolution of the Simiiformes coincide with those that are also more affected by rearrangements in human pathology. Thus, HSA 1, 3, and 7 are the ones that more frequently show pericentric inversions (Fryns et al. 1986) while paracentric inversions affect mainly chromosomes HSA 1, 3, and 6 (Kaiser 1984). In cancer patients who have undergone radio and/or chemotherapy the chromosomes most frequently affected by reorganizations are HSA 1, 3 and 7 (Barrios 1987; Bauchinger and Gotz 1979; Lee and Kamra 1981; Berger et al. 1985a, Kano and Little 1986), while the chromosomes less frequently affected in this type of patients seem to be HSA 13, 15, 21, and 22 (Barrios 1987). The phylogenetic study of human chromosomes also indicates that these are among the more stable chromosomes in the evolution of the Simiiformes. As shown in Fig. 19, chomosomes 13 and 21 would have acquired their present morphology in the common ancestor to the Simiiformes, and according to Dutrillaux et al. (1982b) the same morphology can also be found in other mammalian species. HSA 15 and 22 (Fig. 19) would have adopted its present morphology after divergence of the Cebidae. Furthermore, these chromosomes show few reorganizations in the different Primate families studied so far.

The most frequent of the different types of reorganization detected in the evolution of the Simiiformes are inversions (especially pericentric), changes in the amount and localization of heterochromatin, fusions and fissions, and changes in the location of centromeres due to activation/inactivation mechanisms. Much less frequent are reciprocal translocations, deletions, and insertions. The reasons for and consequences of the different "classic" types of reorganizations, such as inversions, fissions, etc., have been discussed by others (Chiarelli and Egozcue 1967; White 1973, 1978; de Grouchy 1978; Lande 1979; Bengston 1980; Marks 1983; Coyne 1984; Dutrillaux 1986; King 1986; Baker et al. 1987). However in our opinion, two types of reorganization, i.e., the changes in the amount and location of heterochromatin and the changes in the location of the centromere due to activation/inactivation mechanisms, deserve special attention.

The biological role of constitutive heterochromatin is controversial. To some authors, changes in the amount and location of heterochromatin would have no effect on the individual or the species and would be maintained as polymorphisms in the general population (McKenzie and Lubs 1975; Arrighi et al. 1976; Baimai 1977; Dutrillaux 1979b; Dutrillaux et al. 1981; Seuánez et al. 1983, 1986; King 1986). To others, such changes could have a selective effect, and their study would be extremely important from a phylogenetic point of view (White 1978; Stanyon and Chiarelli 1982; García et al. 1983). Our results indicate that such changes in the amount and location of heterochromatin have been extremely frequent in the evolution of the Simiiformes and that they are probably involved in the evolution of the species, although their role is still unknown.

Heterochromatin is generally believed to correspond to inactive regions of the chromosomes (Sieger et al. 1970), although some authors have described low levels of genetic activity in these regions (Sadamory and Sandberg 1983). On the other hand, constitutive heterochromatin has been related to gene regulation (Britten and Davidson 1971; Hsu 1975; Brown 1981) and its variations have been associated with different pathological conditions such as mental retardation and embryopathies (Lubs et al. 1977; Matsaura et al. 1978; Tharapel and Summit 1978; Funderburg et al. 1980; Podugolnikova and Blumina 1983), spontaneous abortion (de Grouchy et al. 1964; Hamerton et al. 1965, 1972; de la Chapelle et al. 1974; Patil and Lubs 1977; Hommings and Burns 1979; Verp et al. 1983) and cancer (Atkin and Picktall 1977; Atkin and Baker 1977; Berger et al. 1979, 1985b; Le Coniat et al. 1981; Rajasekariah and Garson 1981; Shabtai et al. 1985).

The evolutionary studies carried out so far seem to indicate that the euchromatic regions of the chromosomes in the different species analyzed are quite similar (Dutrillaux 1979b; Dutrillaux et al. 1981; Miró et al. 1986, 1987; Clemente et al. 1987). The main differences in these species are due to the different amounts and localization of heterochromatin. In our work on the Simiiformes, we have observed that some chromosomes preferentially show changes in the amount and location of heterochromatin. These data are in agreement with those of Dutrillaux et al. (1981) according to which heterochromatin is not distributed at random in the chromosomes, but is usually found in the same regions, depending on the species or genera studied. This suggests the existence of specific chromosomal regions with a potential to develop increased amounts of heterochromatin, maybe through a mechanism of DNA amplification.

Furthermore, the limits of the regions where heterochromatin is found in some Primate species are very frequently involved in chromosome rearrangements observed in their homeologues in other species. For instance, band HSA 2q13 corresponds to the region where the fusion that originated HSA 2 took place, and in the acrocentric chromosomes of the Cebidae, Cercopithecidae, and Hominidae it also shows terminal heterochromatin in PTR and GGO and interstitial hetero-

chromatin in LLA. And it is one of the bands implicated in the pericentric inversion needed to establish the homeology between the corresponding acrocentric chromosomes found in the orangutan and different Cebidae species with the chromosome present in PTR, GGO, and different species of the family Cercopithecidae (unpublished data). These data are in agreement with previous publications (Miró 1981; García et al. 1983; Miró et al. 1986, 1987; Clemente et al. 1987) indicating that the limits of heterochromatic regions would be more prone to breakage and reunion mechanisms and, as a result, would be involved in most reorganizations produced during chromosome evolution.

The proposed changes of location of centromeres have been described as frequent reorganizations in the evolution of the Cercopithecidae (Dutrillaux et al. 1982a), the Platyrrhini (Viegas-Péquignot et al. 1985; Clemente et al. 1987), and the Prosimians (Rumpler et al. 1983). These differences in the localization of the centromeres might result from a simple inactivation/activation mechanism if latent, interstitial centromeres are present in the chromosome. The existence of latent centromeres has been proposed by several authors (Raoul 1970; Dutrillaux 1975, 1979b; Holmquist and Dancis 1980; Miró et al. 1986, 1987; Clemente et al. 1987), and Raoul (1970) and Holmquist and Dancis (1980) have demonstrated that at least some reorganizations imply the activation of a latent centromere and the inactivation of the previous one. Since the displacement of a centromere in heterozygosis can give rise to abnormal meiotic segregations, this may have had as important a role in cladogenesis as any other type of chromosome reorganization.

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