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Comparative Cytogenetics Allows the Reconstruction of Human Chromosome History: The Case of Human Chromosome 13

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Abstract

Comparative cytogenetics permits the identification of human chromosomal homologies and rearrangements between species, allowing the reconstruction of the history of each human chromosome. The aim of this work is to review evolutionary aspects regarding human chromosome 13. Classic and molecular cytogenetics using comparative banding, chromosome painting, and bacterial artificial chromosome (BAC) mapping can help us formulate hypotheses about chromosome ancestral forms; more recently, sequence data have been integrated as well. Although it has been previously shown to be conserved when compared to the ancestral primate chromosome, it shows a degree of rearrangements in some primate taxa; furthermore, it has been hypothesised to have a complex origin in eutherian mammals which has still not been completely clarified.

Keywords: FISH, evolution, mammals, human syteny

1. Introduction

Comparative cytogenetics has been widely applied to many mammalian species [1–3] through banding methods and, later, with fluorescence *in situ* hybridization (FISH) of whole chromosomes and bacterial artificial chromosome (BAC) probes; these approaches permit the definition of regions of chromosomal homology, rearrangements, and breakpoints, as well as elucidate phylogenetic relationships between taxa [4]. In addition, the comparative cytogenetic approach is particularly useful in the reconstruction of human chromosome (HSA) history.

Indeed, parsimony analysis of homologies and rearrangements permits us to define ancestral chromosomal syntenies (synteny is the colocalization of two or more genetic loci) and derived ones [2]. Banding allows us to first evaluate rearrangements between species; the mapping of whole chromosomes through the chromosomal painting approach allows researchers to better define rearrangements at the molecular level, such as Robertsonian ones and breakpoints. At a finer level, the use of DNA cloned inside vectors such as yeast artificial chromosomes (YACs) or BAC, used as mapping probes, permits the evaluation of chromosomal dynamics [5, 6], defining marker orders and intrachromosome rearrangements. Moreover, the use of specific loci or repetitive probes permits the localization of specific sequences, such as repetitive ones, which are often supposed to be responsible for the plasticity of chromosomes [7–10] and human genes involved in cancers [11].

More recently, the integration of cytogenetic data with sequence data has been proposed [12–16]. These kinds of data are available from genomic browsers and are helpful for testing previously proposed phylogenomic hypotheses and chromosomal organisation reconstructions.

In this review, we report the principal approach which has proven useful for studying human chromosome history by analysing previous cytogenetic and sequence data regarding human chromosome 13.

2. The reconstruction of human chromosome history

At least three or four principal approaches can be used to reconstruct human synteny history. In a comparative perspective, the analysis of banding data permits the identification of chromosomal homologies. In particular, the analysis of the banding patterns obtained by the enzymatic digestion of chromosomes in metaphases using proteolysis and Giemsa solution staining permits the identification of chromosomal homologies and principal rearrangements occurring between species. Consequently, by focusing attention on a single chromosome, it is possible to track the principal evolutionary steps involving each individual human chromosome [1].

Another approach is the analysis of comparative painting data; the painting approach consists of a whole chromosome undergoing FISH on cytogenetic preparations, allowing the identification of molecular level homologies, interchromosomal rearrangements and genomic breakpoints. First, human chromosome probes are mapped onto metaphases of target species (chromosome painting [CP]) [17], then, for a better comparison, animal chromosomal probes are mapped onto human metaphases in a reciprocal hybridization (RP) [18]. Subsequently, whole animal chromosomes are mapped onto other animal metaphases in an approach known as ZOO-FISH, Z-F [19]. The analysis of these data regarding a single chromosome, consequently, permits the tracking of each change involving the human chromosome under study.

In addition, human chromosome evolution can be studied using another kind of probe, the BAC probe, containing an insert of 50–300 Kb of the human genome. It can be mapped by FISH onto the metaphases of many species. BACs are available for each human chromosome and can be purchased from the BAC/PAC Resource Center (Chori), and some of them are commercially available for medical diagnosis. These probes are very useful in detecting

small interchromosomal rearrangements which are not detectable by painting and in defining marker order along chromosomes, thus revealing inversions, new centromere evolutions (new centromeres arise without the occurrence of inversions, maintaining the marker order), and duplications [3].

Comparative cytogenetics has been applied to reconstructing most human chromosome history; these published works have mainly been done by reviewing previous painting data or by mapping BAC probes on primates (see review in [2]) and other eutherian mammals; some works have analysed only specific chromosome regions (see **Table 1** for representative works).

Furthermore, alignments of sequences (SA) of many mammal species, obtainable from the NCBI, UCSC, and Ensemble genome browsers, can be integrated with molecular cytogenetic information in order to shed light on the history and peculiar features characterising each human chromosome.

2.1. The evolutionary history of HSA 13

Human chromosome 13 has been sequenced, and it has been shown to be the largest acrocentric chromosome in the human karyotype. Currently, the NCBI reports 1381 total genes, 41 novel genes, and 477 pseudogenes for a size of 114.36 MB [47]. It is among the human chromosomes with the lowest percentage of duplicated sequences [48].

The analyses of classical and molecular cytogenetics, using comparative banding and chromosome painting, have allowed researchers to formulate hypotheses about its ancestral forms. In this report, we delineate the principal steps regarding the history of human chromosome 13, tracked through the analysis of previous cytogenetics literature and sequence data. We have reported a list of species analysed by painting or sequence information, chromosome homologues to human chromosome 13, human associations with HSA 13, chromosome type if available, references and methods from which we obtained the data, such as CP, RP, Z-F, and SA (see **Table 2**). The principal steps in the evolution of human chromosome 13 are illustrated in a graphical reconstruction of the mammal phylogenetic tree, **Figure 1**; the mammal phylogenetic tree has been drawn in agreement with previous ones [16, 49], with some modifications, and was created using Mesquite v.2.75 [50]. Among mammals, three major groups are distinguishable: monotremes (Prototheria, platypus), marsupials (Metatheria, opossum), and placental mammals (eutherian), with these last two known as Theria; among placental mammals, Afrotheria, Xenarthra, and Boroautherian are recognized, with the latter comprising Laurasiatheria and Euarchontoglires (or Supraprimates) [49]. In the mammalian phylogenetic tree are shown the orthologue blocks that correspond to human chromosome 13—in yellow—in representative eutherian species for which reciprocal chromosome painting is available; for some of them also DNA sequence alignments have been previously showed, see **Table 2** for reference. For each species are reported chromosome ideograms on which human synteny 13 is found, and on the left of the ideograms are reported the species' chromosome number and on the right HSA synteny; the black circle is the centromere. Syntenies homologues of human chromosome 13 in platypus (Monotremata) are on chromosomes 2, 10, and 20, in opossum (Metatheria) are on chromosomes 4 and 7, and in chicken (Aves) are on chromosome 1. These chromosomes are reported in box because they are representative eutherian mammal

HSA chr.	Methods	References
1	Region study by BAC mapping	[20]
	History by multidisciplinary approach	[21]
	History by BAC mapping	[2]
2	Region study by BAC mapping	[22]
	History by BAC mapping	[2]
3	Region study by BAC mapping	[23–25]
	Review	[26]
4	Region study by BAC mapping	[27]
	History by BAC mapping	[2]
	Region study by BAC mapping	[28, 29]
5	Region study by BAC mapping	[30, 31]
	review	[2]
6	History by BAC mapping	[32, 33]
7	Painting	[34]
	Review	[35]
	Region study by BAC mapping	[36]
8	Brief history by BAC mapping	[2]
9	Region study by BAC mapping	[37]
10	History by BAC mapping	[37, 38]
11	History by BAC mapping	[39]
12	Brief history by BAC mapping	[2]
13	History by BAC mapping	[40]
14	Region study by BAC mapping	[41]
15	Region study by BAC mapping	[41, 42]
16	History by BAC mapping,	[43]
	Painting	[34]
17	History by BAC mapping	[2]
18	Region study by BAC mapping,	[44]
	History by BAC mapping	[2]
19	Painting,	[34]
	Brief history by BAC mapping	[2]
20	History by BAC mapping	[45]
21	Region study by BAC mapping	[23]
	Brief history by BAC mapping	[2]
22	Brief history by BAC mapping	[2]
X	Brief history by BAC mapping	[2]
y	Region study by BAC mapping	[46]

Table 1. List of representative works, (references and methods) analyzing each human chromosome evolution and/or marker order in particular chromosomal region.

	Chromosome type	Chr.	Human association	References	Methods
Dermoptera					
<i>Galeopterus variegatus</i>	Acrocentric	13		[58]	RP
Proboscidea					
<i>Loxodonta africana</i>	Acrocentric	16,26	13, 6/13/3	[59]	CP
	Submetacentric			[12, 16]	SA
<i>Elephas maximus</i>	Acrocentric	16, 26	13, 6/13/3	[59]	CP
	Submetacentric				
Tubulidentata					
<i>Orycteropus afer</i>	Submetacentric	1	19/16/13/2/8/4	[59, 60]	CP SA
Afrosoricida					
<i>Chrysochloris asiatica</i>	Metacentric	8	13/18	[61, 60]	RP SA
Macroscelidea					
<i>Elephantulus rupestris</i>	Submetacentric	2	13/3/21/5	[61]	CP
<i>Elephantulus edwardii</i>				[60]	SA
<i>Macroscidelis proboscideus</i>	Submetacentric	2	13/3/21/5	[53]	CP
Sirenia					
<i>Trichechus manatus</i>	Metacentric	19	13/3	[62]	CP
Eulipotyphla					
<i>Sorex araneus</i>	Metacentric	bc	9/5/2/13/8/7	[16, 63]	CP, SA
<i>Blarinella griselda</i>	Submetacentric	3	13/10/13/4/5	[63]	CP
<i>Neotetracus sinensis</i>	Submetacentric	3,10	13/4/20/10,	[63]	CP
	Acrocentric		1/13/10/12/22		
<i>Hemiechinus auritus</i>				[64]	CP
<i>Talpa europaea</i>	Metacentric	6	2/13	[65]	CP
Cingulata					
<i>Dasypus novemcinctus</i>	Submetacentric	19		[66]	CP
Pilosa					
<i>Choloepus didactylus</i>	Acrocentric	17		[64]	CP
<i>Coniochaeta hoffmannii</i>	Acrocentric	12		[66]	CP
<i>Tamandua tetradactyla</i>	Metacentric	4, (2*)	13/1	[64, *66]	CP
<i>Bradypus torquatus</i>	Acrocentric	12		[67]	CP
<i>Bradypus variegatus</i>	Acrocentric	17		[67]	CP
Carnivora					
<i>Mustela putorius</i>				[68]	CP

	Chromosome type	Chr.	Human association	References	Methods
<i>Vulpes vulpes</i>	Submetacentrics	6,9	13/14, 2/8/13/3/19	[69]	RP
<i>Canis lupus familiaris</i>	Acrocentrics	(25*) 22, 28		[*70]	RP
				[69]	CP
				[71, 72]	Z-F
				[16]	SA
<i>Felis silvestris catus</i>	Acrocentric	A1		[69]	CP
				[12, 13, 51]	SA
<i>Mephitis mephitis</i>	Submetacentric	19		[73]	CP
<i>Procyon lotor</i>	Metacentric	3	13/2	[73]	CP
Perissodactyla					
<i>Equus caballus</i>	Acrocentric	17		[74]	RP
				[13, 16]	SA
				[19]	Z-F
				[40]	BAC
<i>Equus asinus</i>		11		[19]	Z-F
<i>Equus burchelli</i>	Submetacentric	6q	13/9	[19]	RP
					Z-F
<i>Equus grevyi</i>		6q	13/9	[19]	Z-F
<i>Equus zebra hartmannae</i>		15		[19]	Z-F
<i>Equus hemionus onager</i>		5q	12/13/22	[19]	Z-F
<i>Equus przewalskii</i>		16		[19]	Z-F
<i>Diceros bicornis</i>	Acrocentric	10		[19]	Z-F
<i>Ceratotherium simum</i>		10		[19]	Z-F
<i>Tapirus bairdii</i>		1		[19]	Z-F
<i>Tapirus indicus</i>	Acrocentric	18		[19]	Z-F
<i>Tapirus pinchaque</i>		13		[19]	Z-F
<i>Tapirus terrestris</i>		8		[19]	Z-F
<i>Hemiechinus auritus</i>	Submetacentrics	5q,6	5/13, 2/22/12/13/12	[64]	CP
Pholidota					
<i>Manis javanica</i>	Submetacentric	1,9q	13/5/2p, 18/13	[64]	CP
	Metacentric			[75]	CP
<i>Manis pentadactyla</i>	Submetacentric	1q, 17	13/5/2, 13	[75]	CP
	Acrocentric				
Cetartiodactyla					
<i>Bos taurus</i>	Acrocentric	12		[12, 16]	SA
				[76]	RP

	Chromosome type	Chr.	Human association	References	Methods
<i>Sus scrofa</i>	Metacentric	11		[12, 16] [76]	SA RP
<i>Camelus dromedarius</i>	Metacentric	14		[76]	RP
<i>Globicephala melas</i>	Metacentric	15		[77]	Z-F
<i>Hippopotamus amphibious</i>	Metacentric	15		[77]	Z-F
<i>Giraffa camelopardalis</i>	Metacentric	12	14/15/13	[77]	Z-F
<i>Okapia johnstoni</i>	Acrocentric	11		[77]	Z-F
<i>Moschus moschiferus</i>	Acrocentric	17		[77]	Z-F
Lagomorpha					
<i>Oryctolagus cuniculus</i>	Submetacentric	8	13/12	[78] [51]	RP SA
Rodentia					
<i>Mus musculus</i>		3,5,8,14,14		[13] [79] [16]	SA SA SA
<i>Rattus norvegicus</i>		2,12,15,15,16		[13] [16]	SA SA
<i>Sciurus carolinensis</i>	Submetacentric	6	10/13	[80] [81]	RP RP
<i>Petaurista albiventer</i>	Metacentric	11	10/13	[81]	CP
<i>Tamias sibiricus</i>	Metacentric	10	10/13	[81]	CP
<i>Castor fibre</i>	Submetacentric	4	8/13	[79]	CP
<i>Pedetes capensis</i>	Submetacentric	6	13/12/22	[79]	CP
<i>Sicista betulina</i>	Metacentric, Submetacentric	1,9	13/4/10/11/9/10, 3/6/313/19	[79]	CP
Chiroptera					
<i>Eonycteris spelaea</i>	Submetacentric	E11	13/4/8/13	[82]	CP
<i>Rhinolophus mehelyi</i>	Acrocentric	R6	13/4/8/13	[82]	CP
<i>Hipposideros larvatus</i>	Metacentric	H1	13/3/21	[82, 83]	CP
<i>Mormopterus planiceps</i>	Metacentric	M7	13/18	[82]	CP
<i>Myotis myotis</i>	Metacentric	V5/6	4/8/13/12/22	[82]	CP
<i>Aselliscus stoliczkanus</i>	Metacentric	1	22/12/13/4/8/13	[83]	CP
<i>Megaderma spasma</i>	Metacentric	12	20/13/8b/4c	[84]	CP
<i>Taphozous melanopogon</i>	Submetacentric	1	4c/8b/13/16b/7c/5a	[84]	CP

	Chromosome type	Chr.	Human association	References	Methods
Primates					
Strepsirrhini					
<i>Avahi laniger</i>		12		[85]	CP
<i>Daubentonia madagascariensis</i>		8p	10/13	[85]	CP
<i>Eulemur fulvus</i>		12		[85]	CP
<i>Haplemur griseus griseus</i>		15		[85]	CP
<i>Indri indri</i>	Submetacentric	3p	13/17	[85]	CP
<i>Lemur catta</i>	Acrocentric	13		[85, 86]	BAC CP
<i>Lepilemur ankaranensis</i>		14		[87]	CP
<i>Lepilemur dorsalis</i>		6p		[85, 87]	CP
<i>Lepilemur edwardsi</i>		6p		[87]	CP
<i>Lepilemur leucopus</i>		1q ter		[87]	CP
<i>Lepilemur microdon</i>		5p		[87]	CP
<i>Lepilemur mittermeieri</i>		7p		[87]	CP
<i>Lepilemur mustelinus</i>		8 ter		[87, 85]	CP
<i>Lepilemur jamesi</i>		5q ter		[87]	CP
<i>Lepilemur ruficaudatus</i>		5q prox		[85, 87]	CP
<i>Lepilemur septentrionalis</i>		14		[85, 87]	CP
<i>Microcebus murinus</i>	Submetacentric	13		[85, 87]	CP
<i>Propithecus verreauxi</i>		6q	5/13	[85]	CP
<i>Otolemur crassicaudatus</i>	Acrocentric	14		[88]	CP
<i>Galago moholi</i>	Metacentric	5	13/16/12	[88]	CP
<i>Otolemur garnettii</i>	Submetacentric	14		[89]	RP
<i>Nycticebus coucang</i>	Submetacentric	18 17		[89, 90]	RP CP
Platyrrhini					
<i>Alouatta belzebul</i>	Acrocentric	14		[91]	CP
<i>Alouatta caraya</i>	Acrocentric	15 (20*)		[92, *93]	CP
<i>Alouatta guariba guariba</i>	Acrocentric	14		[93]	CP
<i>Alouatta seniculus arctoidea</i>		16		[91]	CP
<i>Alouatta seniculus macconnelli</i>	Submetacentric	4q	13/19	[92]	CP
<i>Alouatta seniculus sara</i>		12		[91]	CP

	Chromosome type	Chr.	Human association	References	Methods
<i>Aotus lemurinus griseimembra</i>	Acrocentric	17		[93, 94]	CP
<i>Aotus nancymaae</i>	Acrocentric	19		[95]	CP
<i>Ateles geoffroyi</i>				[96]	CP
<i>Ateles belzebuth hybridus</i>	Acrocentric	12		[97]	CP
<i>Ateles belzebuth marginatus</i>	Submetacentric	12		[98]	CP
<i>Ateles paniscus paniscus</i>	Metacentric	4	13a/13b/3c/7b/1a2	[98]	CP
<i>Brachyteles arachnoides</i>	Acrocentric	20		[98]	CP
<i>Callicebus donacophilus pallescens</i>	Acrocentric	15		[99]	CP
<i>Callicebus lugens</i>	Submetacentric	1	1/13–12/13	[100]	CP
<i>Callicebus moloch</i>	Acrocentric	21		[101]	CP
<i>Callicebus cupreus</i>	Submetacentric Acrocentric	7,17	3/21/13, 13/17	[102]	CP
<i>Callimico goeldii</i>	Acrocentrics	19,17	13/9/22, 13/17	[18, 103]	CP RP
<i>Callithrix argentata</i>	Submetacentrics	2,1	13/9/22, 20/17/13	[18, 103]	CP RP
<i>Callithrix jacchus</i>	Submetacentrics	1,5	13/9/22, 20/17/13	[18, 103]	CP RP
<i>Cebuella pygmaea</i>	Submetacentrics	1,4	13/9/22,20/17/13	[18, 103]	CP
<i>Saguinus oedipus</i>	Submetacentrics	1,2	9/13/22,20/17/13	[18, 103]	CP
<i>Cebus apella (Sapajus)</i>	Acrocentric	17		[104, 105]	CP Z-F
<i>Sapajus a. paraguayanus</i>	Acrocentric	17		[105]	Z-F
<i>Sapajus A. robustus</i>	Acrocentric	17		[105]	Z-F
<i>Cebus capucinus</i>	Acrocentric	11		[105]	CP
<i>Cebus nigrivittatus</i>	Acrocentric	17		[97]	CP
<i>Chiropotes israelita</i>	Acrocentric	15		[95]	CP
<i>Chiropotes utahicki</i>	Acrocentric	15		[95]	CP
<i>Lagothrix lagotricha</i>	Submetacentric	8		[106]	CP
<i>Leontopithecus chrysomelas</i>	Submetacentrics	1,2	9/13/22,13/17/20	[107]	CP
<i>Pithecia irrorata</i>	Submetacentric	8	22/13	[108]	CP
<i>Cacajao calvus rubicundus</i>	Acrocentric	13		[108]	CP
<i>Saimiri sciureus</i>	Acrocentric	16		[18, 101]	CP

	Chromosome type	Chr.	Human association	References	Methods
Catarrhini					
<i>Chlorocebus aethiops</i>	Metacentric	3		[109]	CP
<i>Cercopithecus erythrogaster</i>	Submetacentric	12		[110]	Z-F
<i>Cercopithecus neglectus</i>	Metacentric	19		[111]	RP
<i>Cercopithecus stampflii</i>	Submetacentric	13		[110]	Z-F
<i>Presbytis cristata</i>	Metacentric	19		[112]	CP
<i>Colobus guereza</i>	Metacentric	19		[113]	CP
<i>Erythrocebus patas</i>	Submetacentric	15		[111]	RP
<i>Hylobates concolor</i>	Metacentrics	5,9	1/13; 1/4/10/13	[114]	CP
<i>Hylobates klossii</i>		4q	3/13	[115]	CP
<i>Hylobates lar</i>	Metacentric	4q	3/13	[17]	CP
<i>Hylobates moloch</i>		4q	3/13	[115]	CP
<i>Macaca fuscata</i>	Submetacentric	16		[116]	CP
<i>Nasalis larvatus</i>	Metacentric	15		[117]	CP
<i>Pygathrix nemaeus</i>	Submetacentric	17		[118]	CP
<i>Semnopithecus francoisi</i>	Metacentric	9		[119]	CP
<i>Semnopithecus phayrei</i>	Metacentric	9		[115]	CP
<i>Symphalangus syndactylus</i>		15		[17]	CP
<i>Pongo pygmaeus</i>	Acrocentric	14		[17]	CP
<i>Gorilla gorilla</i>	Acrocentric	14		[17]	CP
<i>Pan troglodytes</i>	Acrocentric	14		[17]	CP
Scandentia					
<i>Tupaia belangeri</i>	Acrocentric	17		[120]	CP
<i>Tupaia minor</i>	Acrocentric	16		[121]	CP
Galliformes					
<i>Gallus gallus</i>		1		[51, 52]	SA
Monotremata					
<i>Ornithorhynchus anatinus</i>	Submetacentric	2,10,20		[51]	SA
	Metacentrics				
Didelphimorphia					
<i>Monodelphis domestica</i>	Submetacentrics	4,7		[51, 52]	SA

Table 2. List of species analyzed by chromosomal painting (CP or reciprocal P) and/or sequence alignments (SA) and the references used. For each species is reported the human chromosome 13 homologous and eventually, if present other human associations.

outgroups and data come just from sequence alignments. When HSA 13 synteny, in yellow, is rearranged with just few human syntenies, these are represented in different colours and are reported on the right of the ideogram (e.g., in Indri chromosome 3, synteny 13 is fused

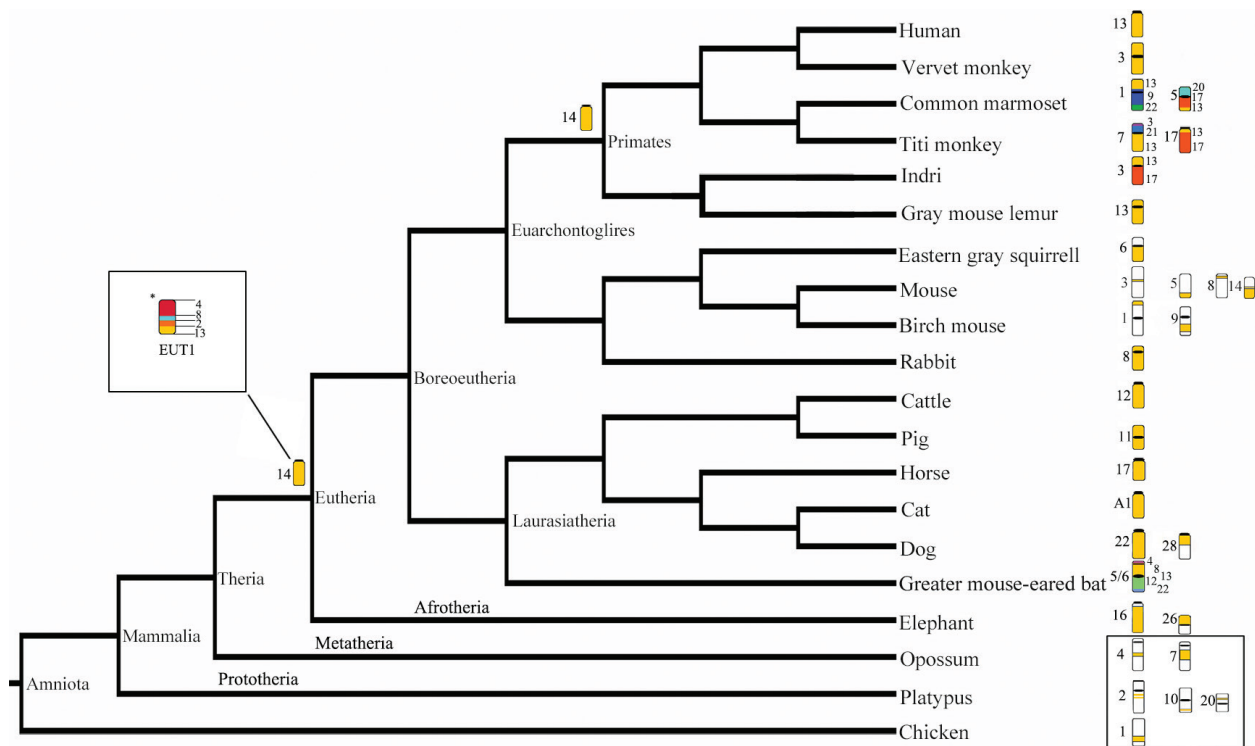


Figure 1. The mammalian phylogenetic tree showing the orthologue blocks that correspond to human chromosome 13—in yellow—in representative eutherian species for which reciprocal chromosome painting is available. For some species also DNA sequence alignments have been previously showed, see **Table 2** for citation; in the tree, it is reported the ancestral synteny 13 form described by painting data analysis and in the box the eutherian ancestral chromosome 13 alternative reconstruction obtained through sequence data* [17]. The platypus (Monotremata), opossum (Metatheria) and chicken (Aves) chromosomes homologues are reported in the box to the low right; these last species are representative outgroups. Different colours represent HSA human synteny which are reported on the right of the ideogram; white region represents parts of chromosomes covered by many different human synteny; on the left of the ideogram are reported the species' chromosome number of the 13 human homologues; the black circle is the centromere.

with synteny 17 in red), whereas when HSA 13, in yellow, is rearranged with many human synteny, these are represented by white segments for logistic issue (e.g., on chicken chromosome 1). Through painting and sequence analysis in mammals, human chromosome 13 has been previously shown to be conserved, with some exceptions (**Table 2**, **Figure 1**). Indeed, the homologues to human chromosome 13 are found as single conserved chromosomes in most representative mammalian orders analysed by chromosome painting, for example in Dermoptera, Pilosa, Carnivori (cat—*Felis silvestris catus* ch A1), Lagomorpha (rabbit—*Oryctolagus cuniculus* ch 8), Perissodactyla (horse—*Equus caballus* ch 17), and Cetartiodactyla (cattle—*Bos tauros* ch 12 and pig—*Sus scrofa* ch 11; in pig, the synteny is metacentric due to a new centromere formation). Human synteny 13 has gone to many rearrangements such as translocation and fission in other different groups; indeed, it is associated with one or more human synteny due to translocation, as in Tubulidentata, Afrosoricida, Eulipotyphla, Macroscelidea, Sirenia, Pholidota, Chiroptera (**Table 2**). For example, among Chiroptera in Greater mouse-eared bat, on *Myotis myotis* ch 5/6 is present human synteny 13 associated with many other human synteny (8 lightgreen/4 bordoux/13 yellow/12 green/22 darkgreen) and among Rodentia in eastern grey squirrel, *Sciurus carolinensis* ch 6, human synteny 13 in yellow is associated with other human synteny (reported in white in **Figure 1**). Furthermore, human synteny 13 is fragmented into two segments or into many segments and associated

with other HSA syntenies, for example in Carnivori (*Canis*—*Canis lupus familiaris* ch 22, 28), in Proboscidea (elephant—*Loxodonta Africana* ch 16, 26), and in Rodentia species such as birch mouse (*Sicista betulina* ch 1, 9; in these last species, many other human syntenic associations are reported in white segments for logistic concern in **Figure 1**).

Through genome assembly analysis (alignments of sequences, SA), chromosome 13 has also been shown to be conserved in many mammals such as pigs, horses, and cats [13], very rearranged in mice (*Mus musculus* ch 3, 5, 8, 14) [14] and fragmented in platypus (*Ornithorhynchus anatinus* ch 2, 10, 20) [51]; moreover, it has also been shown to be present in the outgroups Opossum (*Monodelphis domestica* ch 4, 7) and chicken (*Gallus gallus* ch 1) [52] (**Table 2, Figure 1**). More recently, researchers analysing more than 19 placental mammals have hypothesised that the eutherian homologue 13 ancestor was fused with other human syntenies (HSA 4, and parts of HSA 2 and 8) [16]. This alternative reconstruction obtained through sequence data (in **Figure 1** reported in the box*) see synteny 13 on EUT ch 1 associated with other HSA syntenies (2 orange/8 lightgreen/4 bordoux) according with previous sequence alignments work [17]. Part of this human associations (13/2/8/4) involving human synteny 13 is found through painting just in Greater mouse-eared bat ch 5/6, HSA syntenies 4/8/13/12/22, and for this reason, the alternative reconstruction do not find support through painting. Thus, the two reconstructions, by painting and by sequence analysis, regarding the ancestral synteny 13 in eutherian are not in agreement. Better analysis is needed in order to clarify this complex origin. The main issue to be considered to shed light on this issue is the use of appropriate outgroups in the reconstruction of the ancestral eutherian chromosome forms and the incomplete set of taxa analysed. Indeed, the lack of comparative chromosome painting between eutherians and other mammals, such as monotreme and marsupials, and on the other hand the lack of data on many genomes do not permit an exact reconstruction [16, 53].

Human chromosome 13 has also been analysed by mapping BAC probes onto representative Mammalian orders [40]; this work has especially focused attention on the history of this chromosome, with particular focus on intrachromosomal rearrangements and the potential relationships between evolutionarily new centromeres (ENCs) and neocentromeres occurring in clinical cases. Indeed, it has been hypothesised that neocentromere formation, a typical event in many tumours, could occur in correspondence to ENC position arising during evolution [54]. BAC mapping has permitted the study of small intrachromosomal rearrangements along the human 13 homologues and the identification of the occurrence of new evolutionary centromeres. Among mammals, evolutionary centromere repositioning on HSA 13 homologues have been shown in pigs and many primates such as for example on *Lagothrix lagotricha* chromosome 8 [40]; furthermore, a small inversion is common in nonprimate mammals [3, 40].

Although human chromosome 13 has been previously shown to be conserved, when compared to ancestral primate chromosomes, it shows some degree of rearrangements in certain primate taxa. Conflicting interpretations of classical banding data on human and great ape chromosome 13 have been published [1, 55, 56]. Among Hominoids, humans, chimpanzees, and orangutans share the same acrocentric form from which the gorillas' differs by only a small paracentric inversion [57]. Among Strepsirrhini, it is a single conserved chromosome as seen for example in grey mouse lemur (*Microcebus murinus* ch 13); however, in this species, synteny 13 is metacentric presumably due to an inversion or alternatively for the occurrence of a new centromere. Synteny 13 has gone to different rearrangements in other species such as, for example, in indri (*Indri indri* ch 3), where it is fused with synteny 17 in red (**Figure 1**).

Among Catarrhines (Old World monkeys), the HSA 13 homologues differ in the presence of new centromeres, for example Vervet monkey (*Chlorocebus aethiops*); the *Chlorocebus* chromosome 3 are, indeed, metacentric if compared with the acrocentric human form (**Figure 1**).

Even if human chromosome 13 is presumably conserved in the ancestors of platyrrhines, HSA 13 homologue has gone into many rearrangements in New World monkeys; indeed, synteny 13 has gone to fission and subsequent translocation with other HSA syntenies in Common marmosets (*Callithrix jacchus*), resulting in chromosome 1 and 5 (covered, respectively, by HSA 13 yellow/9 blue/22 darkgreen and 13 yellow/17 red/20 lightgreen), and in Titi monkeys (*Callicebus cupreus*) resulting in ch 7 and 17 (covered, respectively, by HSA 3 fuxia/21 lightblue/13 yellow and 13 yellow/17 red; **Figure 1**). Furthermore, some intrachromosomal rearrangements, such as inversions and new centromeres, have been shown by BAC in other Platyrrhini [40].

3. Conclusion

Classic cytogenetics, using banding, and molecular cytogenetics, using painting or other mapping probes such as BAC, are useful methods for reconstructing human chromosome history in a comparative approach with mammals. Although human chromosome 13 has previously been shown to be conserved in mammals, it is less conserved than previously claimed; indeed, some interchromosomal rearrangements have been demonstrated through painting, and intrachromosomal rearrangements have been shown by BAC mapping in various taxa; for this reason, further analysis is needed. Furthermore, the ancestral eutherian form has yet to be elucidated, as contrasting results continue to be shown through painting and sequence data comparison.

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Conflict of interest

We have no conflicts of interest.

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References

- [1] Dutrillaux B. Chromosomal evolution in primates: Tentative phylogeny from *Microcebus murinus* (Prosimian) to man. *Human Genetics*. 1979;**48**:251-314
- [2] Stanyon R, Rocchi M, Capozzi O, Roberto R, Misceo D, Ventura M, et al. Primate chromosome evolution: Ancestral karyotypes, marker order and neocentromeres. *Chromosome Research*. 2008:17-39
- [3] Rocchi M, Archidiacono N, Schempp W, Capozzi O, Stanyon R. Centromere repositioning in mammals. *Heredity*. 2012;**108**(1):59-67
- [4] Dumas F, Mazzoleni S. Neotropical primate evolution and phylogenetic reconstruction using chromosomal data. *The Italian Journal of Zoology*. 2017;**84**(1):1-18
- [5] Sineo L, Dumas F, Vitturi R, Picone B, Privitera O, Stanyon R. Williams-Beuren mapping in *Callithrix argentata*, *Callicebus cupreus* and *Alouatta caraya* indicates different patterns of chromosomal rearrangements in neotropical primates. *Journal of Zoological Systematics and Evolutionary Research*. 2007;**45**(4):366-371
- [6] Picone B, Dumas F, Stanyon R, Lannino A, Bigoni F, Privitera O, et al. Exploring evolution in Ceboidea (Platyrrhini, primates) by Williams-Beuren probe (HSA 7q11.23) chromosome mapping. *Folia Primatologica*. 2008;**79**(5):417-427
- [7] Dumas F, Sineo L, Ishida T. Taxonomic identification of *Aotus* (Platyrrhinae) through cytogenetics | Identificazione tassonomica di *Aotus* (Platyrrhinae) mediante la citogenetica. *Journal of Biological Research*. 2015;**88**(1):65-66
- [8] Dumas F, Cuttaia H, Sineo L. Chromosomal distribution of interstitial telomeric sequences in nine neotropical primates (Platyrrhini): Possible implications in evolution and phylogeny. *Journal of Zoological Systematics and Evolutionary Research*. 2016;**54**(3):226-236
- [9] Mazzoleni S, Schillaci O, Sineo L, Dumas F. Distribution of interstitial telomeric sequences in primates and the pygmy tree shrew (Scandentia). *Cytogenetic and Genome Research*. 2017;**151**(3):141-150
- [10] Mazzoleni S, Rovatsos M, Schillaci O, Dumas F. Cytogenetics evolutionary insight on localization of 18S, 28S rDNA genes on homologous chromosomes in Primates genomes. *Comparative Cytogenetics*. 2018;**12**(1):27-40
- [11] Hrubá M, Dvorák P, Weberová L, Subrt I, Hrubá M, Dvorák P, et al. Independent coexistence of clones with 13q14 deletion at reciprocal translocation breakpoint and 13q14 interstitial deletion in chronic lymphocytic leukemia. *Leukemia & Lymphoma*. 2012;**53**(10):2054-2062
- [12] Froenicke L. Origins of primate chromosomes—As delineated by Zoo-FISH and alignments of human and mouse draft genome sequences. *Cytogenetic and Genome Research*. 2005;**108**:122-138

- [13] Murphy WJ, Larkin DM, Der WAE, Bourque G, Tesler G, Auvil L, et al. Dynamics of mammalian chromosome evolution inferred from multispecies comparative maps. *Science*. 2005;**309**(5734):613-617
- [14] Ma J, Zhang L, Suh BB, Raney BJ, Burhans RC, Kent WJ, et al. Reconstructing contiguous regions of an ancestral genome. *Genome Research*. 2006;**16**(12):1557-1565
- [15] Robinson TJ, Ruiz-herrera A, Froenicke L. Dissecting the mammalian genome—New insights into chromosomal evolution. *Trends in Genetics*. 2006;**22**(6):297-301
- [16] Kim J, Farré M, Auvil L, Capitanu B, Larkin DM, Ma J, et al. Reconstruction and evolutionary history of eutherian chromosomes. *PNAS*. 2017;**114**(27):E5379-E5388
- [17] Jauch A, Wienberg J, Stanyon R, Arnoldt N, Tofanelli S, Ishidai T, et al. Reconstruction of genomic rearrangements in great apes and gibbons by chromosome painting. *PNAS*. 1992;**89**:8611-8615
- [18] Dumas F, Stanyon R, Sineo L, Stone G, Bigoni F. Phylogenomics of species from four genera of New World monkeys by flow sorting and reciprocal chromosome painting. *BMC Evolutionary Biology*. 2007;**7**(Suppl 2):S11
- [19] Trifonov VA, Stanyon R, Nesterenko AI, Fu B, Perelman PL, O'Brien PCM, et al. Multi-directional cross-species painting illuminates the history of karyotypic evolution in Perissodactyla. *Chromosome Research*. 2008;**16**(1):89-107
- [20] Weise A, Starke H, Mrasek K, Claussen U, Liehr T. New insights into the evolution of chromosome 1. *Cytogenetic and Genome Research*. 2005;**108**:217-222
- [21] Murphy WJ, Froenicke L, O'Brien SJ, Stanyon R. The origin of human chromosome 1 and its homologs in placental mammals. *Genome Research*. 2003;**13**(8):1880-1888
- [22] Fan Y, Linardopoulou E, Friedman C, Williams E, Trask BJ. Genomic structure and evolution of the ancestral chromosome fusion site in 2q13-2q14.1 and paralogous regions on other human chromosomes. *Genome Research*. 2002;**12**(11):1651-1662
- [23] Müller S, Stanyon R, Finelli P, Archidiacono N, Wienberg J. Molecular cytogenetic dissection of human chromosomes 3 and 21 evolution. *PNAS*. 2000;**97**(1):206-211
- [24] Tsend-Ayush E, Grützner F, Yue Y, Grossmann B, Hänsel U, Sudbrak R, et al. Plasticity of human chromosome 3 during primate evolution. *Genomics*. 2004;**83**(2):193-202
- [25] Yue Y, Grossmann B, Tsend-ayush E, Grützner F, Yang F, Haaf T. Genomic structure and paralogous regions of the inversion breakpoint occurring between human chromosome 3p12.3 and orangutan chromosome. *Cytogenetic and Genome Research*. 2005;**108**(1-3):98-105
- [26] Ruiz-Herrera A, Robinson TJ. Evolutionary plasticity and cancer breakpoints in human chromosome 3. *BioEssays*. 2008;**30**(11-12):1126-1137
- [27] Marzella R, Viggiano L, Miolla V, Storlazzi CT, Ricco A, Gentile E, et al. Molecular cytogenetic resources for chromosome 4 and comparative analysis of phylogenetic chromosome IV in great apes. *Genomics*. 2000;**63**(3):307-313

- [28] Dumas F, Sineo L. Chromosomal dynamics in platyrrhinae by mapping BACs probes. *Journal of Biological Research*. 2012;**LXXXV**:299-301
- [29] Dumas F, Sineo L. The evolution of human synteny 4 by mapping sub-chromosomal specific probes in Primates. *Caryologia*. 2014;**67**(4):281-291
- [30] Marzella R, Viggiano L, Ricco AS, Tanzariello A, Fratello A, Archidiacono N, et al. A panel of radiation hybrids and YAC clones specific for human chromosome. *Cytogenetics and Cell Genetics*. 1997;**77**(3-4):232-237
- [31] Szamalek JM, Goidts V, Chuzhanova N, Hameister H, Cooper DN, Keherer-Sawatzki H. Molecular characterization of the pericentric inversion that distinguishes human chromosome 5 from the homologous chimpanzee chromosome. *Human Genetics*. 2005;**117**(2-3):168-176
- [32] Capozzi O, Purgato S, Addabbo PD, Archidiacono N, Battaglia P, Spada F, et al. Evolutionary descent of a human chromosome 6 neocentromere: A jump back to 17 million years ago. *Genome Research*. 2009;**19**(5):778-784
- [33] Eder V, Ventura M, Ianigro M, Teti M, Rocchi M, Archidiacono N. Chromosome 6 phylogeny in primates and centromere repositioning. *Molecular Biology and Evolution*. 2003;**20**(9):1506-1512
- [34] Richard F, Lombard M, Dutrillaux B. Phylogenetic origin of human chromosomes 7, 16, and 19 and their homologs in placental mammals. *Genome Research*. 2000;**10**(5):644-651
- [35] Müller S, Finelli P, Neusser M, Wienberg J. The evolutionary history of human chromosome 7. *Genomics*. 2004;**84**:458-467
- [36] Dumas F, Sineo L. Chromosomal dynamics in Cercopithecini studied by Williams-Beuren probe mapping. *Caryologia*. 2010;**63**(4):435-442
- [37] Montefalcone G, Tempesta S, Rocchi M, Archidiacono N. Centromere repositioning. *Genome Research*. 1999;**9**(12):1184-1188
- [38] Carbone L, Ventura M, Tempesta S. Evolutionary history of chromosome 10 in primates. *Chromosoma*. 2002:267-272
- [39] Cardone MF, Lomiento M, Teti MG, Misceo D, Roberto R, Capozzi O, et al. Evolutionary history of chromosome 11 featuring four distinct centromere repositioning events in Catarrhini. *Genomics*. 2007;**90**(1):35-43
- [40] Cardone MF, Alonso A, Pazienza M, Ventura M, Montemurro G, Carbone L, et al. Independent centromere formation in a capricious, gene-free domain of chromosome 13q21 in Old World monkeys and pigs. *Genome Biology*. 2006;**7**(10):R91
- [41] Ventura M, Mudge JM, Palumbo V, Burn S, Blennow E, Pierluigi M, Giorda R, et al. Neocentromeres in 15q24Y26 map to duplicons which flanked an ancestral centromere in 15q25. *Genome Research*. 2003;**13**(9):2059-2068
- [42] Locke DP, Jiang Z, Pertz LM, Misceo D, Archidiacono N, Eichler EE. Molecular evolution of the human chromosome 15 pericentromeric region. *Genome Biology*. 2005;**108**:73-82

- [43] Misceo D, Ventura M, Eder V, Rocchi M, Archidiacono N. Human chromosome 16 conservation in primates. *Chromosome Research*. 2003;**11**(4):323-326
- [44] Goits V, Szamalek JM, Hameister H, Kehrer-Sawatzki H. Segmental duplication associated with the human-specific inversion of chromosome 18: A further example of the impact of segmental duplications on karyotype and genome evolution in primates. *Human Genetics*. 2004:116-122
- [45] Misceo D, Cardone MF, Carbone L, D'Addabbo P, de Jong PJ, Rocchi M, et al. Evolutionary history of chromosome 20. *Molecular Biology and Evolution*. 2005;**22**(2):360-366
- [46] Wimmer R, Kirsch S, Rappold GA, Schempp W. The evolution of the azoospermia factor region AZFa in higher primates. *Cytogenetic and Genome Research*. 2005;**108**:211-216
- [47] Dunham A, Matthews LH, Burton J, Ashurst JL, Howe KL, Ashcroft KJ, et al. The DNA sequence and analysis of human chromosome 13. *Nature*. 2004;**428**:522-528
- [48] Bailey JA, Gu Z, Clark RA, Reinert K, Samonte RV, Schwartz S, et al. Recent segmental duplications in the human genome. *Science*. 2002;**297**:1003-1007
- [49] Murphy WJ, Eizirik E, Johnson WE, Zhang YP, Ryder OA, O'Brien SJ. Molecular phylogenetics and the origins of placental mammals. *Nature*. 2001;**409**(6820):614-618
- [50] Maddison WP, Maddison DRV. Mesquite: A modular system for evolutionary analysis. 2008;**11**:1103-1118. <http://mesquiteproject>
- [51] Graphodatsky A, Ferguson-Smith MA, Stanyon R. A short introduction to cytogenetic studies in mammals with reference to the present volume. *Cytogenetic and Genome Research*. 2012;**137**(2-4):83-96
- [52] Robinson TJ, Ruiz-herrera A. Defining the ancestral eutherian karyotype: A cladistic interpretation of chromosome painting and genome sequence assembly data. *Chromosome Research*. 2008;**16**:1133-1141
- [53] Svartman M, Stone G, Page JE, Stanyon R. A chromosome painting test of the basal Eutherian karyotype. *Chromosome Research*. 2004;**12**:45-53
- [54] Alonso A, Mahmood R, Li S, Cheung F, Yoda K, Warburton PE. Genomic microarray analysis reveals distinct locations for the CENP-A binding domains in three human chromosome 13q32 neocentromeres. *Human Molecular Genetics*. 2003;**12**(20):2711-2721
- [55] Clemente IC, Ponsa M, Garcia M, Egozcue J. Evolution of the Simiiformes and the phylogeny of human chromosomes. *Human Genetics*. 1990;**84**:493-506
- [56] Yunis JJ, Prakash O. The origin of man: A chromosomal pictorial legacy. *Science*. 1982;**215**(4539):1525-1530
- [57] Muller S, Wienberg J. "Bar-coding" primate chromosomes: molecular cytogenetic screening for the ancestral hominoid karyotype. 2001;**109**:85-94
- [58] Nie W, Fu B, O'Brien PCM, Wang J, Su W, Tanomtong A, et al. Flying lemurs—The "flying tree shrews"? Molecular cytogenetic evidence for a Scandentia-Dermoptera sister clade. *BMC Biology*. 2008;**6**:18

- [59] Yang F, Alkalaeva EZ, Perelman PL, Pardini AT, Harrison WR, O'Brien PCM, et al. Reciprocal chromosome painting among human, aardvark, and elephant (superorder Afrotheria) reveals the likely eutherian ancestral karyotype. *PNAS*. 2003;**100**:1062-1066
- [60] Ruiz-Herrera A, Robinson TJ. Chromosomal instability in Afrotheria: Fragile sites, evolutionary breakpoints and phylogenetic inference from genome sequence assemblies. *BMC Evolutionary Biology*. 2007;**7**:199
- [61] Robinson TJ, Fu B, Ferguson-Smith MA, Yang F. Cross-species chromosome painting in the golden mole and elephant-shrew: Support for the mammalian clades Afrotheria and Afroinsectiphillia but not Afroinsectivora. *The Royal Society*. 2004;**271**:1477-1484
- [62] Kellogg ME, Burkett S, Dennis TR, Stone G, Gray BA, McGuire PM, et al. Chromosome painting in the manatee supports Afrotheria and Paenungulata. *BMC Evolutionary Biology*. 2007;**7**:6
- [63] Ye J, Biltueva L, Huang L, Nie W, Wang J, Jing M, et al. Cross-species chromosome painting unveils cytogenetic signatures for the Eulipotyphla and evidence for the polyphyly of Insectivora. *Chromosome Research*. 2006;**14**(2):151-159
- [64] Yang F, Graphodatsky AS, Li T, Fu B, Dobigny G, Wang J, et al. Comparative genome maps of the pangolin, hedgehog, sloth, anteater and human revealed by cross-species chromosome painting: Further insight into the ancestral karyotype and genome evolution of eutherian mammals. *Chromosome Research*. 2006;**14**:283-296
- [65] Volleth M, Müller S. Zoo-FISH in the European mole (*Talpa europaea*) detects all ancestral Boreo-Eutherian human homologous chromosome associations. *Cytogenetic and Genome Research*. 2006;**115**:154-157
- [66] Svartman M, Stone G, Stanyon R. The ancestral Eutherian karyotype is present in Xenarthra. *PLoS Genetics*. 2006;**2**(7):1006-1011
- [67] Azevedo NF, Svartman M, Manchester A, de Moraes-Barros N, Stanyon R, Vianna-Morgante AM. Chromosome painting in three-toed sloths: A cytogenetic signature and ancestral karyotype for Xenarthra. *BMC Evolutionary Biology*. 2012;**15-21**:12-36
- [68] Cavagna P, Menotti A, Stanyon R. Genomic homology of the domestic ferret with cats and humans. *Mammalian Genome*. 2000;**11**:866-870
- [69] Yang F, O'Brien PCM, Milne BS, Graphodatsky AS, Solanky N, Trifonov V, et al. A complete comparative chromosome map for the dog, red fox, and human and its integration with canine genetic maps. *Genomics*. 1999;**62**:189-202
- [70] Breen M, Thomas R, Binns MM, Carter NP, Langford CF. Reciprocal chromosome painting reveals detailed regions of conserved synteny between the karyotypes of the domestic dog (*Canis familiaris*) and human. *Genomics*. 1999;**61**(2):145-155
- [71] Yang F, Graphodatsky AS, O'Brien PCM, Colabella A, Solanky N, Squire M, et al. Reciprocal chromosome painting illuminates the history of genome evolution of the domestic cat, dog and human. *Chromosome Research*. 2000;**8**:393-404

- [72] Graphodatsky AS, Perelman PL, Sokolovskaya NV, Beklemisheva VR, Serdukova NA, Dobigny G, et al. Phylogenomics of the dog and fox family (Canidae, Carnivora) revealed by chromosome painting. *Chromosome Research*. 2008;**16**(1):129-143
- [73] Perelman PL, Graphodatsky AS, Dragoo JW, Serdyukova NA, Stone G, Cavagna P, et al. Chromosome painting shows that skunks (Mephitidae, Carnivora) have highly rearranged karyotypes. *Chromosome Research*. 2008;**16**(8):1215-1231
- [74] Yang F, Fu B, O'Brien PCM, Nie W, Ryder OA, Ferguson Smith MA. Refined genome-wide comparative map of the domestic horse, donkey and human based on cross-species chromosome painting: Insight into the occasional fertility of mules. *Chromosome Research*. 2004;**12**:65-76
- [75] Nie W, Wang J, Su W, Wang Y, Yang F. Chromosomal rearrangements underlying karyotype differences between Chinese pangolin (*Manis pentadactyla*) and Malayan pangolin (*Manis javanica*) revealed by chromosome painting. *Chromosome Research*. 2009;**17**:321-329
- [76] Balmus G, Trifonov VA, Biltueva LS, O'Brien PCM, Alkalaeva ES, Fu B, et al. Cross species painting among camel, cattle, pig and human: Further insights into the putative Cetartiodactyla ancestral karyotype. *Chromosome Research*. 2007;**15**:499-514
- [77] Kulemzina AI, Trifonov VA, Perelman PL, Rubtsova NV, Volobuev V, Ferguson-Smith MA, et al. Cross-species chromosome painting in Cetartiodactyla: Reconstructing the karyotype evolution in key phylogenetic lineages. *Chromosome Research*. 2009;**17**(3):419-436
- [78] Korstanje R, O'Brien PCM, Yang F, Rens W, Bosma AA, van Lith HA, et al. Complete homology maps of the rabbit (*Oryctolagus cuniculus*) and human by reciprocal chromosomal painting. *Cytogenetics and Cell Genetics*. 1999;**83**:317-322
- [79] Graphodatsky AS, Yang F, Dobigny G, Romanenko SA, Biltueva LS, Perelman PL, et al. Tracking genome organization in rodents by Zoo-FISH. *Chromosome Research*. 2008;**16**(2):261-274
- [80] Stanyon R, Stone G, Garcia M, Froenicke L. Reciprocal chromosome painting shows that squirrels, unlike murid rodents, have a highly conserved genome organization. *Genomics*. 2003;**82**(2):245-249
- [81] Li T, O'Brien PCM, Biltueva L, Fu B, Wang J, Nie W, et al. Evolution of genome organizations of squirrels (Sciuridae) revealed by cross-species chromosome painting. *Chromosome Research*. 2004;**12**(4):317-335
- [82] Volleth M, Heller KG, Pfeiffer RA, Hameister H. A comparative ZOO-FISH analysis in bats elucidates the phylogenetic relationships between Megachiroptera and five microchiropteran families. *Chromosome Research*. 2002;**10**(6):477-497
- [83] Mao X, Nie W, Wang J, Su W, Ao L, Feng Q, et al. Karyotype evolution in *Rhinolophus* bats (Rhinolophidae, Chiroptera) illuminated by cross-species chromosome painting and G-banding comparison. *Chromosome Research*. 2007;**15**(7):835-847

- [84] Mao X, Nie W, Wang J, Su W, Feng Q, Wang Y, et al. Comparative cytogenetics of bats (Chiroptera): The prevalence of Robertsonian translocations limits the power of chromosomal characters in resolving interfamily phylogenetic relationships. *Chromosome Research*. 2008;**16**(1):155-170
- [85] Warter S, Hauwy M, Dutrillaux B, Rumpler Y. Application of molecular cytogenetics for chromosomal evolution of the Lemuriformes (Prosimians). *Cytogenetic and Genome Research*. 2005;**108**(1-3):197-203
- [86] Cardone MF, Ventura M, Tempesta S, Rocchi M, Archidiacono N. Analysis of chromosome conservation in *Lemur catta* studied by chromosome paints and BAC/PAC probes. *Chromosoma*. 2002;**111**(5):348-356
- [87] Rumpler Y, Warter S, Hauwy M, Fausser JL, Roos C, Zinner D. Comparing chromosomal and mitochondrial phylogenies of sportive lemurs (Genus *Lepilemur*, Primates). *Chromosome Research*. 2008;**16**(8):1143-1158
- [88] Stanyon R, Koehler U, Consigliere S. Chromosome painting reveals that galagos have highly derived karyotypes. *American Journal of Physical Anthropology*. 2002;**117**(4):319-326
- [89] Stanyon R, Dumas F, Stone G, Bigoni F. Multidirectional chromosome painting reveals a remarkable syntenic homology between the greater galagos and the slow loris. *American Journal of Primatology*. 2006;**68**:349-359
- [90] Nie W, O'Brien PCM, Fu B, Wang J, Su W, Ferguson-Smith MA, et al. Chromosome painting between human and lorisiform prosimians: Evidence for the HSA 7/16 synteny in the primate ancestral karyotype. *American Journal of Physical Anthropology*. 2006;**129**(2):250-259
- [91] Consigliere S, Stanyon R, Koehler U, Arnold N, Wienberg J. In situ hybridization (FISH) maps chromosomal homologies between *Alouatta belzebul* (Platyrrhini, Cebidae) and other primates and reveals extensive interchromosomal rearrangements between howler monkey genomes. *American Journal of Primatology*. 1998;**46**(2):119-133
- [92] De Oliveira EHC, Neusser M, Figueiredo WB, Nagamachi C, Pieczarka JC, Sbalqueiro IJ, et al. The phylogeny of howler monkeys (*Alouatta*, Platyrrhini): Reconstruction by multicolor cross-species chromosome painting. *Chromosome Research*. 2002;**10**(8):669-683
- [93] Ruiz-Herrera A, Garcia F, Aguilera M, Garcia M, Fontanals MP. Comparative chromosome painting in *Aotus* reveals a highly derived evolution. *American Journal of Primatology*. 2005;**65**(1):73-85
- [94] Stanyon R, Garofalo F, Steinberg ER, Capozzi O, Di Marco S, Nieves M, et al. Chromosome Painting in two genera of South American monkeys: Species identification, conservation, and management. *Cytogenetic and Genome Research*. 2011:1-11
- [95] Stanyon R, Bigoni F, Slaby T, Müller S, Stone G, Bonvicino CR, et al. Multi-directional chromosome painting maps homologies between species belonging to three genera of New World monkeys and humans. *Chromosoma*. 2004;**113**(6):305-315

- [96] Morescalchi MA, Schempp W, Wienberg J, Stanyon R. Mapping chromosomal homology between humans and the black-handed spider monkey by fluorescence in situ hybridization. *Chromosome Research*. 1997;5(8):527-536
- [97] García F, Ruiz-Herrera A, Egozcue J, Ponsà M, Garcia M. Chromosomal homologies between *Cebus* and *Ateles* (Primates) based on ZOO-FISH and g-banding comparisons. *American Journal of Primatology*. 2002;57(4):177-188
- [98] De Oliveira EHC, Neusser M, Pieczarka JC, Nagamachi C, Sbalqueiro IJ, Müller S. Phylogenetic inferences of Atelinae (Platyrrhini) based on multi-directional chromosome painting in *Brachyteles arachnoides*, *Ateles paniscus paniscus* and *Ateles b. marginatus*. *Cytogenetic and Genome Research*. 2005;108(1-3):183-190
- [99] Barros RMS, Nagamachi CY, Pieczarka JC, Rodrigues LRR, Neusser M, de Oliveira EH, et al. Chromosomal studies in *Callicebus donacophilus pallescens*, with classic and molecular cytogenetic approaches: Multicolour FISH using human and *Saguinus oedipus* painting probes. *Chromosome Research*. 2003;11(4):327-334
- [100] Stanyon R, Bonvicino CR, Svartman M, Seuánez HN. Chromosome painting in *Callicebus lugens*, the species with the diploid number ($2n = 16$) known in primates. *Chromosome Research*. 2003;112(4):201-206
- [101] Stanyon R, Consigliere S, Müller S, Morescalchi A, Neusser M, Wienberg J. Fluorescence in situ hybridization (FISH) maps chromosomal homologies between the dusky titi and squirrel monkey. *American Journal of Primatology*. 2000;50(2):95-107
- [102] Dumas F, Bigoni F, Stone G, Sineo L, Stanyon R. Mapping genomic rearrangements in titi monkeys by chromosome flow sorting and multidirectional in-situ hybridization. *Chromosome Research*. 2005:85-96
- [103] Neusser M, Stanyon R, Bigoni F, Wienberg J, Müller S. Molecular cytotaxonomy of New World monkeys (Platyrrhini)—Comparative analysis of five species by multi-color chromosome painting gives evidence for a classification of *Callimico goeldii* within the family of Callitrichidae. *Cytogenetics and Cell Genetics*. 2001;94:206-215
- [104] García F, Nogués C, Ponsà M, Ruiz-Herrera A, Egozcue J, Garcia Caldés M. Chromosomal homologies between humans and *Cebus apella* (Primates) revealed by ZOO-FISH. *Mammalian Genome*. 2000;11:399-401
- [105] Richard F, Lombard M, Dutrillaux B. ZOO-FISH suggests a complete homology between human and capuchin monkey (Platyrrhini) euchromatin. *Chromosome Research*. 1996;36:417-423
- [106] Stanyon R, Consigliere S, Bigoni F, Ferguson-Smith M, O'Brien PCM, Wienberg J. Reciprocal chromosome painting between a New World primate, the woolly monkey, and humans. *Chromosome Research*. 2001;9(2):97-106
- [107] Gerbault-Serreau M, Bonnet-Garnier A, Richard F, Dutrillaux B. Chromosome painting comparison of *Leontopithecus chrysomelas* (Callitrichine, Platyrrhini) with man and its phylogenetic position. *Chromosome Research*. 2004;12(7):691-701

- [108] Finotelo LFM, Amaral PJS, Pieczarka JC, de Oliveira EHC, Pissinati A, Neusser M, Müller S, Nagamachi CY. Chromosome phylogeny of the subfamily Pitheciinae (Platyrrhini, Primates) by classic cytogenetics and chromosome painting. *BMC Evolutionary Biology*. 2010;**10**:189
- [109] Finelli P, Stanyon R, Plesker R, Ferguson-Smith MA, O'Brien PCM, Wienberg J. Reciprocal chromosome painting shows that the great difference in diploid number between human and African green monkey is mostly due to non-Robertsonian fissions. *Mammalian Genome*. 1999;**10**(7):713-718
- [110] Moulin S, Gerbault-Seureau M, Dutrillaux B, Richard FA. Phylogenomics of African guenons. *Chromosome Research*. 2008;**16**:783-799
- [111] Stanyon R, Bruening R, Stone G, Shearin A, Bigoni F. Reciprocal painting between humans, De Brazza's and patas monkeys reveals a major bifurcation in the Cercopithecini phylogenetic tree. *Cytogenetic and Genome Research*. 2005;**108**(1-3):175-182
- [112] Bigoni F, Koehler U, Stanyon R, Ishida T, Wienberg J. Fluorescence in situ hybridization establishes homology between human and silvered leaf monkey chromosomes, reveals reciprocal translocations between chromosomes homologous to human Y/5, 1/9, and 6/16, and delineates an $X_1X_2Y_1Y_2/X_1X_1X_2X_2$ sex-chromosome system. *American Journal of Physical Anthropology*. 1997a;**23**:315-327
- [113] Bigoni F, Stanyon R, Koehler U, Morescalchi AM, Wienberg J. Mapping homology between human and black and white colobine monkey chromosomes by fluorescent in situ hybridization. *American Journal of Primatology*. 1997b;**42**(4):289-298
- [114] Koehler U, Bigoni F, Wienberg J, Stanyon R. Genomic reorganization in the concolor gibbon (*Hylobates concolor*) revealed by chromosome painting. *American Journal of Physical Anthropology*. 1995;**292**:287-292
- [115] Müller S, Hollatz M, Wienberg J. Chromosomal phylogeny and evolution of gibbons (Hylobatidae). *Human Genetics*. 2003;**113**(6):493-501
- [116] Wienberg J, Stanyon R, Jauch A, Cremer T. Homologies in human and *Macaca fuscata* chromosomes revealed by in situ suppression hybridization with human chromosome specific DNA libraries. *Chromosoma*. 1992;**101**:265-270
- [117] Bigoni F, Stanyon R, Wimmer R, Schempp W. Chromosome painting shows that the proboscis monkey (*Nasalis larvatus*) has a derived karyotype and is phylogenetically nested within Asian colobines. *American Journal of Primatology*. 2003;**60**(3):85-93
- [118] Bigoni F, Houck ML, Ryder OA, Wienberg J, Stanyon R. Chromosome painting shows that *Pygathrix nemaeus* has the most basal karyotype among Asian colobinae. *International Journal of Primatology*. 2004;**25**(3):679-688
- [119] Nie W, Liu R, Chen Y, Wang J, Yang F. Mapping chromosomal homologies between humans and two langurs (*Semnopithecus francoisi* and *S. phayrei*) by chromosome painting. *Chromosome Research*. 1998;**6**(6):447-453

- [120] Müller S, Stanyon R, O'Brien PCM, Ferguson-Smith MA, Plesker R, Wienberg J. Defining the ancestral karyotype of all primates by multidirectional chromosome painting between tree shrews, lemurs and humans. *Chromosoma*. 1999;**108**(6):393-400
- [121] Dumas F, Houck ML, Bigoni F, Perelman P, Romanenko SA, Stanyon R. Chromosome painting of the pygmy tree shrew shows that no derived cytogenetic traits link primates and scandentia. *Cytogenetic and Genome Research*. 2012;**136**(3):175-179

