The evolution of human synteny 4 by mapping sub-chromosomal specific probes in Primates

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Abstract

Comparative cytogenetic data concerning the ortholog to human chromosome 4 in primates shows that this chromosome is conserved between humans and non-human primates. However, the degree of conservation is not as high as previously estimated. In primates it is a large submetacentric chromosome but many exceptions are known especially in taxa characterized by a high level of chromosomal rearrangements. The rearrangements that have been visualized by chromosome painting so far, mostly interchromosomal changes, are only a fraction of the actual chromosomal changes that have occurred during evolution. Intrachromosome changes can be analyzed through classical cytogenetic approach or by mapping sub-chromosomal specific probes. In order to study human synteny 4 evolution we mapped diverse subchromosomal specific probes, on chromosomes of representative species of the main Primates taxa, with the aim to verify markers order conservation along the orthologues to human chromosome 4 allowing us the detection of possible intra-chromosomal rearrangements. The mapping of these probes permitted us to test previous cytogenetic hypothesis on human synteny 4 evolution, and to show a markers order conservation between orthologues to human synteny 4 in Catarrhini and Platyrrhini, but with a different position of the centromeres. This data permitted us to hypothesize the occurrence of a new centromeres evolution in one of the two lineages. Moreover we analysed literature data regarding HSA4 homologous in Primates with particular attention to Platyrrhini allowing us the reconstruction of the changes that synteny 4 has undergone during evolution. Lastly we highlight the value of the subchromosomal specific probes mapping approach in the detection of intrachromosomal rearrangements that can be crucial for a more refined comparative mapping and for phylogenetic reconstruction.

Keywords: human chromosome 4; chromosomal rearrangements; Platyrrhini, Phylogeny; Evolution.

Introduction

Molecular cytogenetics by chromosomal painting provides a tentative reconstruction of ancestral genomes for the major branching of Mammals trees. Starting from the proposed ancestral genome of Primates (Ferguson-Smith and Trifonov 2007; Robinson and Ruiz-Herrera 2008) it has been possible to...
reconstruct the most important steps leading to the formation of human chromosomes over the last 100 million years (Stanyon et al. 2008). However, chromosome painting gives considerable data on inter-chromosomal rearrangements (translocations) but the knowledge of intra-chromosomal rearrangements in the different lineages remains limited. This creates several problems on interpretation of results applied to phylogeny. Intrachromosomal rearrangement can be hypothesized through the study of classical cytogenetics data such as G-band patterns and can be confirmed, at the molecular level, using subchromosomal probes (Sineo et al. 2007, Dumas and Sineo 2010) obtained or by cloning DNA in vectors such as Yeast Artificial Chromosomes (YACs) and Bacterial Artificial Chromosomes (BACs) or by microdissection. This approach is a useful tool as it allows researchers the definition of markers order along chromosomes and eventually detect inversions and the occurrence of evolutionary new centromeres (Stanyon et al. 2008), which are considered important genomic structures promoting chromosomal evolution (Villasante et al. 2007). Indeed, it has been possible to appreciate that the pericentromeric regions are rich in duplicons, transpons, retroelements, all currently considered to be characteristic of “hot spots” of chromosomes in both evolution and in diseases. Evolutionary new centromeres (ENC) arise in a novel chromosomal region without any change in marker order and are accompanied by the inactivation of the old centromere (Marshall et al. 2008; Rocchi et al. 2009).

One of the most debated topics of evolutionary history involves human chromosome 4. The human synteny 4 evolution has been recently studied in Eutherian mammals by comparative karyological and genomic data analysis (Picone et al. 2010, Dumas, 2012b). In most mammals the homologues to human chromosome 4 are associated with the small arm of the human chromosome 8 (4/8p) (Richard et al. 2001; Svartman et al. 2004; Wienberg et al. 2005; Dumas et al. 2012). For this reason, and because of the 4/8 association is present in the marsupial Monodelphis domestica, (Mikkelsen et al. 2007) and the bird Gallus gallus (Murphy et al. 2005; Robinson and Herrera 2008), it has been considered as an ancestral association in the reconstruction of the ancestral karyotype of all eutherian mammals (Ferguson- Smith and Trifonov, 2007; Stanyon et al. 2008). As already demonstrated (Graphodasky et al. 2011), the 4/8 association has been subject to numerous rearrangements forming new associations with other (human) syntenies in Muridae and Canidae or it has even been diversely disrupted in Primates (Stanyon et al. 2008), Sirenia (Kellogs et al. 2007) and Proboscidea (Yang et al. 2003).

The ortholog to human synteny 4 in the ancestral primate karyotype is derived from the fission of the ancestral 4/8 association. In Primates, the HSA 4 homolog has been considered a conserved single submetacentric chromosome (Haig et al. 1999), but many exceptions are known especially in taxa characterized by a high level of chromosomal rearrangements such as Strephirrhini (Nie et al. 2006),
New Word monkeys (De Oliveira et al. 2002, 2012) Cercopithecini (Dumas and Sineo 2010; Moulin et al. 2008) and Hylobatidae (Muller et al. 2003).

In order to refine the dynamic of human synteny 4 in Primates, we hybridized a panel of sub-chromosomal specific probes, (arm probes, BACs and single locus probes) on the orthologous to human chromosome 4 in a representative group of haplorrhini species (table 1). The mapping of these probes permits us to test previous cytogenetic hypothesis on human synteny 4 evolution, and to analyse markers order and intrachromosomal rearrangements. The results, compared and associated with previously published data regarding HSA4 homologous in Primates, allowed us to propose the changes that synteny 4 has undergone during evolution, with a special focus on Platyrrhini.

Materials and methods

Following the standard protocol (Small et al. 1985) metaphases of the taxa listed in table 1, were obtained from primary cultures of lymphoblast or fibroblast cell lines and successively fixed on slides:

<table>
<thead>
<tr>
<th>Infraorder</th>
<th>Scientific name of Taxa</th>
<th>abbreviations of names</th>
<th>Common name</th>
<th>Sample Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platyrrhini</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Saimiri sciureus</em></td>
<td>SSC</td>
<td>Common squirrel monkeys</td>
<td>National Cancer Institute, United States of America</td>
</tr>
<tr>
<td></td>
<td><em>Saguinus oedipus</em></td>
<td>SOE</td>
<td>Cotton top-tamarins</td>
<td>University of Bari, Italy</td>
</tr>
<tr>
<td></td>
<td><em>Callimico goeldii</em></td>
<td>CGO</td>
<td>Goeldi’s tamarin</td>
<td>National Cancer Institute, United States of America</td>
</tr>
<tr>
<td></td>
<td><em>Cebuella pygmaea</em></td>
<td>CPY</td>
<td>Pygmy marmoset</td>
<td>National Cancer Institute, United States of America</td>
</tr>
<tr>
<td></td>
<td><em>Callithrix jacchus</em></td>
<td>CJA</td>
<td>Common marmoset white-tufted-ear</td>
<td>National Cancer Institute, United States of America</td>
</tr>
<tr>
<td></td>
<td><em>Aotus lemurinus griseimembra</em></td>
<td>ALE</td>
<td>Owl monkeys</td>
<td>Tokyo University, Japan</td>
</tr>
<tr>
<td>Catarrhini</td>
<td><em>Lagotricha lagotricha</em></td>
<td>LLA</td>
<td>Woolly monkeys</td>
<td>National Cancer Institute, United States of America</td>
</tr>
<tr>
<td></td>
<td><em>Chlorocebus aethiops</em></td>
<td>CAE</td>
<td>Grivet monkey</td>
<td>National Cancer Institute, United States of America</td>
</tr>
<tr>
<td></td>
<td><em>Erythrocebus</em></td>
<td>EPA</td>
<td>Patas monkey</td>
<td>National Cancer Institute, United States of America</td>
</tr>
</tbody>
</table>
Table 1. List of platyrrhini and catarrhini taxa analysed in the present study and samples source.

<table>
<thead>
<tr>
<th>Primates species classification</th>
<th>United States of America</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cercopithecus albogularis labiatus</td>
<td>Fort Hare University, South Africa</td>
</tr>
<tr>
<td>Macaca arctoides</td>
<td>National Cancer Institute, United States of America</td>
</tr>
<tr>
<td>Pongo p. pygmaeus</td>
<td>National Cancer Institute, United States of America</td>
</tr>
<tr>
<td>Gorilla gorilla</td>
<td>National Cancer Institute, United States of America</td>
</tr>
<tr>
<td>Pan troglodytes</td>
<td>National Cancer Institute, United States of America</td>
</tr>
</tbody>
</table>

The human BAC clones, kindly provided by Prof. M. Rocchi from Bari University, were chosen on the UCSC browser (hg18 assembly, UCSC March 2006 release) and previously used in FISH experiments on human metaphases to validate their mapping. The validated BACs were co-hybridized in FISH experiments.

Two supplementary subchromosomal specific probes commercially available have been mapped on the Primates taxa analysed: the human 4(HSA) p-arm probe (Q-BIOgene – rhodamine labeled/PlatinumBright) and the single locus probe FIP1L1-CHIC2-DDGFRA–HSA 4 q12, (Q-BIOgene – rhodamine labeled/PlatinumBright).

Fluorescence in situ hybridization (FISH) using subchromosomal probes on primates metaphases fixed on slides.

FISH with HSA, BACs probe

Metaphases fixed on slides were performed in 50% formamide (v/v), 10% dextran sulphate, 2 × SSC at 37°C, in the presence of human Cot1 DNA (Gibco-BRL). Hybridization of BACs probes on Primates Post-hybridization washing included 50% formamide, 2 × SSC at 42°C, or 50% formamide, 1 × SSC at 37°C, followed by three washes in 1 × SSC at 42°C. The chromosomes were stained with DAPI (4′,6-diamidino-2-phenylindole).
FISH with HSA 4p-arm probe

Primates metaphases fixed on slides where incubated in 2X SSC 0.5% NP-40, pH 7.0 at 37°C for 15 minutes and dehydrated in ethanol series (70%, 85%, 100%) at room temperature for 2 minutes each. Metaphases were denatured in 70% formamide/ 2X SSC, pH 7.0 at 72°C (± 2°C) for 2 minutes; dehydrated in a 4°C ethanol series (70%, 85% and 100%) for 2 minutes each. The probe was denatured at 90°C for 5-10 minutes and hybridized. Slides after hybridization where incubated overnight at 37°C in a wet chamber. After hybridization slides were washed in 1X Wash buffer (0.4X SSC/0.3% NP-40) for 2 minutes at 72°C without agitation followed by a wash of 2XSSC/0.1% Igepal for a minute at room temperature. Slides were then dehydrated in ethanol series (70%, 85%, 100%) at room temperature for 1 minutes each. On the wet slides was applied 15 μl DAPI antifade (final concentration 0.02 μg/ml ) or PI/antifade (0.3 μg/ml), and a glass cover slip.

FISH with HSA, FIP1L1-CHIC2-DDGFRA, 4p12 probe

Primates metaphases fixed on slides where incubated in 2X SSC 0.5% NP-40, pH 7.0 at 37°C for 30 minutes and a dehydrated in ethanol series (70%, 80%, 95%) at room temperature for 2 minutes each. Metaphases were denatured in 70% formamide/ 2X SSC, pH 7.0 at 72°C (± 2°C) for 2 minutes; and dehydrated in a 4°C ethanol series (70%, 80% and 95%) for 2 minutes each. The probe was denatured at 75°C for 5-10 minutes and hybridized. Slides after hybridization were incubated overnight at 37°C in a wet chamber. After hybridization slides were washed in 1X Wash buffer (0.5 X SSC/ 0.1% SDS) for 5 minutes at 65°C without agitation. On the wet slides was applied 15 μl DAPI antifade (final concentration 0.02 μg/ml) or PI/antifade (0.3 μg/ml), and a glass cover slip.

All digital images were obtained using a Leica DMRXA2 epifluorescence microscope equipped with a cooled CCD camera (Princeton Instruments). Cy3-dCTP, FluorXdCTP, Cy5-dCTP, and DAPI Pseudocoloring; merging of images were performed using Adobe Photoshop software.

Results

All the probes mapped in the present study and the taxa on which they were appropriately hybridized are listed in Table 2. Hybridization are in agreement with painting data regarding the
orthologous to human chromosome 4 in Primates. The primates syntenies reconstructed in this work have been done using the homologies with humans as reference.

<table>
<thead>
<tr>
<th>HSA chromosomal arm international code</th>
<th>Alphabetic order and labelling of probes</th>
<th>Clone name</th>
<th>UCSC browser position of HSA, DNA probes</th>
<th>Human banding position of probes</th>
<th>Taxa and chromosomes on which probes map</th>
</tr>
</thead>
<tbody>
<tr>
<td>p</td>
<td>A</td>
<td>RP11-1150B4</td>
<td>chr4:1,850,027-2,000,642</td>
<td>4p16</td>
<td>SSC1, CJA3, SOE7, CGO9, CPY9, LLA19, MAR4, CAE27, EPA2, GGO10, PPy3, PTR3, CAL 24</td>
</tr>
<tr>
<td>c</td>
<td>centromere</td>
<td></td>
<td></td>
<td></td>
<td>CJA3, SSC1, SOE7, ALE 9</td>
</tr>
<tr>
<td>q</td>
<td>F</td>
<td>FIP1L1-CHIC2-DDGFRA</td>
<td></td>
<td>4q12</td>
<td>SSC1, SOE7, ALE9</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>RP11-637n1</td>
<td>chr4:135,127,036-135,329,748</td>
<td>q28.3</td>
<td>PPy3, SSC1</td>
</tr>
<tr>
<td></td>
<td>L</td>
<td>RP11-166k6</td>
<td>chr4:145,428,129-145,602,514</td>
<td>q31.22</td>
<td>PPy3, SSC1</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>RP11-70L18</td>
<td>chr4:157,931,025-158,098,577</td>
<td>q32.1</td>
<td>PPy3, SSC1</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>RP11-433J23</td>
<td>chr4:166,447,984-66,559,008</td>
<td>q32.3</td>
<td>SSC1, SOE7</td>
</tr>
</tbody>
</table>
Table 2. list of probes used to track HSA 4 evolution. In the first column are listed in order and portioned by the indication of the centromeres position the HSA probes in p and q arms. In the second column are reported the alphabetic letters labelling the probes used in text and figures of the work for the sake of simplicity. In third and fourth columns are listened the specific BAC clones name and their HSA sequence position reported in the UCSC browser. The fifty column is listened the G banding regions from which HSA probes derive. Acronyms in the last column refer to the taxa and the chromosome on which the probes were mapped.

The results can be resumed as follow:

1) Probes A has been mapped on various catarrhini and platyrrhini species (Fig1a-d); it falls in a p-terminal position on submetacentric chromosomes of all Old Word monkeys (PPY 3, PTR 3, GGO 10, MAR 5, EPA 2) with the exception of CAE, where it falls on the acrocentric chromosome 27 and CAL, where it maps in a terminal position of the acrocentric chromosome 24. Probe A falls on New Word monkeys in a q terminal position on the submetacentric chromosomes (SSC 1, SOE 7, CPY 9, CGO 9) but on LLA acrocentric chromosome 19, and on ALE submetacentric chromosome 9 where synteny 4 is fissioned and associated with HSA synteny 15 (imaginnes not shown in the picture).

2) The human 4 p-arm (Fig 1 e-h) and F (HSAq12) probes (Fig 1 i-l) on Platyrhininae maps in a q position on the submetacentric chromosome of CJA (ch. 3), SSC (ch. 1), SOE (ch.7) and ALE (ch. 9),

3) The hybridization of probes I, L, M, N was repeated on Saimiri sciureus (Platyrrhini) and Pongo pygmaeus (Catarrhini) (Fig. 1 m). A co-hybridization of L, M, N probes were performed to assess the relative order of markers with certainty. They mapped respectively in a q arm position on chromosome 3 of PPY and in the p arm position on chromosome 1 of SSC with an opposite orientation (Dumas and Sineo 2011). The obtained data have been compared with BAC probes previously mapped on the homolog to human chromosome 4 in CJA (ch. 3) (Stanyon et al. 2008).

Discussion

Sinteny 4 evolution in Primates

On the basis of previous molecular cytogenetics results present in literature, mainly painting data, we reconstruct a scenario regarding chromosome 4 evolution in Primates (Fig 2). The ortholog to
human synteny 4 in the ancestral primate karyotype, a submetacentric chromosome, is derived from the fission of the ancestral 4/8 association. In Strepsirrhini, synteny 4 was divided into two segments (Stanyon et al., 2002, Stanyon et al., 2006), which in various species have been subject to traslocations (Rumpler et al., 2008). In Platrrhini the orthologous segments are conserved as a single submetacentric chromosome in Cebidae and Pithecidae (Stanyon et al., 2000, Neusser et al., 2001, Dumas et al., 2007) except in Atelidae. In this last family synteny 4 exhibits a high degree of reshuffling and presents up to three fragments (Dumas et al., 2005, De Oliveria et al., 2012). In Catarrhini infraorder the ortholog to human chromosome 4 is a submetacentric chromosome in all the species analysed through painting (Ruiz Herrera et al. 2002; Stanyon et al. 2005; Bigoni et al. 1997a,b, 2003, 2004) with the exception of Cercopithecinae and Hylobatidae (Finelli et al. 1999; Moulin et al 2008; Muller et al. 2003; Dumas and Sineo 2010).

**Marker order along synteny 4 in Primates**

The mapping of subchromosomal specific probes in a few representative of Primates and the comparison with an outgroup (*Felis catus*) leads researchers to hypothesized a markers order conservation in the ancestral form of human synteny 4 in Primates (Stanyon et al. 2008) with some exception in Catarrhini; indeed, through subchromosomal probes mapping in various Old Word monkeys such as *Macaca* (Ventura et al. 2007), *Pongo pygmaeus*, *Gorilla gorilla* and *Pan troglodytes* (Marzella et al. 2000; Clemente et al. 1990) those exception have been demonstrate as previously suggested (Yunish and Prakash 1982) on the base of high resolution GTG banding analysis, probably as result of peri-centromeric inversions.

Our BACs mapping is in agreement with the chromosome painting results, as all probes fall on the orthologous to human chromosomes. The ortholog to human chromosome 4 in the species here considered is a submetacentric chromosome with the exception of *Chlorocebus aethiops* and *Cercopithecus albogularis labiatus* (Catarrhini), where it is fissioned (Finelli et al. 1999, Moulin et al. 2008) with *Lagotrichia lagotricha* and *Aotus lemurinus griseimembra* (Platyrrhini), where respectively human paint 4 maps on two or more chromosomes in association with others syntenies (Neusser et al, 2001; Stanyon et al. 2011).

We found probe A on apparent opposite location in the species analyzed (Fig. 3a): in a terminal position of the short arm (4p), in Catarrhini (*P. pygmaeus* 3, *P. troglodytes* 3, *M. arctoides* 5, *E. patas* 2 and *G. gorilla* 10), and in a terminal position of the long arm (4q) in Platrrhini (*S. sciureus* 3, *S. oedipus* 7, *C. goeldii* 9 and *C. pygmaea* 9); even in *C. albogularis labiatus*, *C. aethiops* (Catarrhini), *A. lemurinus griseimembra* and *L. lagotricha* (Platrrhini) where human synteny 4 has been split in two or
more fragments and, in association with synteny 15, the probe maintained its original location. Indeed probe A falls in a terminal position, on acrocentric chromosomes of *L. lagotricha* 19, *C. aethiops* 27, *C. albogularis labiatus* 24, and in the q arm position on a submetacentric chromosome of *A. lemurinus griseimembra* 9, without other evident rearrangements. The different position of the probe signal in the two lineages can be explained as the result of a large pericentromeric inversion or of the occurrence of a new centromeres activation as it was previously hypothesized through classic banding analysis for the homologues to human chromosome 4 in *Cebus capucinus* (Platyrrhini) (Dutrillaux et al. 1976). To test the two hypothesis we hybridized human 4 p-arm (including the HSA 4 p16.3 region-probe A) and probe F (being in a region close to the centromeres in HSA chromosome -4 but on the other arm, q) in Platyrrhini (*C. jacchus* 3, *S. sciureus* 1, *S. oedipus* 7 and *A. lemurinus griseimembra* 9). We show that both the probes map on the q arm in platyrrhini species; furthermore both in a region far from their centromere position but maintaining their reciprocal position and orientation (Fig. 3b); this evidence shows that the HSA markers order is conserved in the species analysed and the different position seen for probe A in Platyrrhini and Catarrhini is only apparent. Those results allow us to support the hypothesis of a conservation of markers orders as any inversion of the markers occurred, supporting the previous results reported for a few platyrrhini 4 orthologs analysed (Stanyon et al. 2008) and furthermore to suggest that the different apparent position of the A probe signals in New and Old World monkeys considered, as like the differences of 4p-arm and F probes signal position in Platyrrhini and Catarrhini is due to a new centromere activation occurred in one of the two lineages and the two form of chromosome are inverted (upside down). In evaluating the orientation of synteny segments in non-human primates with respect to humans, it is important to note that chromosomes are usually represented with the short arm (p) on top and for each chromosomes the base-pair count conventionally starts from the tip of the short arm; In several Primates chromosomes (Roberto et al., 2008) the centromere index in the genome release could be incorrect because of rearrangements or simply because of centromere repositioning events as it is possible to appreciate in the CCJ chromosome 4 homologues released in the UCSC browser when compared with the present evidences.

In the present work we repeated a previous BACs hybridizations [ (4q 28.3), L (4q 31.22), M (4q32.1), N (4q32.3)] on *S. sciureus* and *P. pygmeus* (Dumas and Sineo 2010). The results has been compared with data present in literature regarding *C. jacchus* (Ch.3), where marker order had been demonstrate to be conserved (Stanyon et al. 2008, Rocchi et. Al. 2009). The comparison permitted us to show a different position and orientation of the probes (block I to N), along the chromosomes homologues of the two platyrrhini species, explainable as result of a large pericentric inversion occurred in *S. sciureus*
This data permits us to underline that there are exceptions respect the conservative status of synteny 4 even in Platyrhini.

Furthermore based on cytogenetic data present in literature (Stanyon et al. 2008, Dumas and Sineo 2011, Ruiz Herrera et al. 2005; Stanyon et al. 2011, Stanyon et al. 2001; Stanyon et al. 2008) we define the chromosomes rearrangements occurred during evolution in New Word monkeys (Fig 3d).

We recognize, through classic banding pattern analysis (Dutrillaux et al. 1979), a first genomic organization of synteny 4 in cebidae species such as *Cebus capucinus* from which derived the others forms by: a new centromere formation in *C. jacchus* 3 as demonstrate by Stanyon and Collegues (2008); a large pericentric inversion in *S. sciureus* 1 (Cebidae) (present work); a robertsonian fission and successive traslocation to form a new syntenic association with human synteny 15 (4a, 4bc/15) in *A. lemurinus griseimembra* (Aotinae- Cebidae); two non centromeric fissions with the production of tree fragments and a traslocation to form the 4/15 association (4a, 4b/15, 4c) in *L. lagotricha* (Atelidae) with chromosome LLA19 (4c) showing a new centromeres. Note that the association 4/15 in *L. lagotricha* has different breakpoints if compared with the one in *Aotus* and does not represent a synapomorphy linking the two species (Picone and Sineo 2010) as supposable even in the *A. lemurinus griseimembra* subspecies.

**Conclusion**

We investigated the evolutionary steps of human synteny 4 by performing original hybridizations and interrogating our data with respect to previous findings on orthologous to human chromosome 4 in primates. We mapped sub-chromosomal probes of interesting critical points on chromosomes of representative group of Anthropoidea (Primates), in order to define and verify marker clustering and possible chromosomal rearrangements. We performed banding pattern and BACs pattern study together that are of great help in joint analysis. Furthermore we reconstructed the evolutionary steps that synteny 4 has undergone during primate evolution with particular attention to Platyrhini by analysing literature data on painting and BACs probes mapping.

Through the mapping of different probes of critical interest we tested previously cytogenetics hypothesis on synteny 4 in New and Old word monkeys allowing us to support the general conservative status of the synteny but with some exceptions. In particular:

1) the mapping of A, p-arm and F probes in catarrhini and platyrhini species analysed permit us to exclude the hypothesis of a pericentromeric inversion as responsible of the apparent differences in between the syntenies 4 in Neotropical and Old word monkeys; conversely we support the hypothesis...
about the markers order conservation in the orthologues to human chromosome 4 in anthropoidea species; indeed we single out that the chromosomes homologous to human synteny 4 in the two lineages are just inverted and they differ merely in the position of the centromeres; this evidence stimulates a innovative hypothesis in which the activation of a new centromere occurred in one of the two lineages;

2) Our analysis of cytogenetic data present in literature regarding human synteny 4 allow us to show the main evolutionary steps that synteny 4 has undergone during Primates evolution with particular attention to Platyrhini. In New World monkeys we show a high level of genomic changes including inter and intrachromosomes rearrangements such as traslocation, fissions, pericentromeric inversion and new centromere activation; rearrangements potentially useful in phylogenetic and genomic studies of sequence assembly.

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References


