The role of chromosomal rearrangements in speciation and adaptation in primates—new tools into human welfare studies?

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Genomics of Non-Classical Model Animals
XXIV Plant and Animal Genomes, San Diego

CHROMOSOMAL REARRANGEMENTS

Fission

Fusion

Translocation

Inversion

Farré & Ruiz-Herrera, 2014

CHROMOSOMAL REARRANGEMENTS and EVOLUTIONARY BREAKPOINT REGIONS (EBRs)

chr1
chr1'
HSB
HSB
HSB
HSB
HSB
HSB
Species A

chr2'
HSB
HSB
Species B

EBR Evolutionary Breakpoint Region
HSB Homologous Synteny Block

CHROMOSOMAL REARRANGEMENTS and EVOLUTIONARY BREAKPOINT REGIONS (EBRs)

Miss-repair of DSBs
Formation of DSBs

Chromosome rearrangements in the germ line

Fixation of the chromosome rearrangements

Models of chromosomal speciation

From Kong et al., 2010

HOW TO STUDY RECOMBINATION

- High density SNPs data using linkage disequilibrium (LD).
- SNPs data from parent-offspring pairs.
- Sperm typing.
- MLH1 detection.

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From Segura et al., 2013

PRIMATES LINEAGE

HUMAN & CHIMPANZEE SPECIATION EVENT

Pair-wise comparisons between human, chimp and orangutan as outgroup

Define HSBs and EBRs

37 EBRs
- EBRs of macroinversions - chrs 1, 4, 5, 9, 12, 15, 16, 17 & 18
- Newly defined indels
- Newly defined microinversions (<1.4 Mbp) - chrs 1, 7, 10, 19, X & Y

From Farré et al., 2013

HUMAN & CHIMPANZEE SPECIATION EVENT

Recombination rate is lower in longer chromosomes

From Farré et al., 2013

GREAT APES LINEAGE

Pair-wise comparisons between human, chimp and orangutan as outgroup

Define HSBs and EBRs

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HUMAN & CHIMPANZEE SPECIATION EVENT

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From Farré et al., 2013
**HUMAN & CHIMPANZEE SPECIATION EVENT**

<table>
<thead>
<tr>
<th>Genome average SRR</th>
<th>Collinear chromosome</th>
<th>Observed non-inverted region</th>
<th>Observed inverted region</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.975</td>
<td>1.001</td>
<td>0.717*</td>
</tr>
</tbody>
</table>

* p-value<0.0001

Farré et al., 2013

**HUMAN & MACAQUE DIVERGENCE NODE**

- Ullastres et al., 2014

**HUMAN & MACAQUE DIVERGENCE NODE**

- We focused on 2 macaque-specific inversions:
  - Human chromosome 4 == Macaque chromosome 5
  - Human chromosome 10 == Macaque chromosome 9
  - Human chromosome 5 == Macaque chromosome 6
Mean Recombination Rate = 35 MLH1 foci/cell

Ullastres et al., 2014

<table>
<thead>
<tr>
<th>CHR</th>
<th>N</th>
<th>p-arm</th>
<th>q-arm</th>
<th>MLH1 foci/SC</th>
<th>Inside inversion</th>
<th>Outside inversion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ch5</td>
<td>87</td>
<td>3.85</td>
<td>4.01</td>
<td>2.01</td>
<td>0.26</td>
<td>0.04*</td>
</tr>
<tr>
<td>ch9</td>
<td>86</td>
<td>3.19</td>
<td>5.56</td>
<td>1.99</td>
<td>0.23</td>
<td>0.03*</td>
</tr>
</tbody>
</table>

* p-value < 0.05

Recombination in inverted region < Recombination in non-inverted region
Recombination in real inverted region < Recombination in simulated inverted region

Ullastres et al., 2014

**SUMMARY**

• Lower recombination rate in the inverted regions of the rearranged chromosomes.

Supporting the suppression of recombination model

• Macaque-specific inversions harbour genes related to immune defense.

• EBRs can represent opportunities for the development of novel functions that may promote the adaptation of the species.

Ullastres et al., 2014

Gene | Macaque Chromosome | Function
-----|---------------------|--------
GNRHR2 | 1 | Gonadotropin receptor
ADIPQ | 2 | Adiponectin precursor
DEF5A | 8 | Defensin precursor
MSMB | 9 | Beta-microseminoprotein
DEFB113 | 10 | Beta-defensins
DEFB118 |  | 
DEFB119 |  | 
DEFB122 |  | 
CCL18 | 16 | C-C motif chemokines
CCL3 |  | 
DC-SIGN | 19 | Pathogen-recognition receptor

Role in neurodevelopment and neurophysiological signaling (Rostene et al. 2011)

Chemokine signaling pathway
p-value=0.015

Metabolism of xenobiotics pathway
p-value=0.003

Play a role during speciation in lineage leading to macaques (Abildskov et al., 2010)

Ugay, A, 2014

EBRs in macaque GO enrichment in Immune Response genes, p-value < 0.004

Macaque-specific inversion in chromosome 5
ACKNOWLEDGEMENTS

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