

Comparative study of the 3D genome in primates

Marc A. Marti-Renom CNAG-CRG · ICREA

Unpublished

http://marciuslab.org http://3DGenomes.org

@mamartirenom

@marciuslab



C. Chothia & A. Lesk (1986) EMBO J. 5(4):823-826



François Serra CNAG-CRG



Yasmina Cuartero CNAG-CRG

In collaboration with: The 4DGenome Unit (CRG) The Marquès Lab (IBE-UPF) The Ruiz-Herrera Lab (UAB) The Navarro Lab (EGA-UPF) The Caceres Lab (UAB)





Chromosome Conformation Capture

Dekker, J., Rippe, K., Dekker, M., & Kleckner, N. (2002). Science, 295(5558), 1306–1311. Lieberman-Aiden, E., et al. (2009). Science, 326(5950), 289–293. Rao, S. S. P., et al. (2014). Cell, 1–29.





Is 3D at all relevant?

Figure adapted from Hui Zheng and Wei Xie. Nature Reviews Molecular Cell Biology (2019)





Flavahan, W. A. et al. Nature 529, 110–114 (2016).



Hi-C matrices from lymphoblasts in seven primates











Synteny breakpoints in 3D

Two regions of at least 100 kb separated by more than 750 kb (including trans chromosomal) Common detections from Ruiz-Herrera's Lab (@300Kb res) and our lab (ENSEMBLE @1Kb res)





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Chimp chr14





Two regions of at least 100 kb separated by more than 750 kb (including trans chromosomal)



Chimpanzee (62 matrices) 0.75 Mł 0.5 Mb · 0.25 Mb · Breakpoint --0.25 Mb --0.5 Mb ·

-0.75 Mb -

Chromosomes



0.75 Mb ·

0.5 Mb

0.25 Mb -

Breakpoint

-0.25 Mb

-0.5 Mb



Macaaue (134

0.75 MB 0.5 MB 0.25 MB BROALDONE 0.25 MB 0.5 MB 0.75 MB



Synteny breakpoints in 3D

Marmoset (151

Mouse (199







— 50-100 kb (origin region) — 100-200 kb (origin region) 200-400 kb (origin region) — 400-600 kb (origin region) — 50-100 kb (copied region) — 100-200 kb (copied region) 200-400 kb (copied region) — 400-600 kb (copied region) interquartile (origin region) interquartile (copied region)











Genome compartments

Conservation of the A/B compartments



Genome Topologically Associating Domains







Genome Topologically Associating Domains

Conservation of TADs











Vietri Rudan, et al. Cell Rep. 2015 Mar 03; 10(8) 1297-1309 Nakahashi et al. Cell Rep. 2013 May 30; 3(5) 1678-1689







LOOPS Conservation of CTCF sites





- >150 K sequences to align (all species together)
- Tree reconstruction using FastTree2
- Reduce the complexity filtering by node support
- Selection of 173 nodes with 0.9 bootstrap
- At least 100 CTCF sites (and at least 50 from single species)

















Motif (nucleotide content)

Insulation/looping (interaction directionality)

• Enrichment in repetitive elements







Few events of genome expansion through transposons involving CTCF sites







Loops Conservation of CTCF sites

LTR13 (Long Terminal Repeat) for HERVK13 endogenous retrovirus



0.03

Loops Conservation of CTCF sites















3' end of L1 retrotransposon, L1PA16_3end subfamily











0.03

Chromosomes

LINE L1 specific of Callithrix jacchus (Marmoset)

- Conservation of 3D structure after chromosomic rearrangements.
- Recently duplicated regions are more isolated from surrounding DNA.
- Compartments are very conserved in primates; detectable changes may not be related to cell-specific features.
- TAD borders conserved with similar selective strength against gain and loss
- New, but few primate specific expansions carrying CTCF sites
- Selection against the creation of new and strong CTCF sites

Summary

http://marciuslab.org http://3DGenomes.org



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