

CHROMATIC reveals chromatinassociated factors contributing to genome topology

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epigenome

gene expression





Fly Chromatin **COLORs** Filion et al. (2010). Cell, 143(2), 212–224.

Position on chr2L (kb)

Who "holds" the genome structure? Serra et al. PLoS Comput Biol (2017) 13(7): e1005665

Position on chr2L (kb)

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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.

Chromatin Immunoprecipitation (ChIP)

Solomon, M. J., Larsen, P. L. & Varshavsky, A. (1988) Cell 53, 937–947. Park, P.J. (2009) Nature Reviews Genetics 10, 669–680.

High-throughput Chromosome Conformation Capture (Hi-C)

Chromatin interaction on a Hi-C map

Chromatin interaction "mediated" by a protein

Hi-ChIP: capturing specific protein-mediated interactions

Mumbach, M.R. et al. (2016) Nature Methods 13(11) 919-922.

SMC1 Hi-ChIP map = Hi-C + ChIP

5 kb res. (mESC mm10)

CHROMATIC

CHROMATIC example

mm10 chr6:48,050,001-52,750,006

Validation with HiChIP as benchmark

mm10 - mESC - 5kb - chr6:48,050,001-52,750,006

Per chromosome

Loops/Hubs

Rest

The role of chromatin factors in genome topology

HoxA cluster (example in ESC)

HoxA

3D interactions are mostly associated with pluripotent TFs

Polycomb **Pluripotency TF** Architectural Activity Repression

Measure the 3D co-localization of factors

CHROMATIC interactions

Overlap (19 factors)

8m 54s

Latent Semantic Analysis

- - -

Types of 3D interactions with LSA in ESC

Polycomb Pluripotency TF Architectural Activity Repression

Types of 3D interactions with LSA in ESC

Annotated using ChIP-Seq and literature

4 major types of 3D interactions in ESC

Higly-, Lowly-expressed and Silent genes

Silent RPKM<1 1<RPKM<10 Low High RPKM>10

A and B compartments

HoxA cluster (example in NPC)

Normalized

ChIP-seq

Global 3D interactions rewiring during mouse development

Total 5kbx5kb pixels = 5,216,011 (0.07%)

Total 5kbx5kb pixels = 6,710,882 (0.09%)

Global 3D interactions rewiring during mouse development **ESC** Total 5kbx5kb pixels = 6,710,882 (0.09%) Total 5kbx5kb pixels = 5,216,011 (0.07%) leuronal Tl 40.2% Pluripotent TFs 73.4% Inactive 24.3% Bivalent Active ESC NPC Active 33.3% PcG-Biva 20.1% **Pluripotent TFs** Unclassified Active **PcG-Bivalent** Active Inactive Neuronal TFs Unclassified Inactive **PcG-Bivalent**

Global 3D interactions rewiring during mouse development

t

3D interactions rewiring at Zfp608 locus during mouse neural development

Take home message...

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

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In collaboration with the Di Croce Lab @CRG

.: Conflict of Interest Statement :. Marc A. Marti-Renom serves as a consultant to Acuity Spatial Genomics, Inc., and receives compensation for these services.

.: Our current sponsors :.

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