3DGenomics

Marc A. Marti-Renom

CNAG-CRG · ICREA

http://marciuslab.org
http://3DGenomes.org
http://cnag.crg.eu

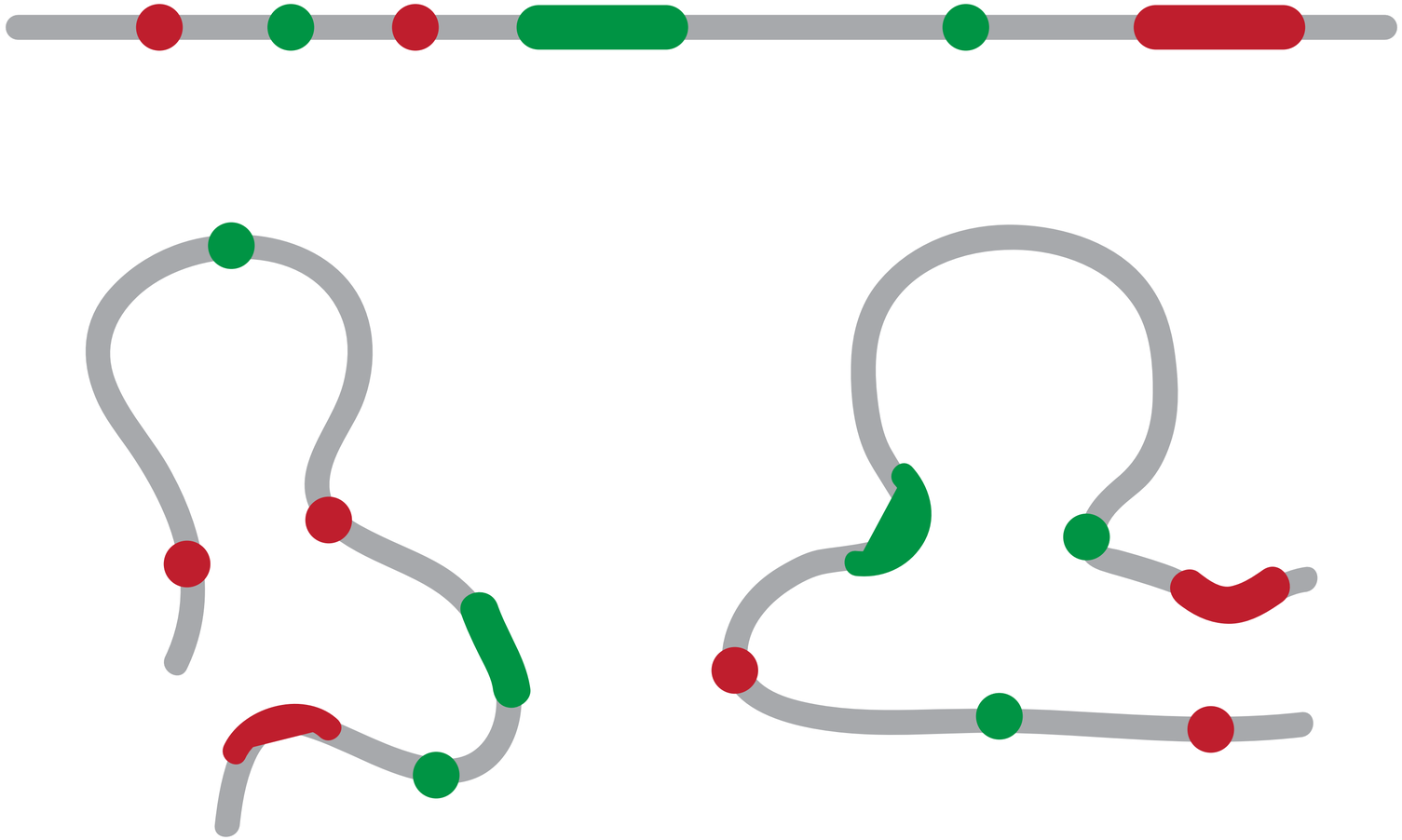
cnag CRG ICREA

All you will see in the screen will be stored here:

http://sgt.cnag.eu/www/presentations/

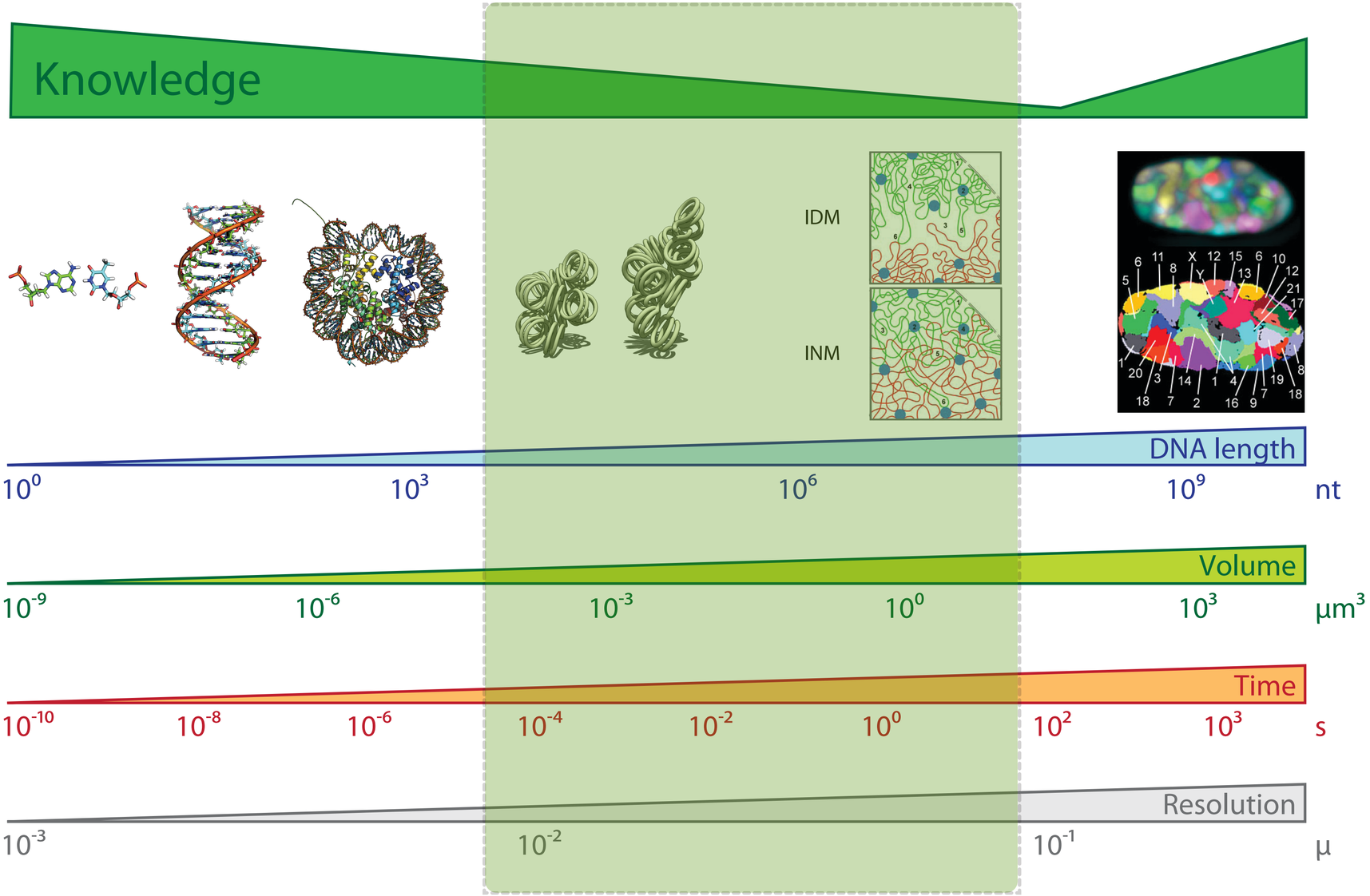
I encourage you to:

You can ask for question any time



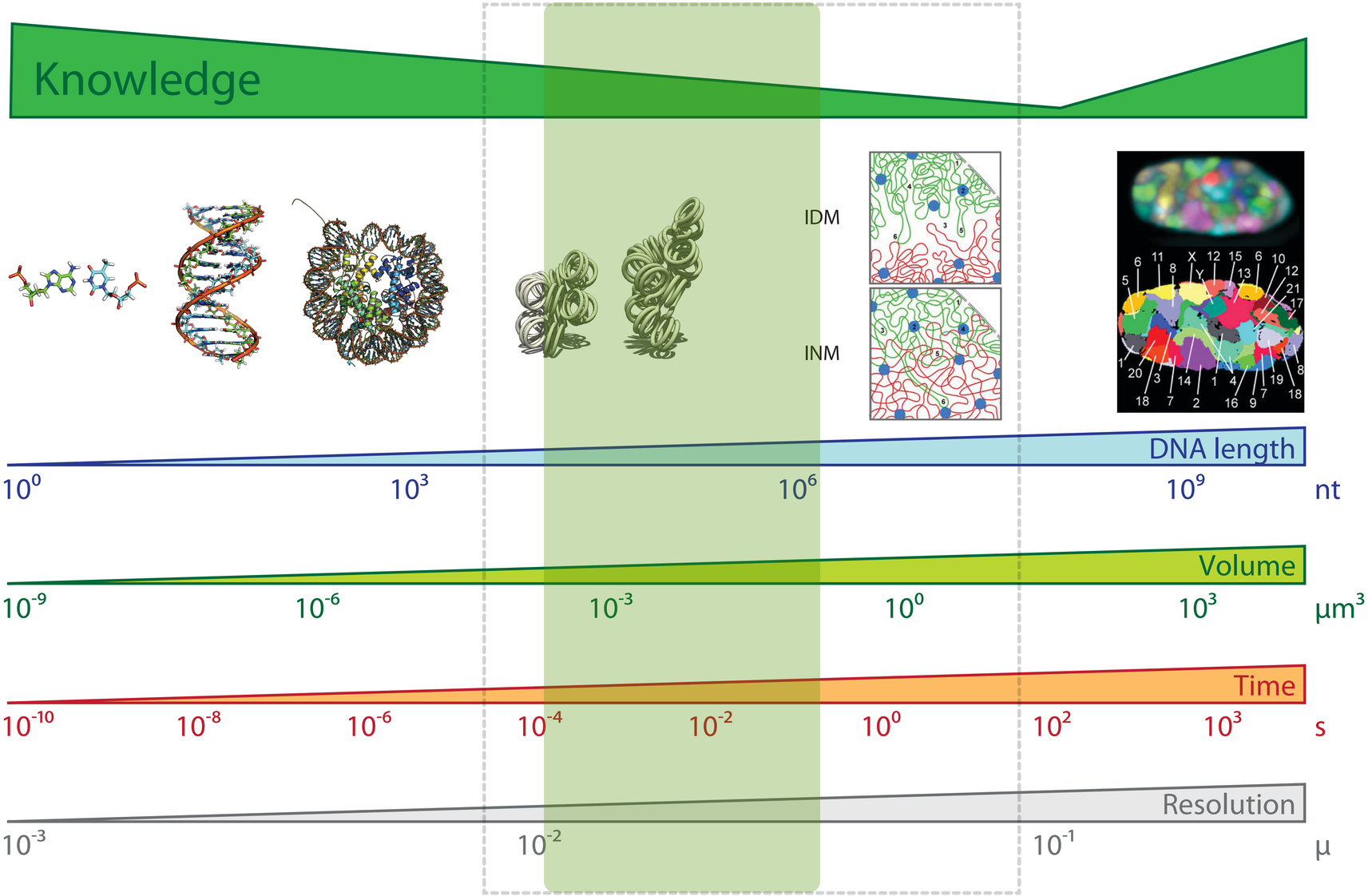
Resolution Gap

Marti-Renom, M. A. & Mirny, L. A. PLoS Comput Biol *7*, e1002125 (2011)



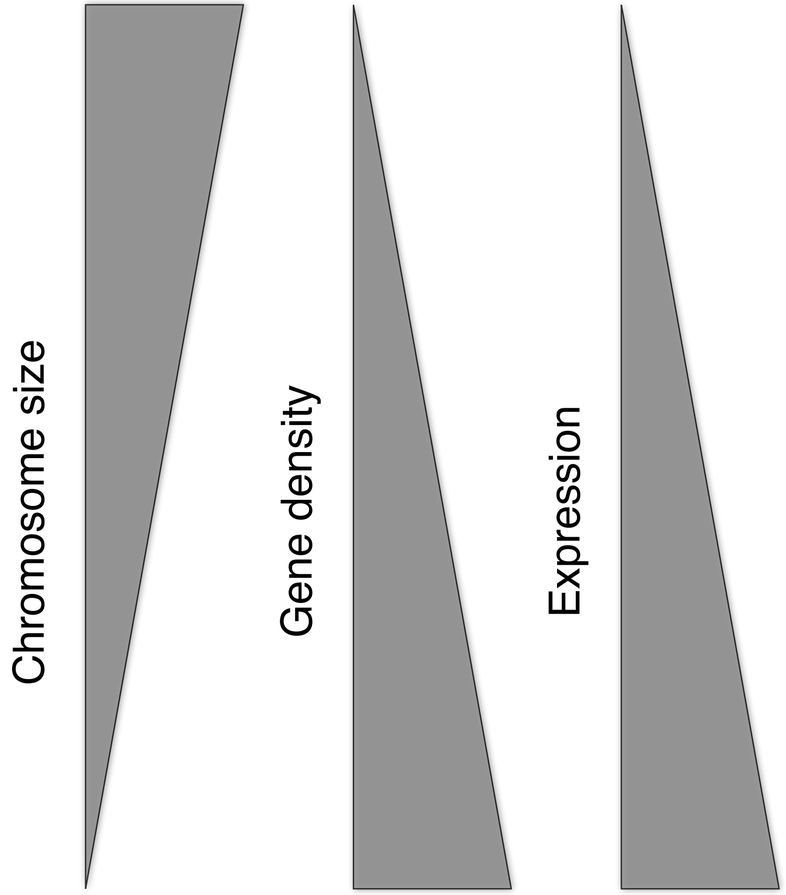
Resolution Gap

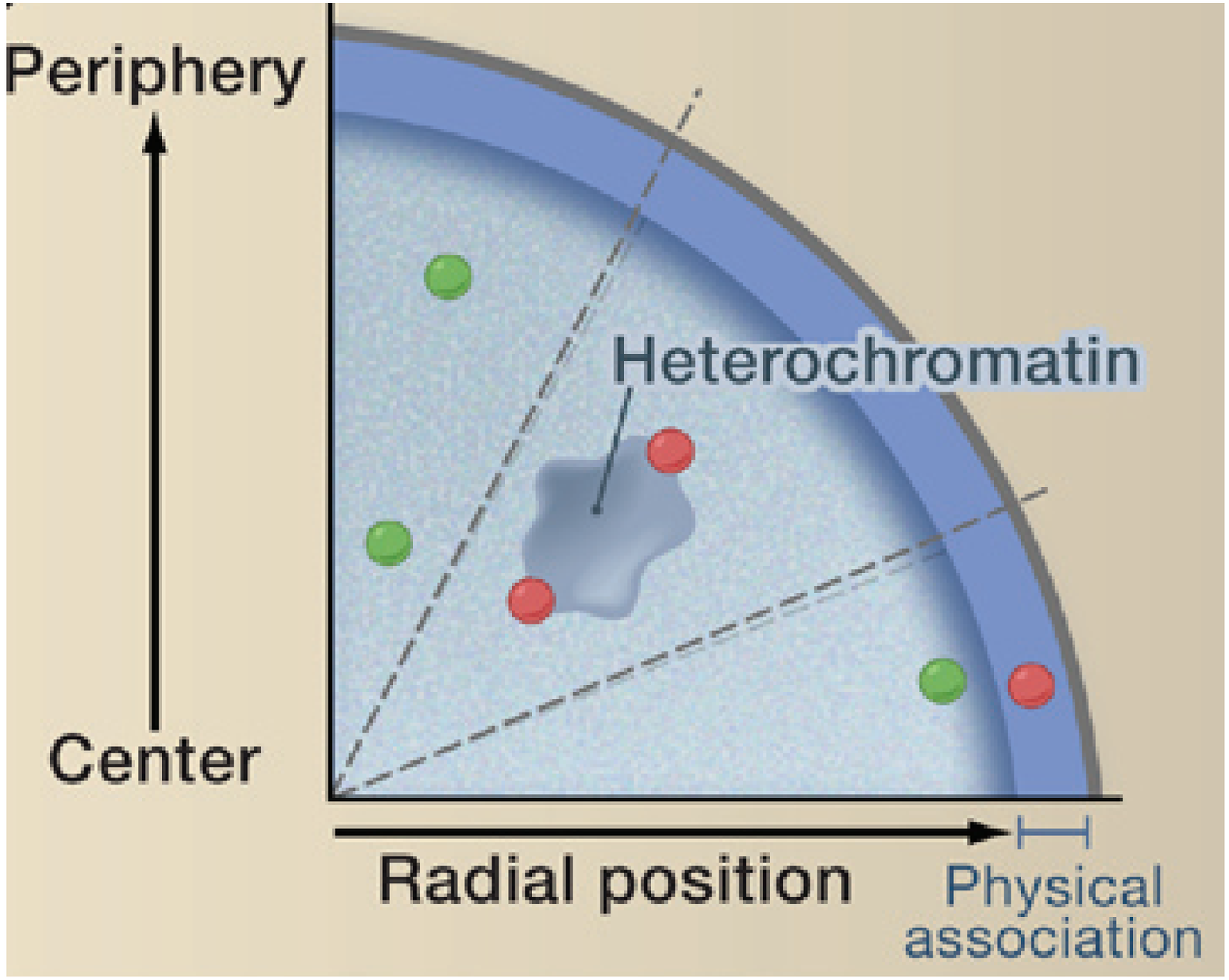
Marti-Renom, M. A. & Mirny, L. A. PLoS Comput Biol *7*, e1002125 (2011)



Level I: Radial genome organization

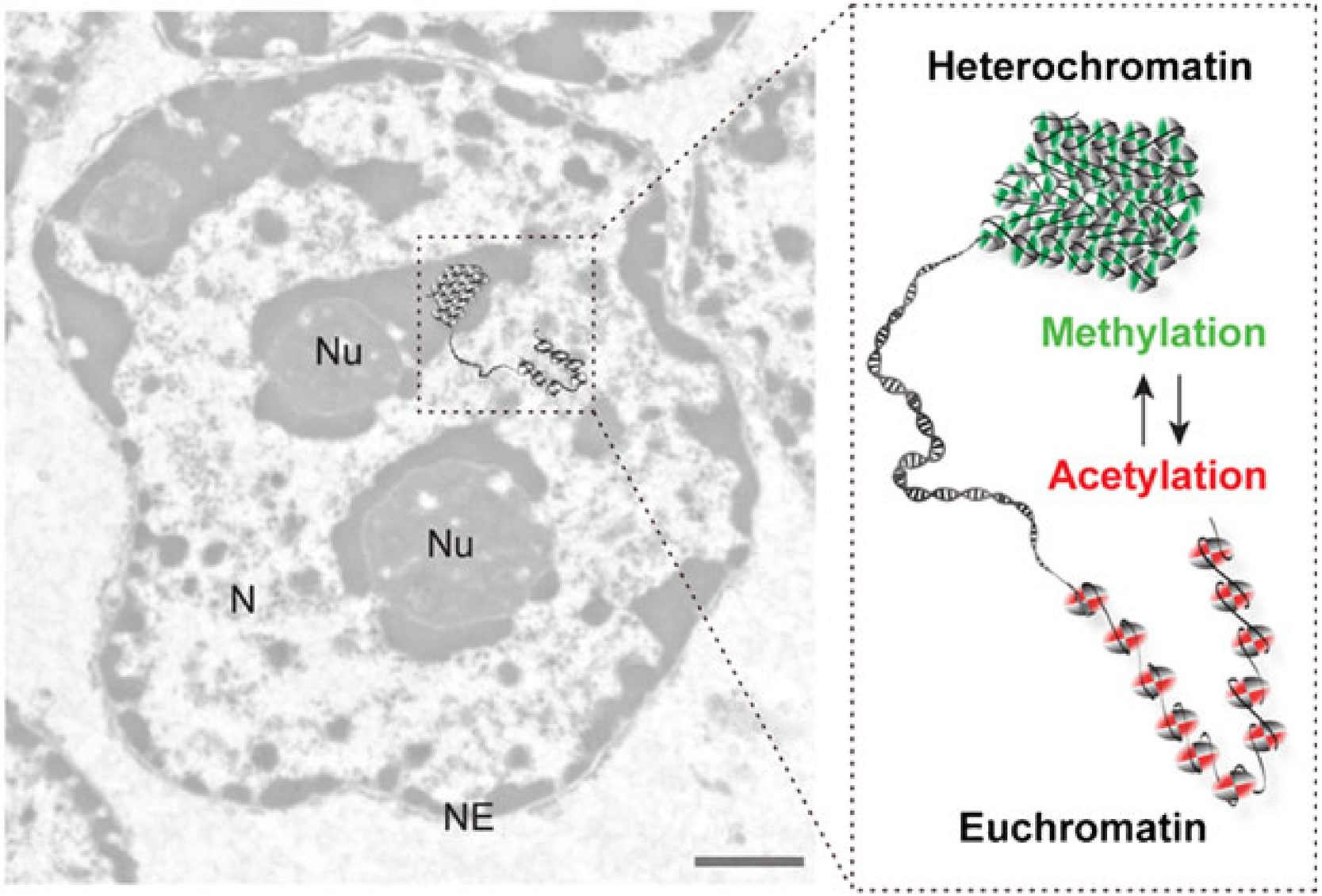
Takizawa, T., Meaburn, K. J. & Misteli, T. The meaning of gene positioning. Cell 135, 9–13 (2008).



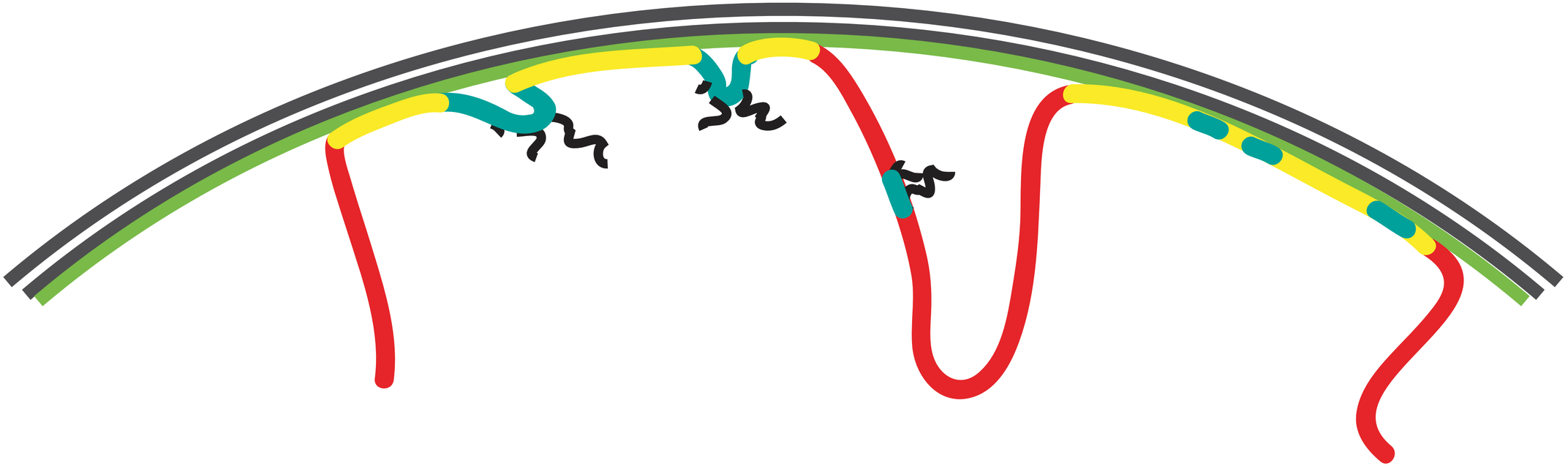


Level II: Euchromatin vs heterochromatin

Electron microscopy



Level III: Lamina-genome interactions



nuclear membrane
nuclear lamina

internal chromatin (mostly active)
lamina-associated domains (repressed)

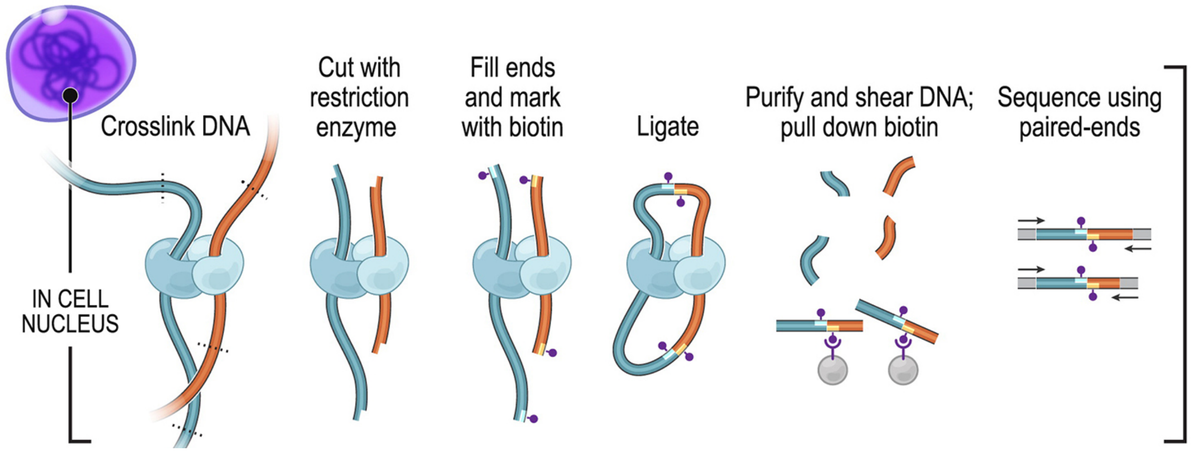
Genes

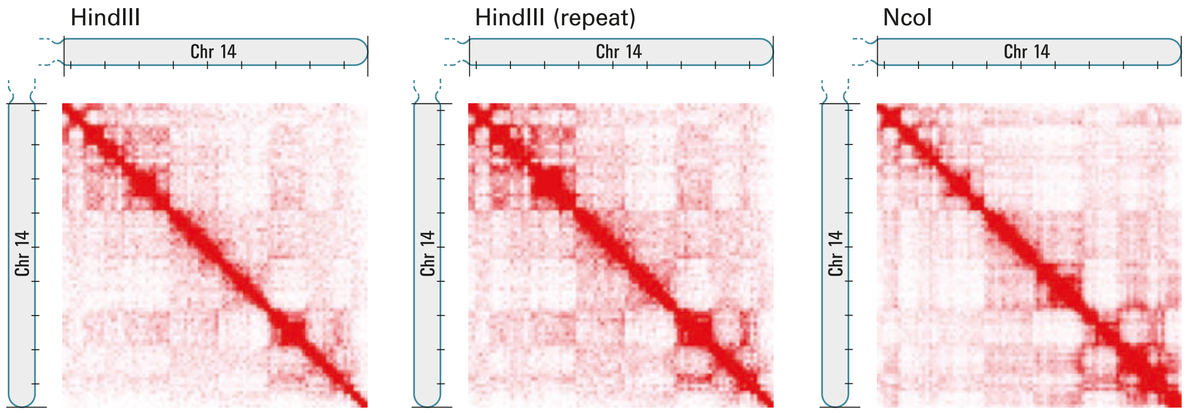
mRNA

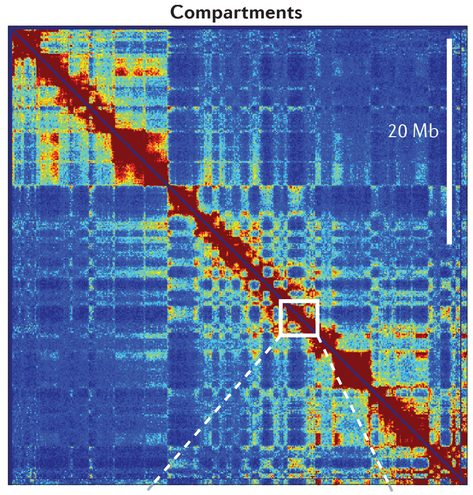
Adapted from Molecular Cell 38, 603-613, 2010

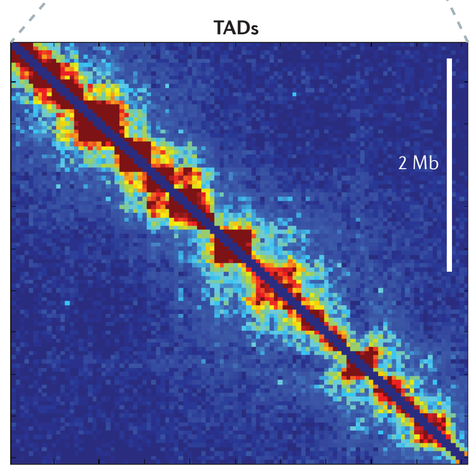
Level IV: Higher-order organization

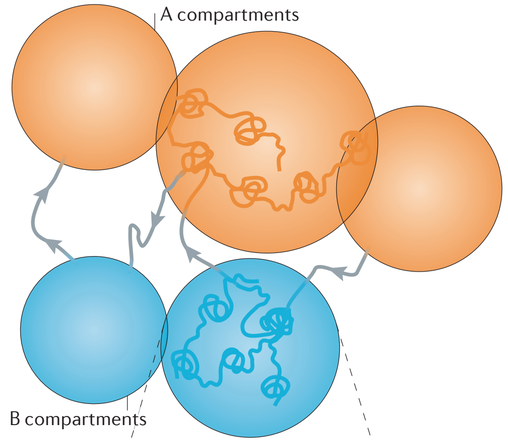
Dekker, J., Marti-Renom, M. A. & Mirny, L. A. Nat Rev Genet 14, 390–403 (2013).

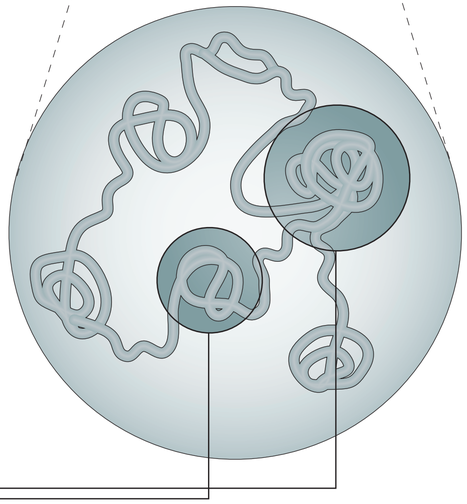




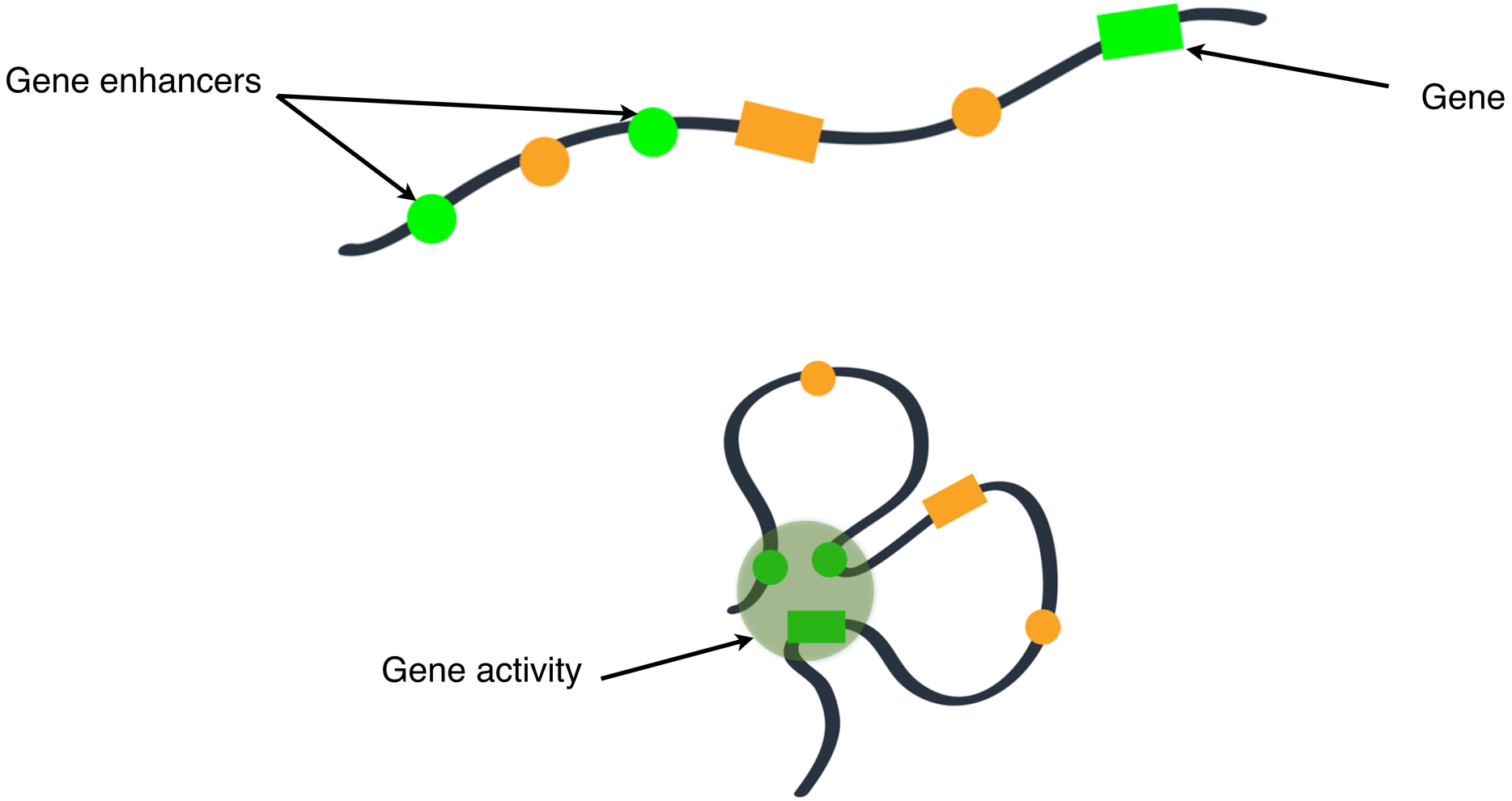






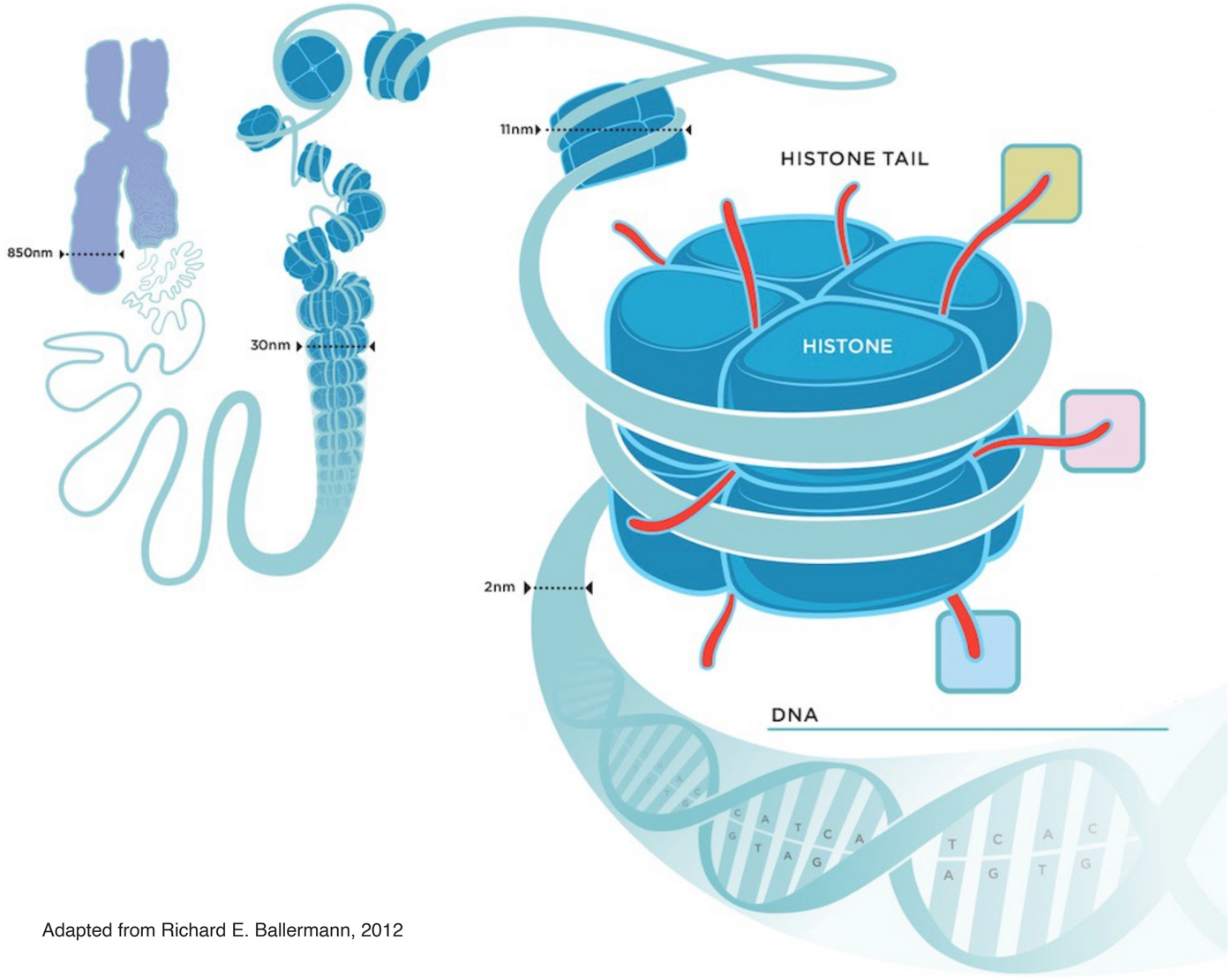


Level V: Chromatin loops



Level VI: Nucleosome

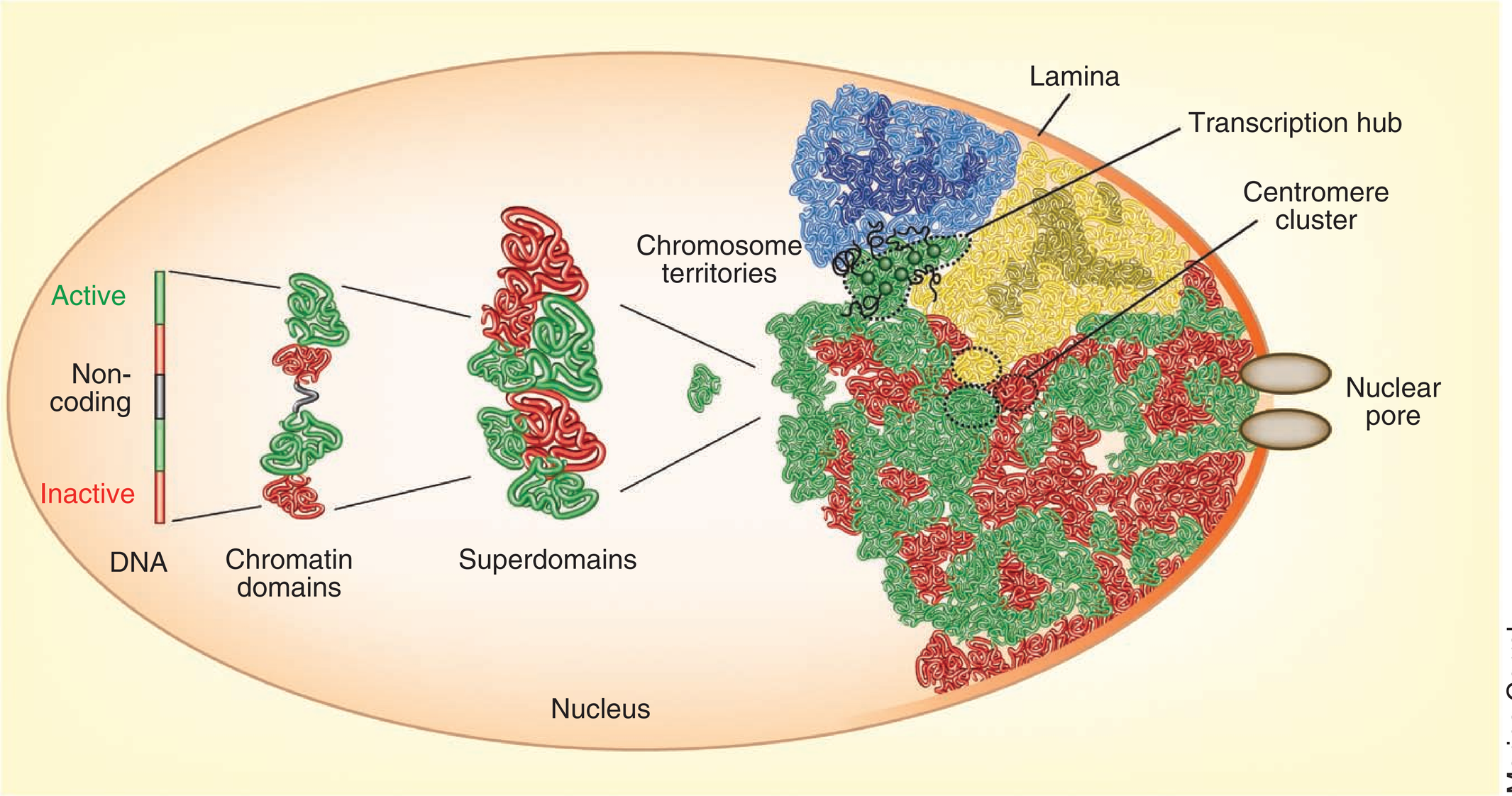
Chromosome **Chromatin fibre** **Nucleosome**



Adapted from Richard E. Ballermann, 2012

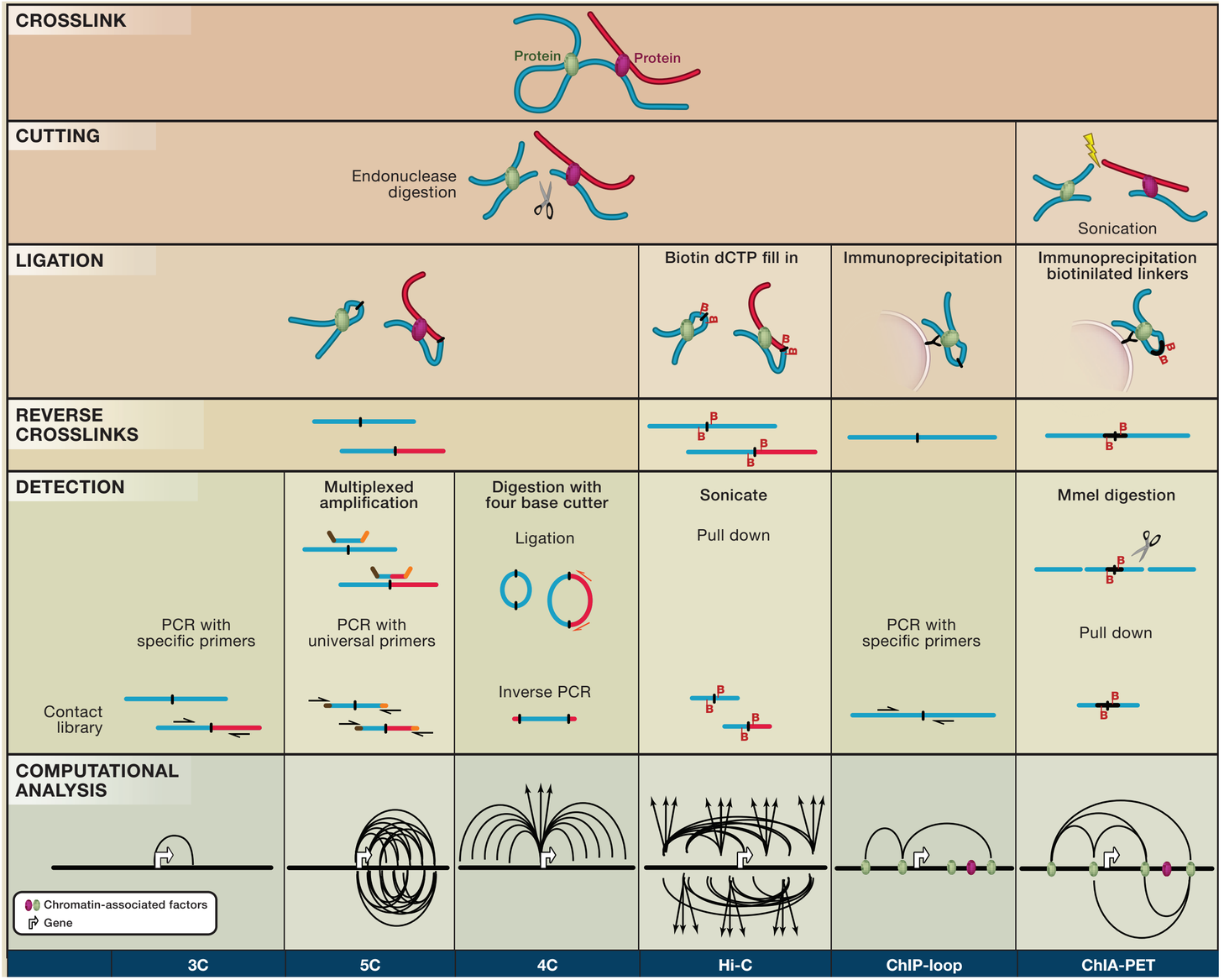
Complex genome organization

Cavalli, G. & Misteli, T. Functional implications of genome topology. Nat Struct Mol Biol 20, 290–299 (2013).



Marina Corral

Chromosome Conformation Capture



Hakim, O., & Misteli, T. (2012). SnapShot: Chromosome Confirmation Capture. Cell, 148(5), 1068–1068.e2.

ARTICLE

doi:10.1038/nature12593

Single-cell Hi-C reveals cell-to-cell variability in chromosome structure

Takashi Nagano[1]*, Yaniv Lubling[2]*, Tim J. Stevens[3]*, Stefan Schoenfelder[1], Eitan Yaffe[2], Wendy Dean[4], Ernest D. Laue[3], Amos Tanay[2] & Peter Fraser[1]

LETTER

doi:10.1038/nature20158

Capturing pairwise and multi-way chromosomal conformations using chromosomal walks

Pedro Olivares-Chauvet[1], Zohar Mukamel[1], Aviezer Lifshitz[1], Omer Schwartzman[1], Noa Oded Elkayam[1], Yaniv Lubling[1], Gintaras Deikus[2], Robert P. Sebra[2] & Amos Tanay[1]

nature genetics
ARTICLES
https://doi.org/10.1038/s41588-018-0161-5

Enhancer hubs and loop collisions identified from single-allele topologies

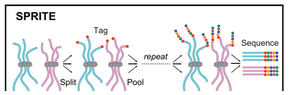
Amin Allahyar[1,2,7], Carlo Vermeulen[3,7], Britta A. M. Bouwman[3], Peter H. L. Krijger[3], Marjon J. A. M. Verstegen[3], Geert Geeven[3], Melissa van Kranenburg[3], Mark Pieterse[3], Roy Straver[1], Judith H. I. Haarhuis[4], Kees Jalink[5], Hans Teunissen[6], Ivo J. Renkens[1], Wigard P. Kloosterman[1], Benjamin D. Rowland[4], Elzo de Wit[4], Jeroen de Ridder[1]* and Wouter de Laat[3]*

Resource

Cell

Higher-Order Inter-chromosomal Hubs Shape 3D Genome Organization in the Nucleus

Graphical Abstract



Authors

Sofia A. Quinodoz, Noah Ollikainen, Barbara Tabak, ..., Patrick McDonel, Manuel Garber, Mitchell Guttman

Correspondence

mguttman@caltech.edu

nature COMMUNICATIONS

ARTICLE

DOI: 10.1038/s41467-018-06961-0 OPEN

Chromatin conformation analysis of primary patient tissue using a low input Hi-C method

Noelia Díaz[1], Kai Kruse[1], Tabea Erdmann[2], Annette M. Staiger[3,4,5], German Ott[3], Georg Lenz[2] & Juan M. Vaquerizas[1]

Article | Published: 11 February 2021

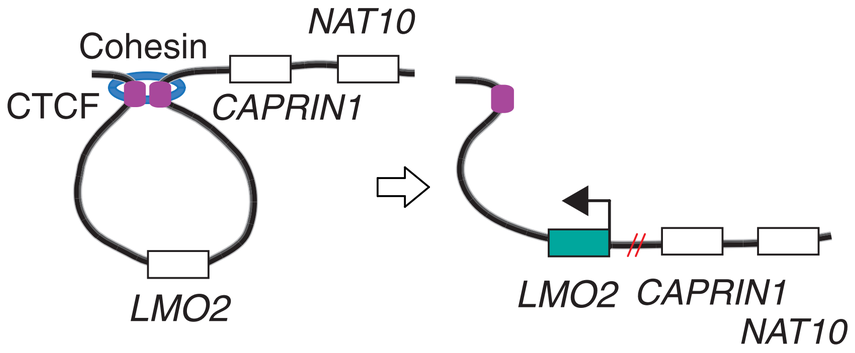
Liquid chromatin Hi-C characterizes compartment-dependent chromatin interaction dynamics

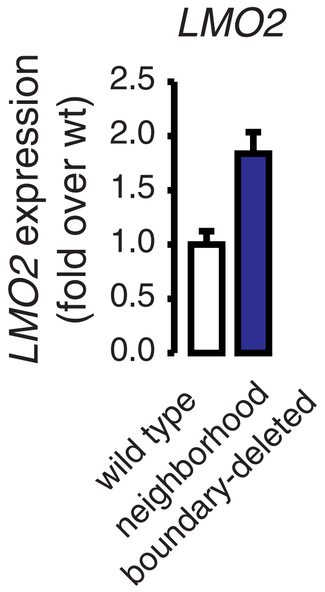
Houda Belaghzal, Tyler Borrman, Andrew D. Stephens, Denis L. Lafontaine, Sergey V. Venev, Zhiping Weng, John F. Marko & Job Dekker

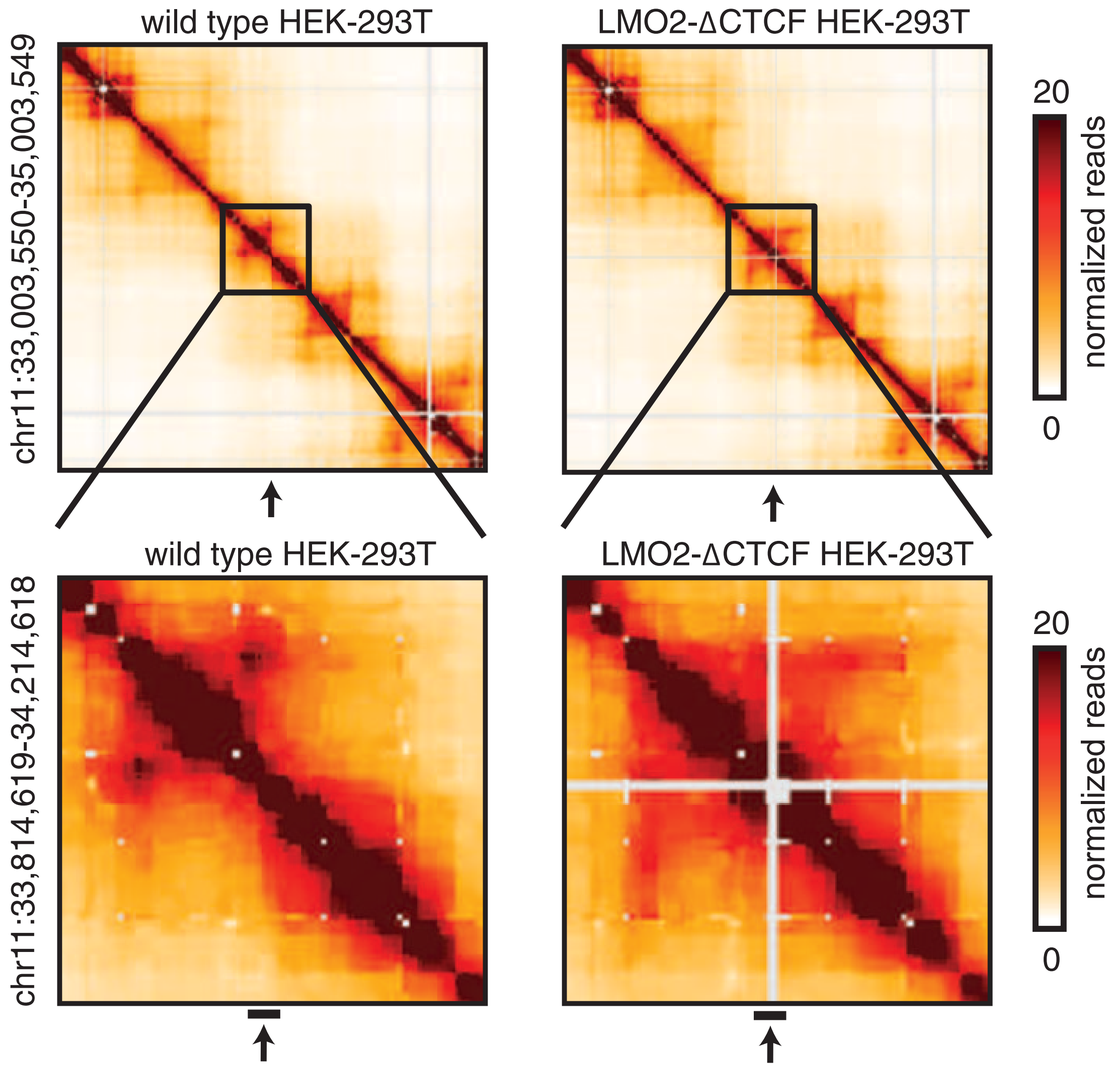
Nature Genetics **53**, 367–378 (2021) | Cite this article

TADs are functional units

Hnisz, D., et al. (2016). Science

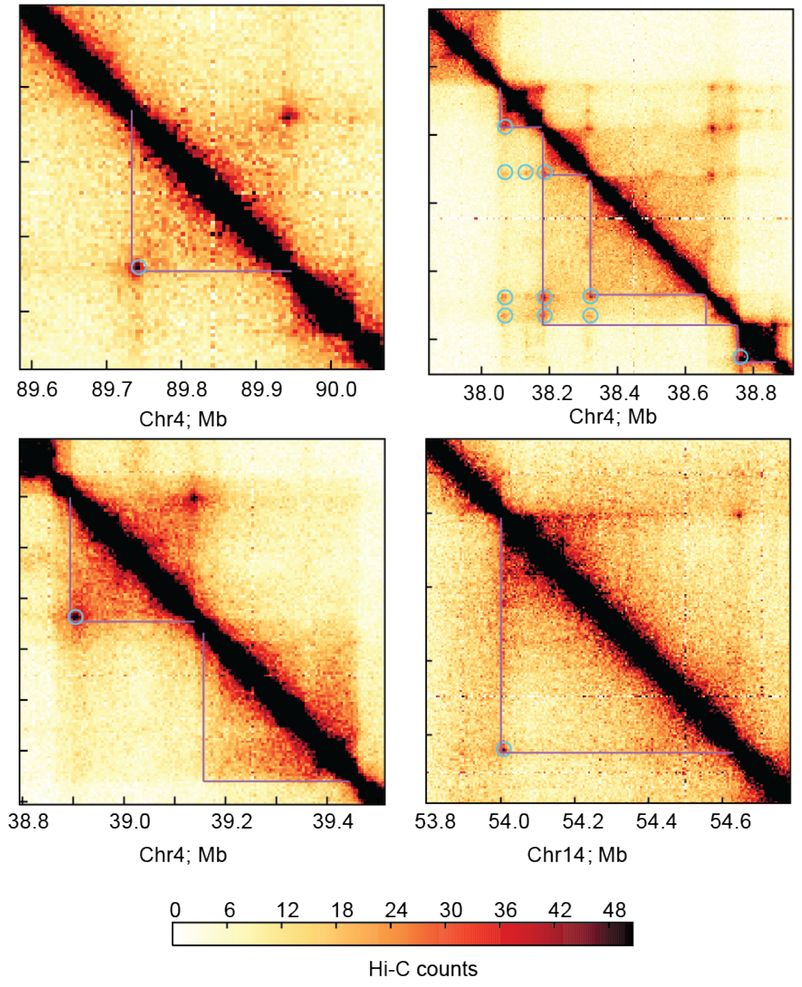


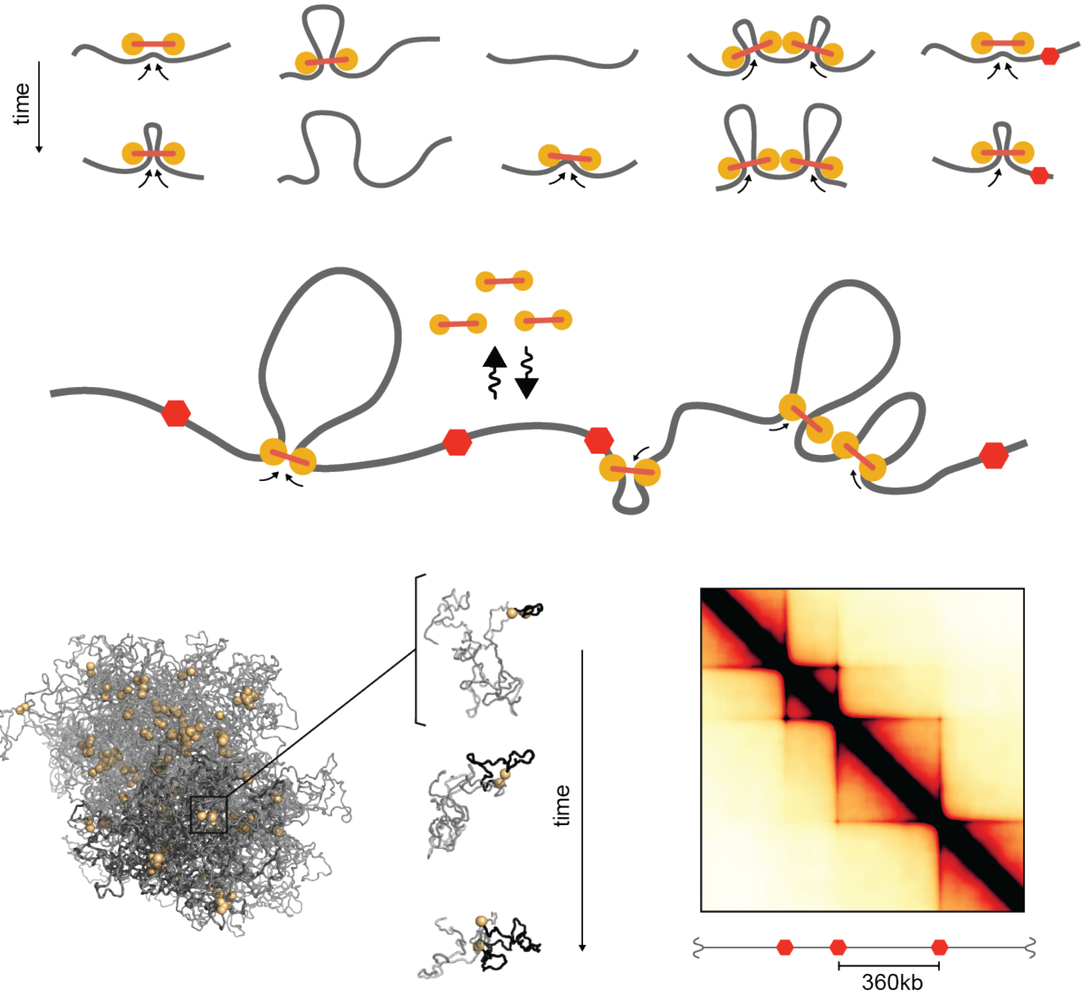




Loop-extrusion as a TAD forming mechanism

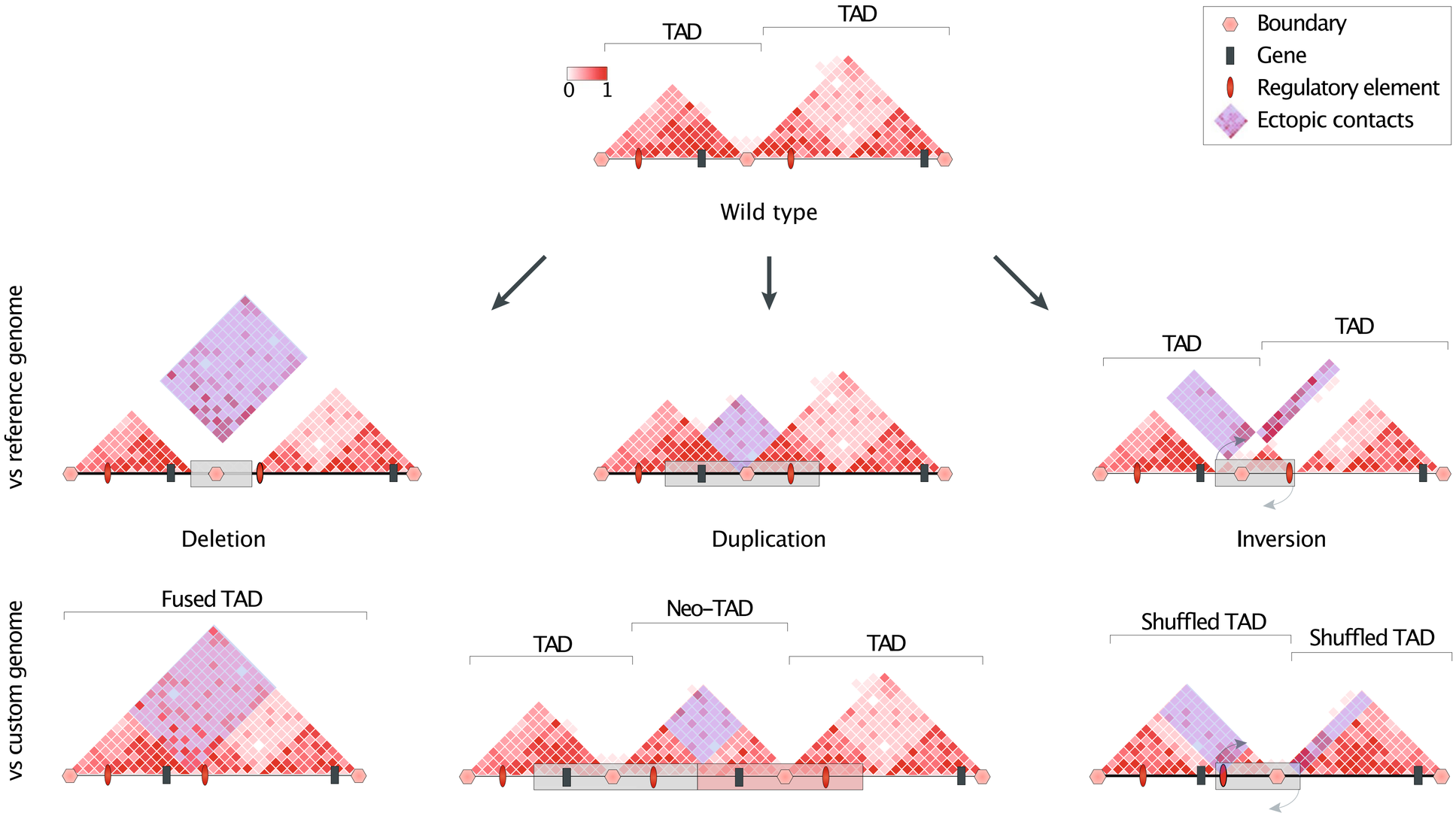
Fudenberg, G., Imakaev, M., Lu, C., Goloborodko, A., Abdennur, N., & Mirny, L. A. (2018).
Cold Spring Harb Symp Quant Biol 2017. 82: 45-55





Are TADs functional units?

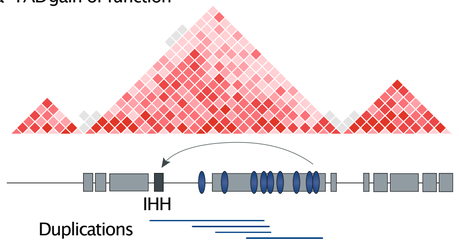
Spielmann Nature Reviews Genetics 2018 (19) 453–467



Clinical examples of structural variants

Spielmann Nature Reviews Genetics 2018 (19) 453–467

Intra–TAD gain of function



Phenotype

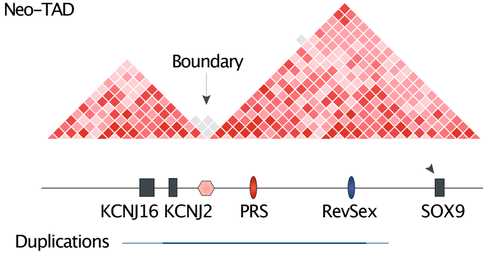
Duplications of enhancer elements cause preaxial synpolydactyly of feet

Examples

Gain of function:
- SOX9 locus: duplications of gonad enhancer cause 46,XX sex reversal
- BCL6 locus: duplications of super enhancers cause B cell lymphomas
- SHH locus: duplications of limb enhancer causes polydactyly

Loss of function:
- PAX6 locus: aniridia
- DLX5 and/or DLX6 loci: split hand foot malformation
- SOX9 locus: deletions of gonad enhancer cause 46,XY sex reversal

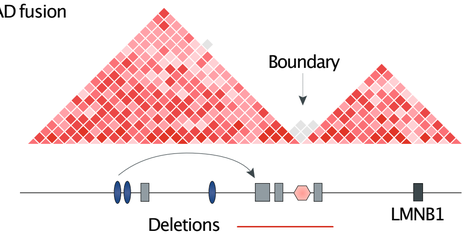
Neo–TAD

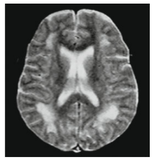


Cooks syndrome: Duplications of TAD boundary, KCNJ2 and KCNJ16 cause aplasia of nails and short digits

- FGF2 locus: colorectal cancer
- PRDM6 locus: medulloblastoma

TAD fusion

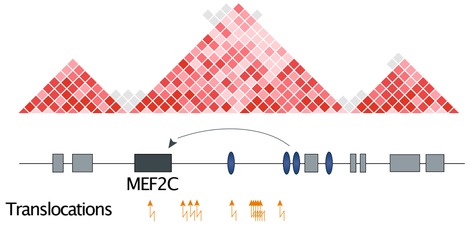


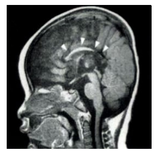


Adult–onset demyelinating leukodystrophy

- GFI1 locus: medulloblastoma
- TAL1 and LMO2 loci: T cell acute lymphoblastic leukaemia
- IRS4 locus: lung squamous carcinoma, sarcoma and cervical squamous carcinoma
- SOX4 locus: mesomelic dysplasia

TAD shuffling: loss of function

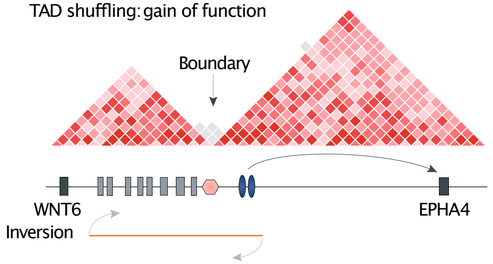




Hypoplastic corpus callosum via loss of function of MEF2C at 5q14.3

- FOXG1 locus: atypical Rett syndrome
- SOX9 locus: campomelic dysplasia
- DLX5 and DLX6 loci: split hand foot malformation

TAD shuffling: gain of function



F–syndrome: syndactyly

- SHH locus: inversion of enhancer causes short digits (Dsh mouse model)
- SHH locus: inversion of enhancer causes polysyndactyly
- GFI1 locus: medulloblastoma
- Translocation at the PITX1 locus: Liebenberg syndrome

Genes Regulatory elements Boundaries

@marciuslab
@mamartirenom

http://marciuslab.org

cnag

CRG Centre for Genomic Regulation

ICREA

Alexander Barclay
Nikolai Bykov
Iana Kim
Peter Hoboth
Anne Lee
Iago Maceda
John Markham
Maria Marti-Marimon
Ana Nikolovska
Mireia Novell
Meritxell Novillo
Maria Roy
Aleksandra Sparavier
Leo Zuber

.: Our current sponsors :.

European Commission

Ministerio de Ciencia e Innovación — Agencia Estatal de Investigación

Generalitat de Catalunya

NIH National Human Genome Research Institute