

# 3D genome and CTCF: known and unknown

Lou Shaoke

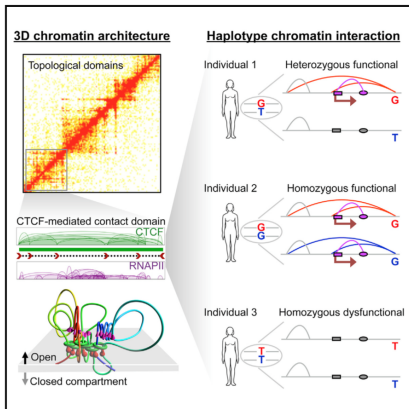
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February 29, 2016

# CTCF-Mediated Human 3D Genome Architecture Reveals Chromatin Topology for Transcription

## Graphical Abstract



## Authors

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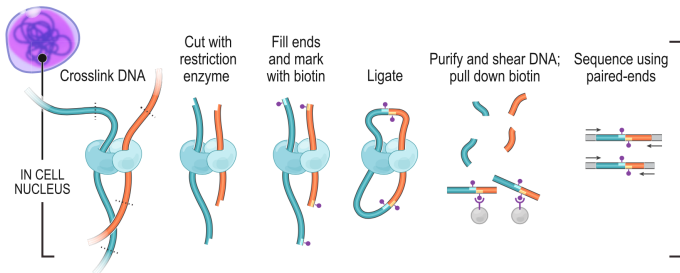
## Correspondence

yijun.ruan@jax.org

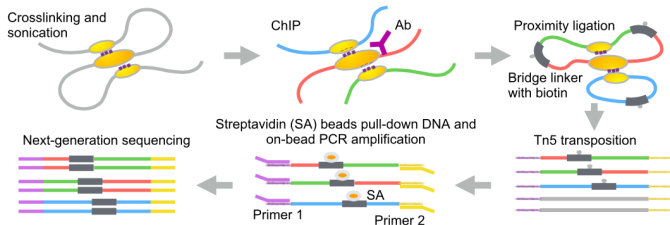
## In Brief

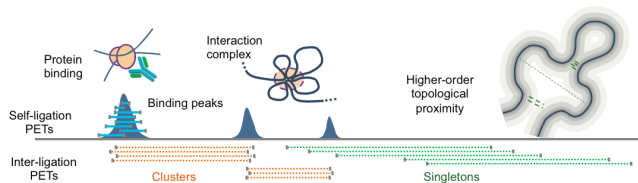
Advanced ChIA-PET shows that CTCF/cohesin and RNA polymerase II arrange spatial organization for coordinated transcription. Haplotype variants exhibit allelic effects on chromatin topology and transcription that link disease susceptibility.

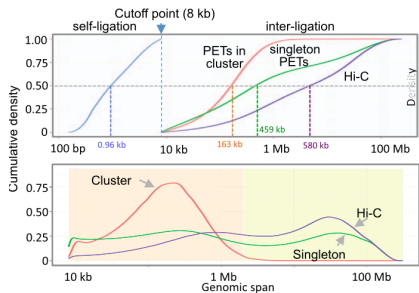
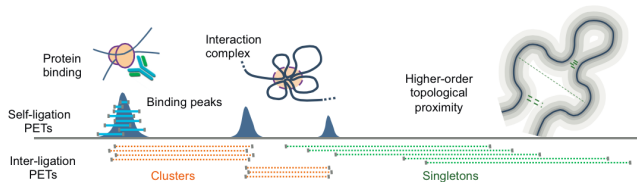
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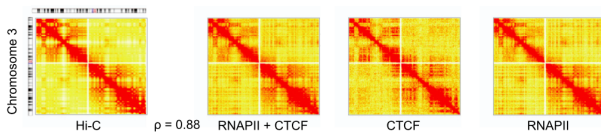
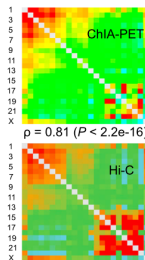
## ChIA-PET





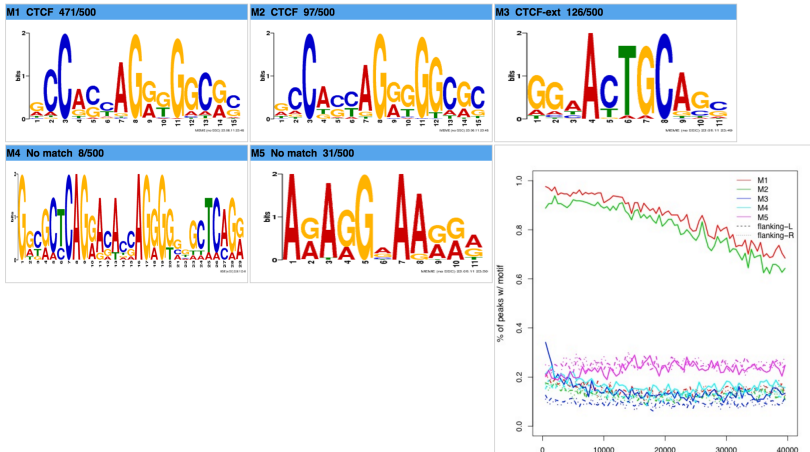


### C Inter-chromosome contacts

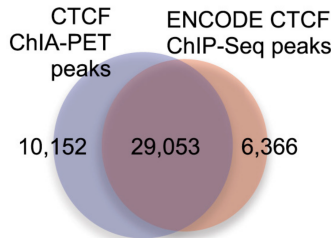
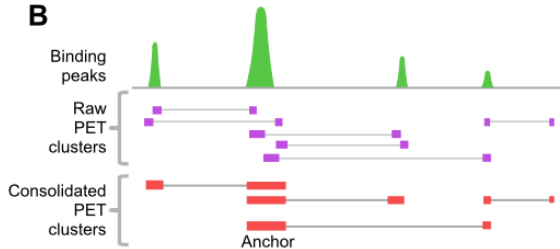


## CTCF: CCCTC-binding factor (zinc finger protein)

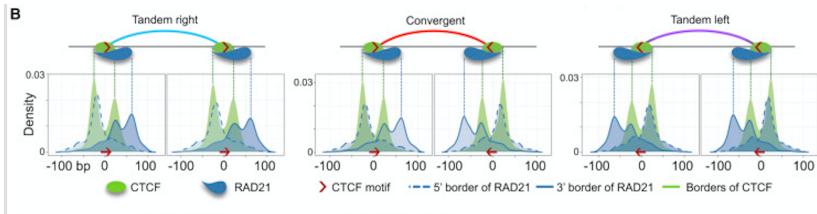
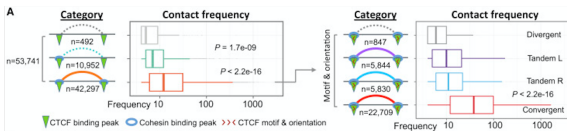
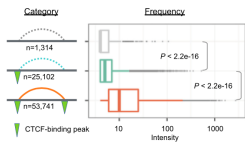
This gene is a member of the BORIS + CTCF gene family and encodes a transcriptional regulator protein with 11 highly conserved zinc finger (ZF) domains. Depending upon the context of the site, the protein can bind a histone acetyltransferase (HAT)-containing complex and function as a transcriptional activator or bind a histone deacetylase (HDAC)-containing complex and function as a transcriptional repressor. If the protein is bound to a **transcriptional insulator element**, it can **block communication between enhancers and upstream promoters**, thereby regulating imprinted expression...(refseq 2010)



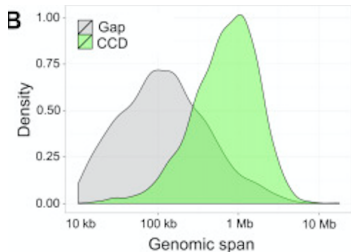
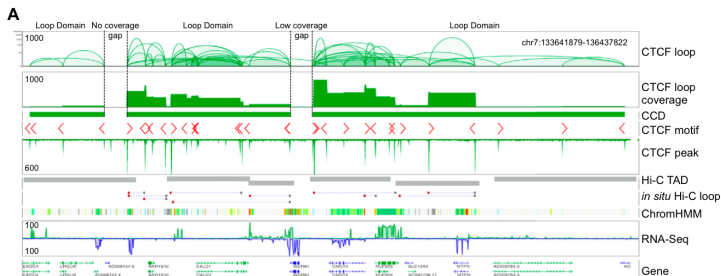
**B**



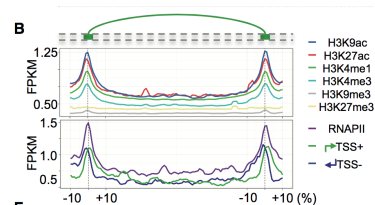
# CTCF: the anchor of interaction







Distribution of genomic span

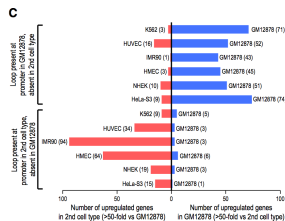
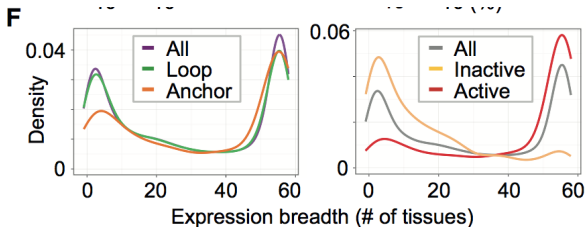
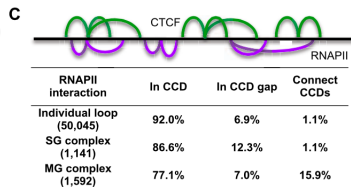
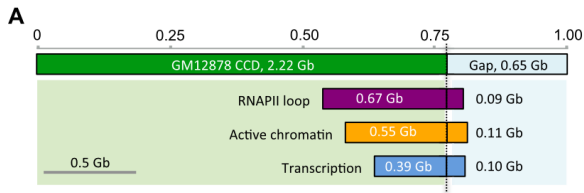


Aggregation plot

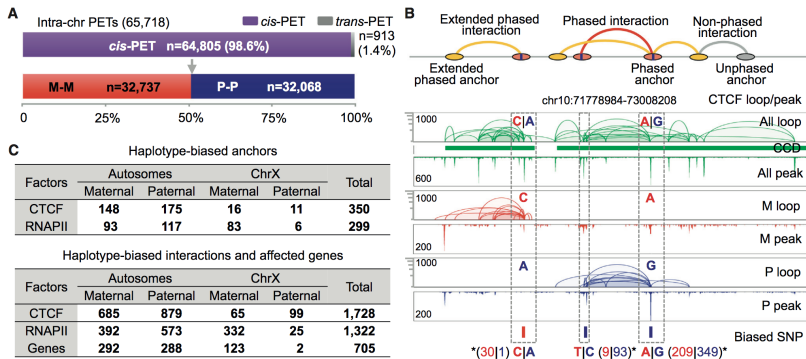
CCD: loop clustering and remove low loop coverage region, remain regions are gaps

# Gene expression with 3d interaction

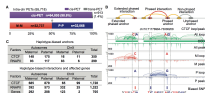
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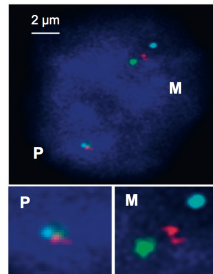
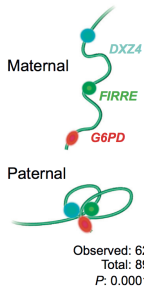
# Haplotype Mapping of Chromatin Interactions

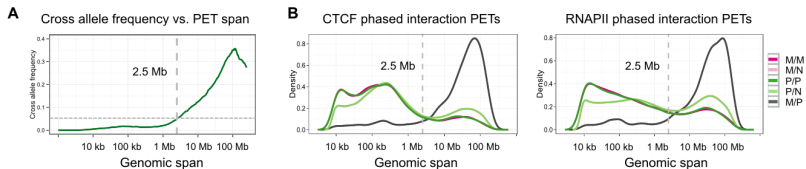


# Haplotype Mapping of Chromatin Interactions

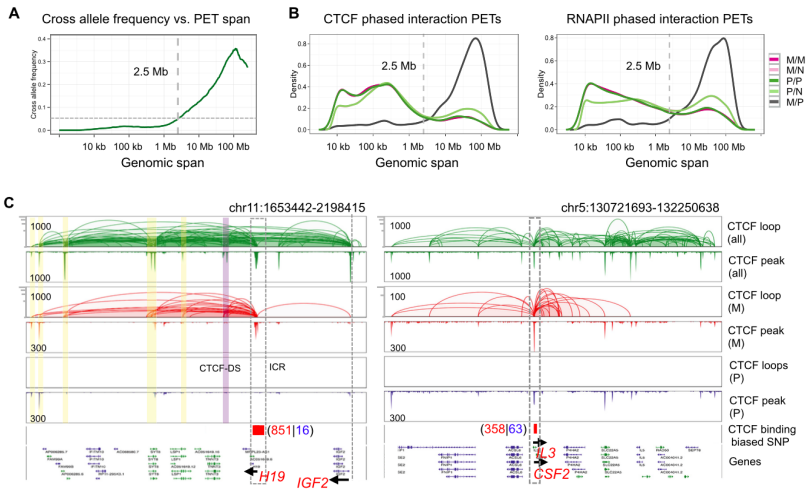


**E**

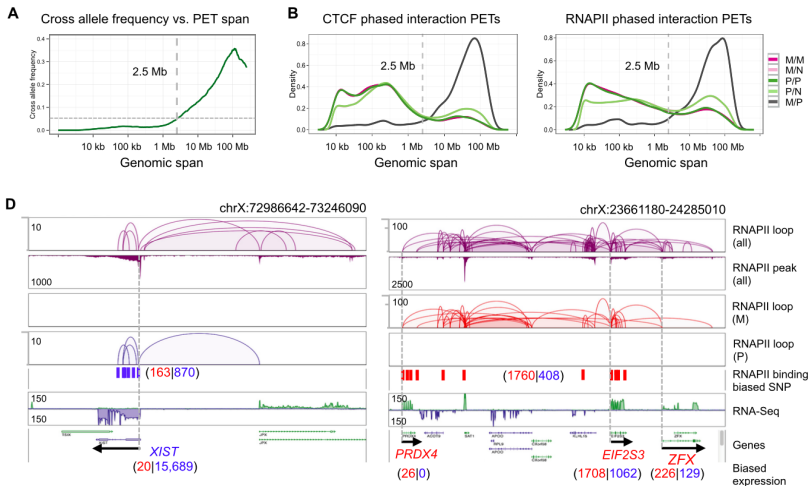




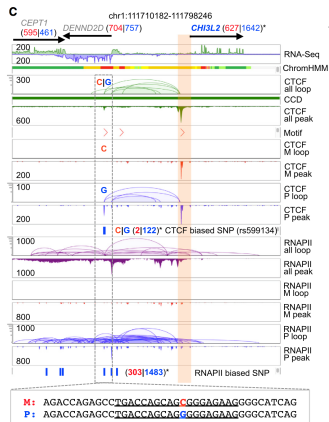
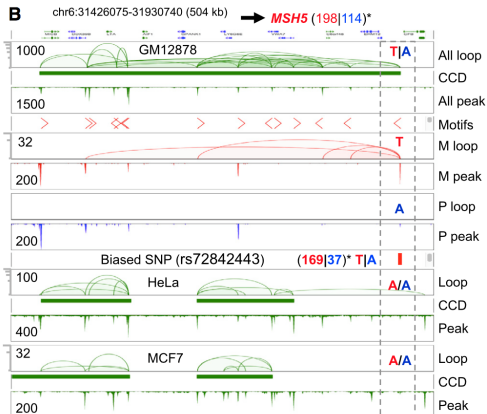
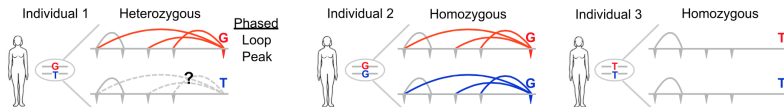
# Chromatin interaction and imprinting region



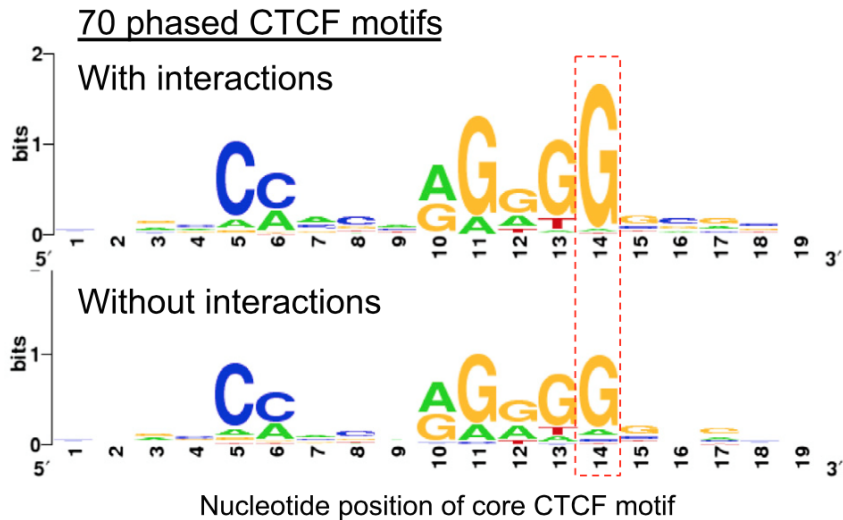
# Chromatin interaction and imprinting region



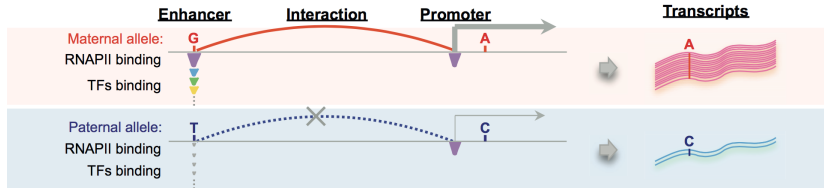
# CTCF ChIA-PET and Allelic specific binding

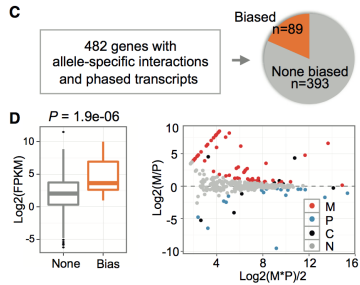
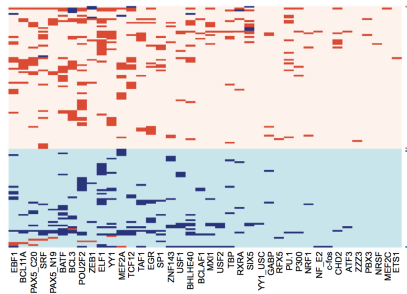
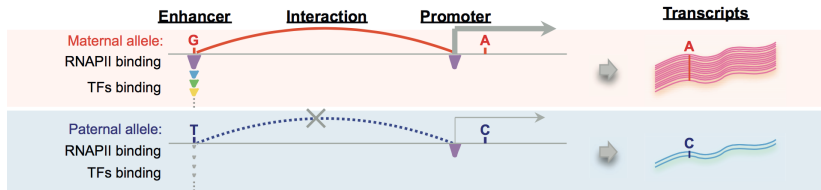




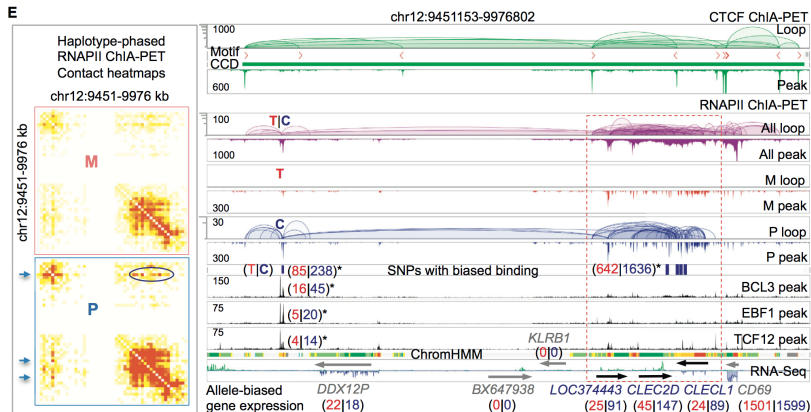
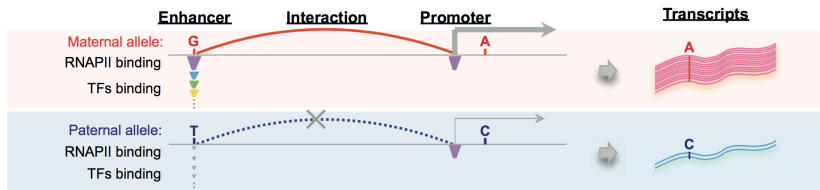


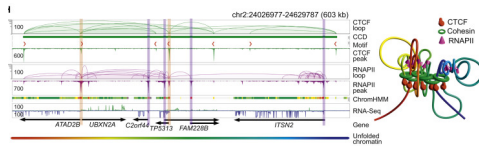
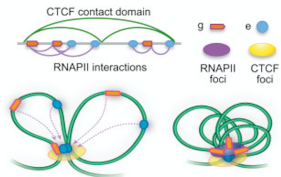
# Pol II ChIA-PET and allelic specific binding

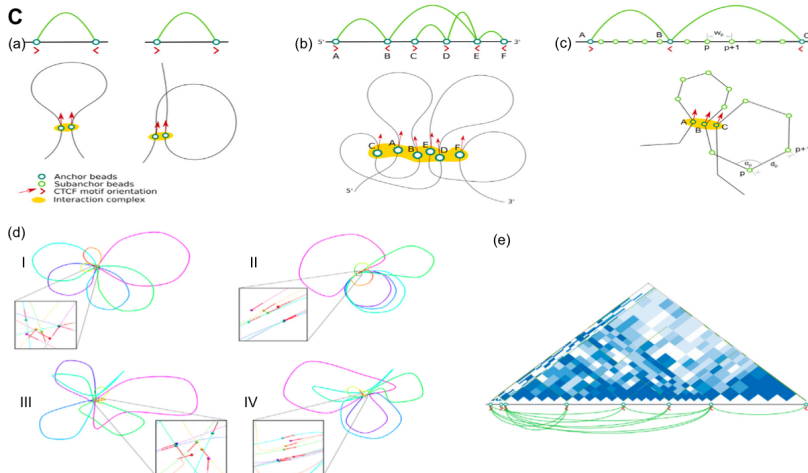




# Pol II ChIA-PET and allelic specific binding







# Chromatin extrusion explains key features of loop and domain formation in wild-type and engineered genomes

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Contributed by Eric S. Lander, September 18, 2015 (sent for review July 27, 2015; reviewed by Frank Alber, Ido Amit, Roger D. Kornberg, Corina E. Tarnita, and Shing-Tung Yau)

## Significance

When the human genome folds up inside the cell nucleus, it is spatially partitioned into numerous loops and contact domains. How these structures form is unknown. Here, we show that data from high-resolution spatial proximity maps are consistent with a model in which a complex, **including the proteins CCCTC-binding factor (CTCF) and cohesin**, mediates the formation of loops by a process of extrusion. Contact domains form as a byproduct of this process. **The model accurately predicts how the genome will fold, using only information about the locations at which CTCF is bound.** We demonstrate the ability to reengineer loops and domains in a predictable manner by creating highly targeted mutations, some as small as a single base pair, at CTCF sites.

(i)

Extrusion complex



CTCF motif



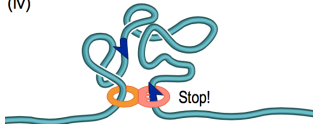
(ii)



(iii)



(iv)

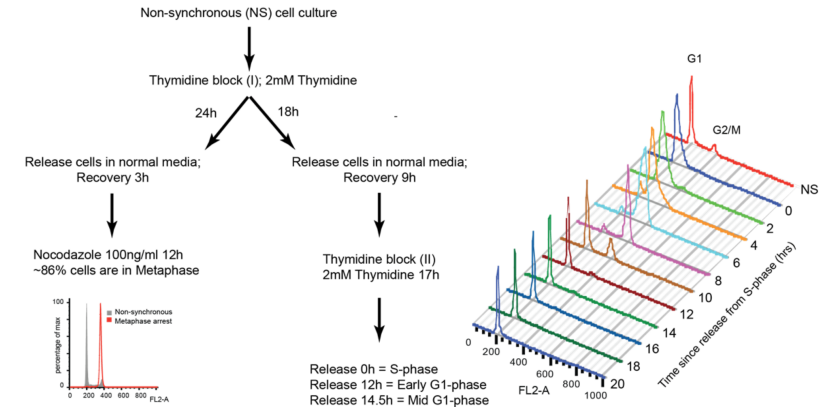


Loop extrusion has given a rational model that not only fit the outcome of chromatin folding, but indicate how the 3d structures are formed.

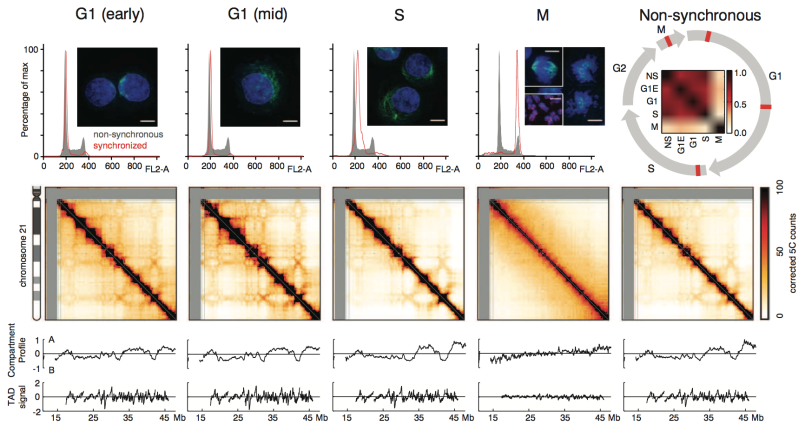
- 1) If this is true, where the loop extrusion enzyme start to fold? Randomly?
- 2) What happened on the gap regions?
- 3) anchor without CTCF binding motif/peak (Motif Gain here? Will check this)
- 4) Rare cross interaction pair;
- 5) The arrangement of anchors of interaction pairs will affect the detection by ChIA-PET?



# Cell cycle and chromatin interactions



(Natalia et. al. Science 22 Nov 2013)



## Organization of chromosome 21 through the cell cycle

(Natalia et. al. Science 22 Nov 2013)

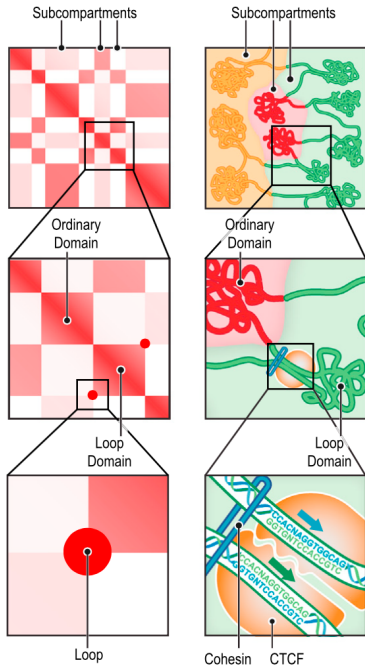
Current knowledge about gene regulation and function are heavily limited into a linear chromosome basis.

Replication timing, histone modification and DNA methylation covary with TAD, even can predict topology structure of chromatin.

The refined chromatin interaction will change the way we think about FunSeq and ENGINE.

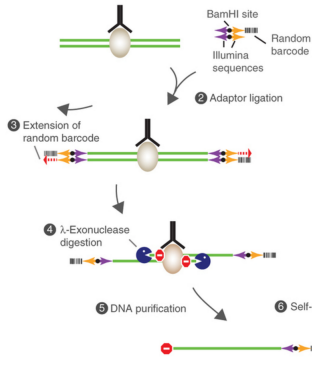
The End!

QA



# ChIP-Nexus

## a ① Chromatin immunoprecipitation



## ⑩ Map first base pair and strand orientation

