

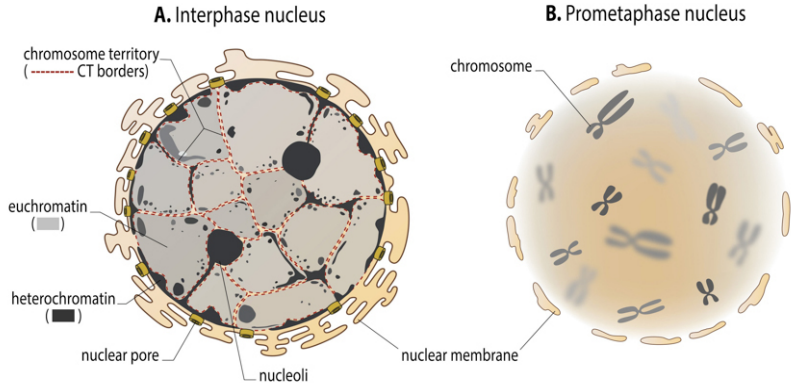
Interaktionen von RNAs und Proteinen

Sonja Prohaska

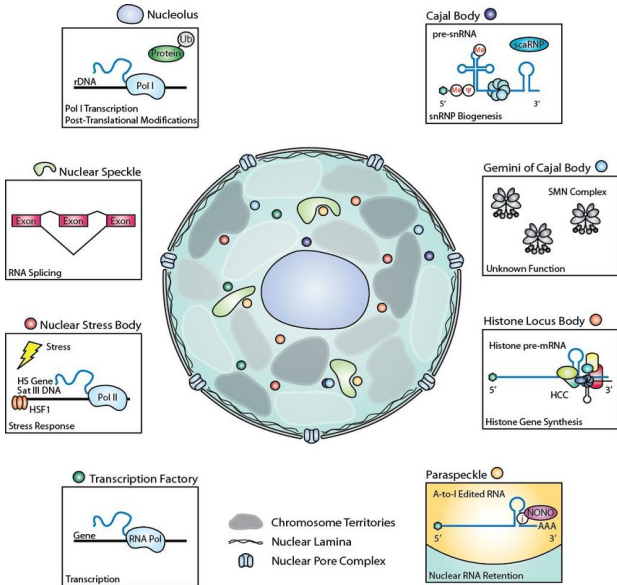
Computational EvoDevo group
Universität Leipzig

SS2019

DNA-DNA Interactions: Nuclear Organization



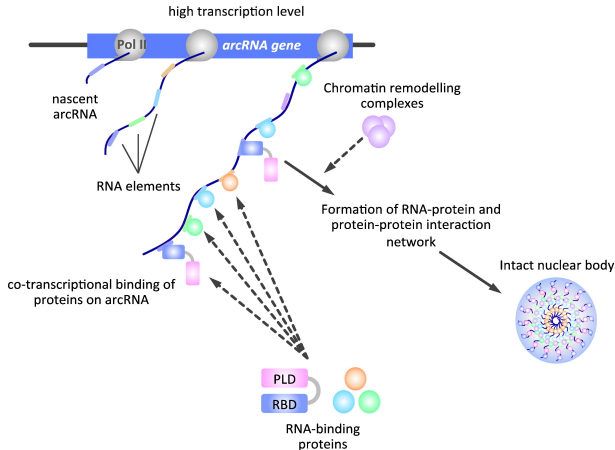
Nuclear Bodies Associated and Their Function



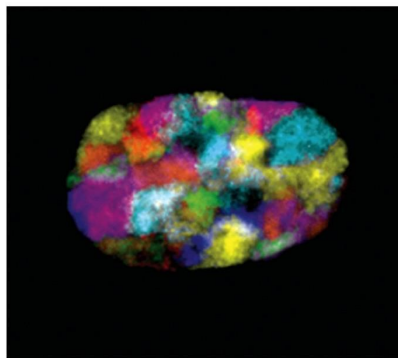
Organization of Nuclear Bodies by Long Noncoding RNAs

arcRNAs: architectural long noncoding RNAs

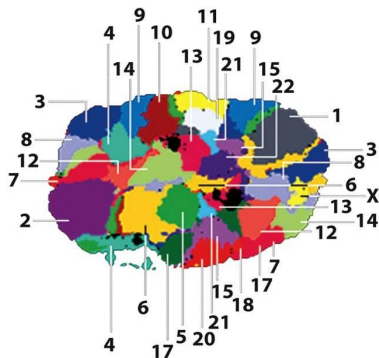
- ▶ nascent arcRNAs serve as scaffold for RNA binding proteins
- ▶ results in strong local enrichment of specific factors



Chromosome Territories

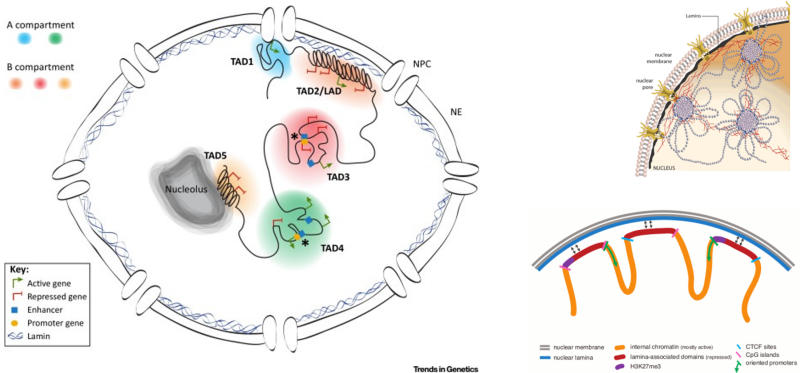


10 μm



Attachment of Chromatin to Nuclear Envelope

- ▶ S/MARs: Scaffold/Membrane attachment regions

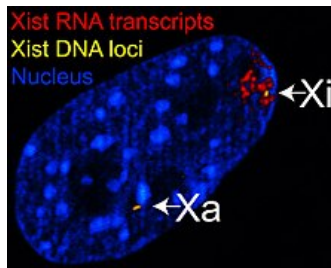
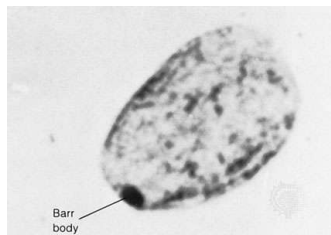


A Special Territory: The Inactive X Chromosome

Dosage compensation in placental mammals

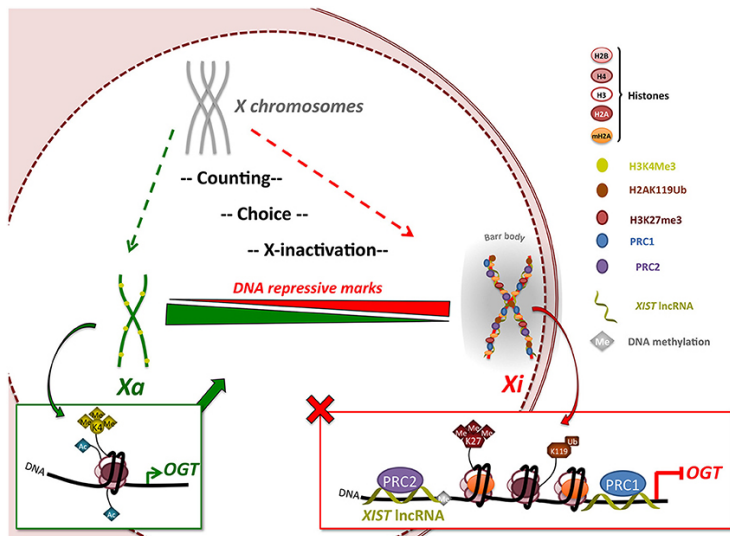
WHAT is happening?

- ▶ random X-inactivation
- ▶ female: $X, X \rightarrow X_a$ (active), X_i (inactive)
- ▶ male: $X, Y \rightarrow X_a$

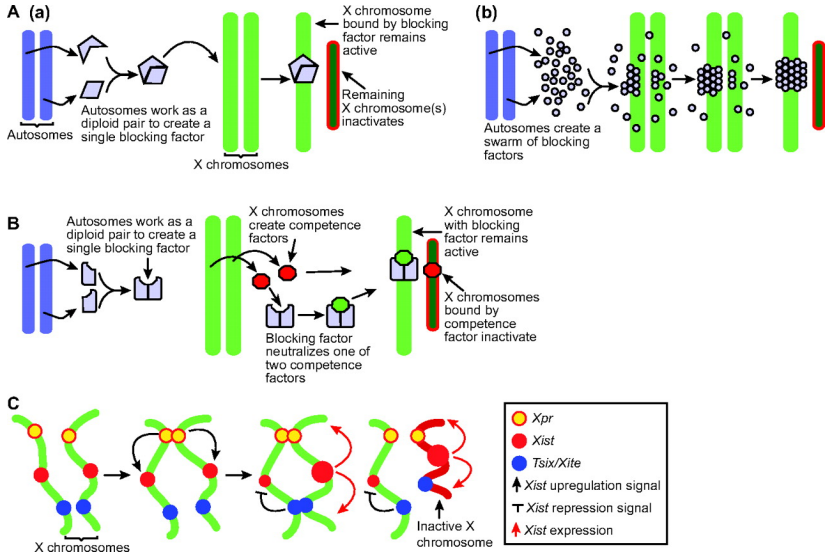


X Chromosome Inactivation (XCI)

HOW is it happening?



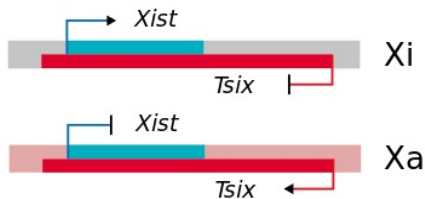
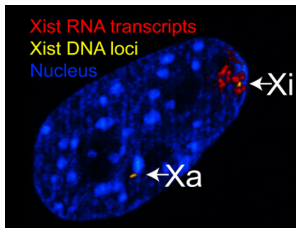
XCI – Counting and Choosing



several model try to explain

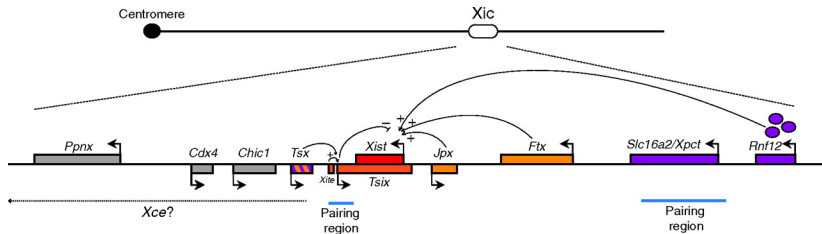
XCI – Main Player(s) Xist (and Tsix)

- ▶ lncRNA **Xist** (X-inactive specific transcript)
expressed from inactive X chromosome
is responsible for silencing the X in *cis* → X_i (inactive)
- ▶ lncRNA **Tsix** (antisense of Xist)
expressed from active X chromosome
is responsible for silencing Xist in *cis* → X_a (active)



The X Inactivation Center (Xic)

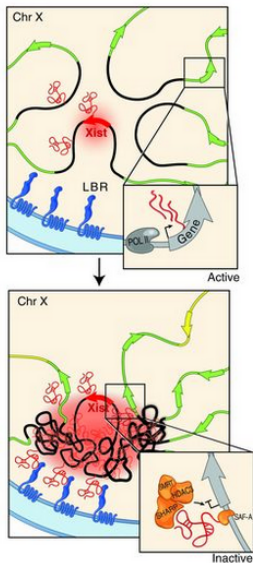
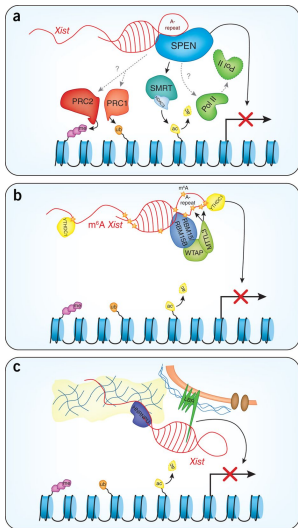
- ▶ **Xist**: X-inactivation specific transcript
17kb, spliced and polyadenylated transcript
- ▶ **Tsix**: antisense RNA of Xist
- ▶ genes (RNA or protein coding) promoting Xist expression
- ▶ genes (RNA or protein coding) suppressing Xist expression



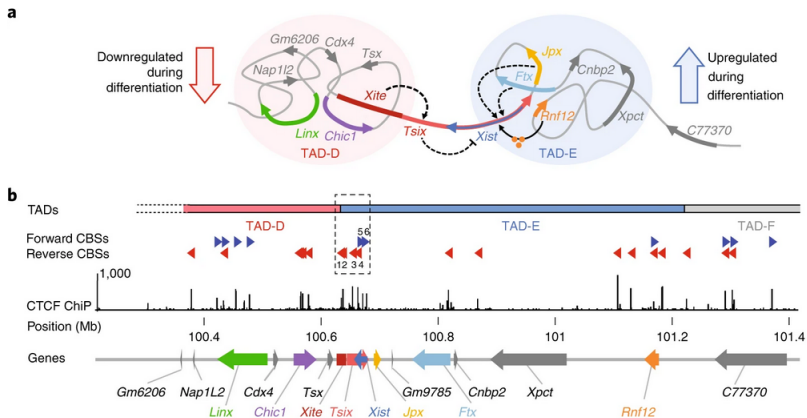
Proposed mechanisms

- ▶ Xist has binding sites for proteins (similar to arcRNAs)
- ▶ SPEN binds “repeatA” on Xist
interacts with SMRT-HDAC3 → deacetylation
may recruit PRC2 → H3K27me3 (repressive mark)
may recruit PRC1 → H2AK119ub (repressive mark)
excludes PolII from Xist-coated chromosome
- ▶ RBM15-WTAP interacts with Xist
recruits m⁶A machinery that methylates Xist
YTHDC1 reads m⁶A enables **transcriptional silencing**
- ▶ **LBR** (lamina binding receptor) links Xist-coated chromatin to lamin in the lamina

Xist Spreading and Lamina Localization



TADs at the Xic

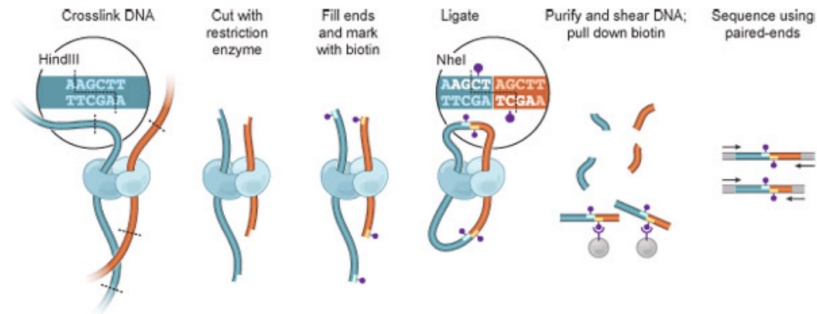


Measuring Chromatin Interactions

Chromosome Conformation Capture

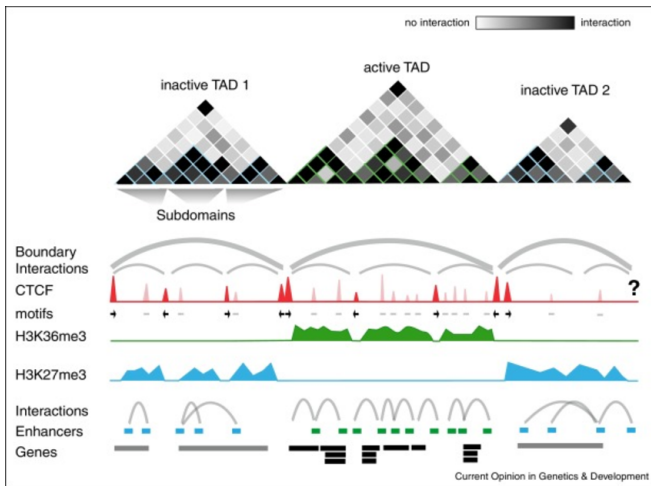
- ▶ a method to measure chromatin-chromatin interactions

Hi-C Method



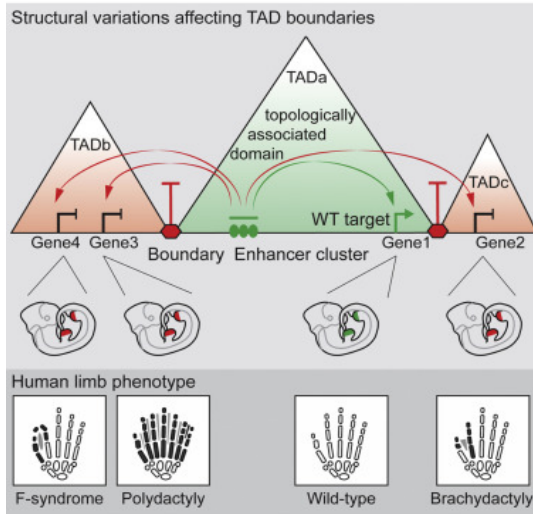
Topologically Associated Domains (TADs)

Structure of TADs



Topologically Associated Domains (TADs)

Functional/Regulatory Relevance



References

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Phase separation drives X-chromosome inactivation: a hypothesis
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- ▶ Chen et al.
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Science 354(6311), 468–472 (2016)
- ▶ Wang et al.
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Novel players in X inactivation: insights into Xist-mediated gene silencing and chromosome conformation
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