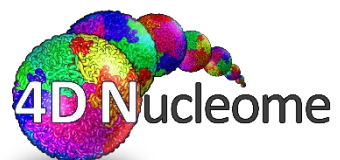


Common Fund 4DN Program

Olivier Blondel, NIDDK
Co-coordinator, 4DN Program

NIH Council Of Councils
Bethesda, January 26, 2018



The NIH 4DN Working Group

Program Co-Chairs:

Dinah S. Singer (NCI)
Phil Smith (NIDDK)
*Roderic Pettigrew (NIBIB)**

Program Coordinators:

Olivier Blondel (NIDDK)
Judy Mietz (NCI)
*Krishna Kandarpa (NIBIB)**

Common Fund Program Leader:

Ananda Roy (NIH OD)

Coordinating Team:

Initiative Leaders:

Lisa H. Chadwick (NIEHS)
Sean Hanlon (NCI)
Lisa Postow (NHLBI)
John Satterlee (NIDA)

Members:

Iddil Bekirov (NIDDK)
Tony Casco (NIH OD)
Richard Conroy (NIH OD)
Mike Pazin (NHGRI)

Working Group Members:

David Balasundaram (CSR)
Terry Bishop (NIDDK)
Anthony Carter (NIGMS)
Joe Gindhart (NIGMS)
Max Guo (NIA)
Matt Reilly (NIAAA)
Robert Riddle (NINDS)
Geetha Senthil (NIMH)
Jill Beaver (NIH OD)

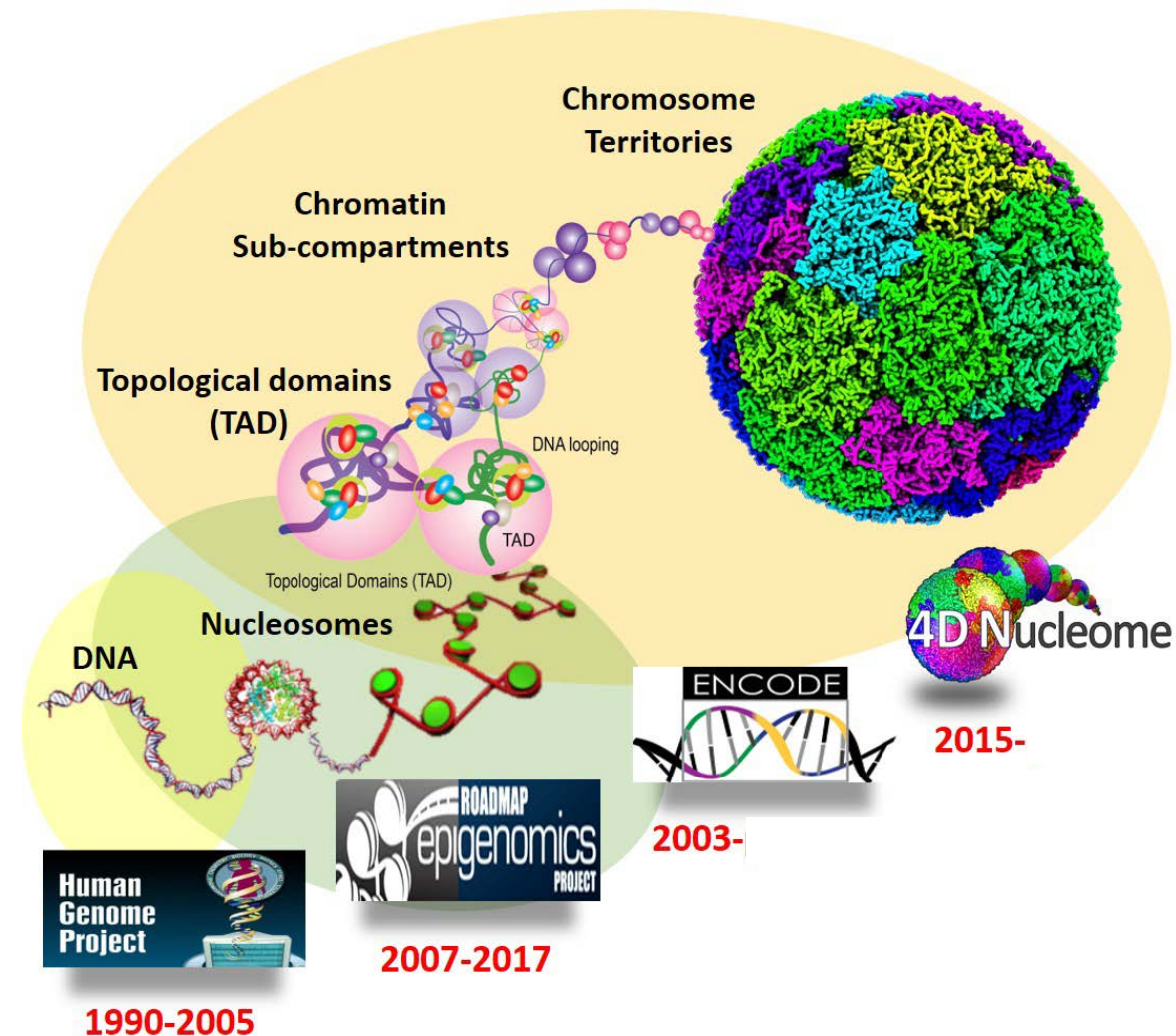
**Former*

Why A 4D Nucleome Program?

A high-resolution structure-function map of nuclear organization will provide critical new insights into our understanding of human health and disease.

Such a large scale challenge requires a concerted effort and technological advancements.

Exploring Genome Organization

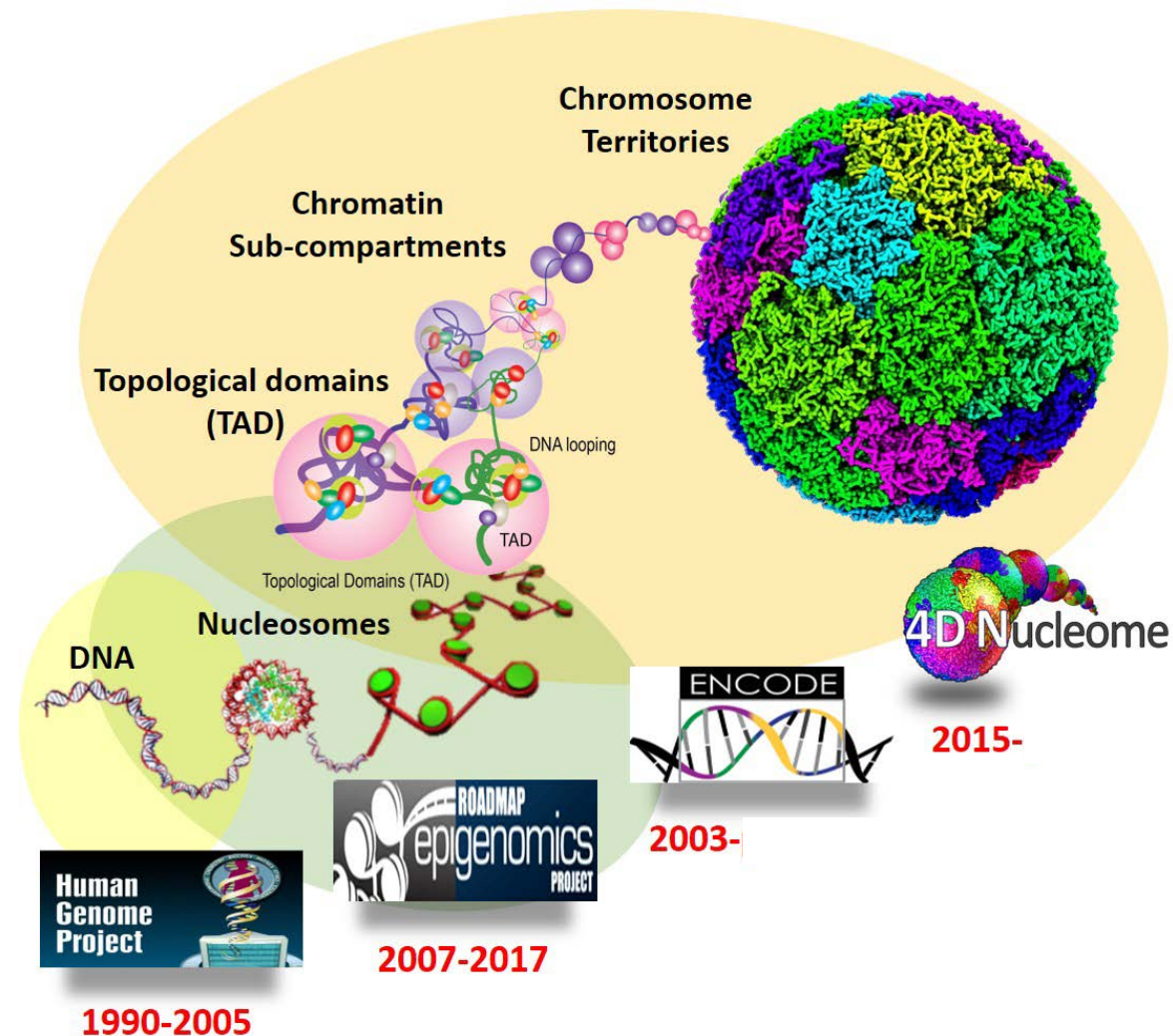


Goals And Deliverables

4DN was started in 2015 for an initial period of 5 years to deliver:

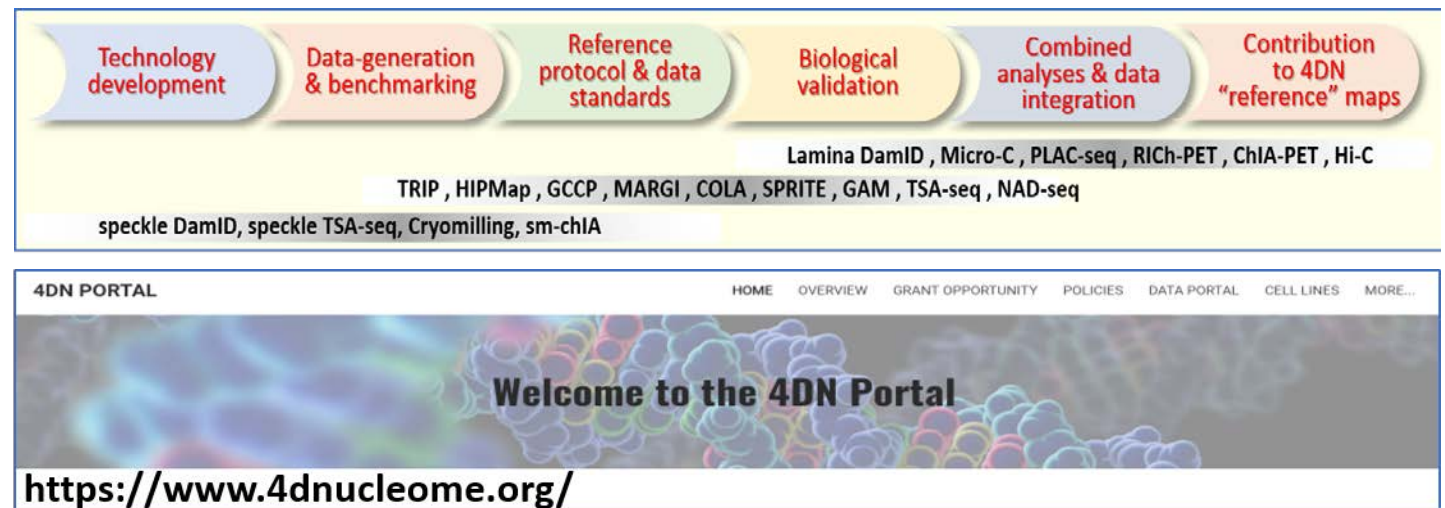
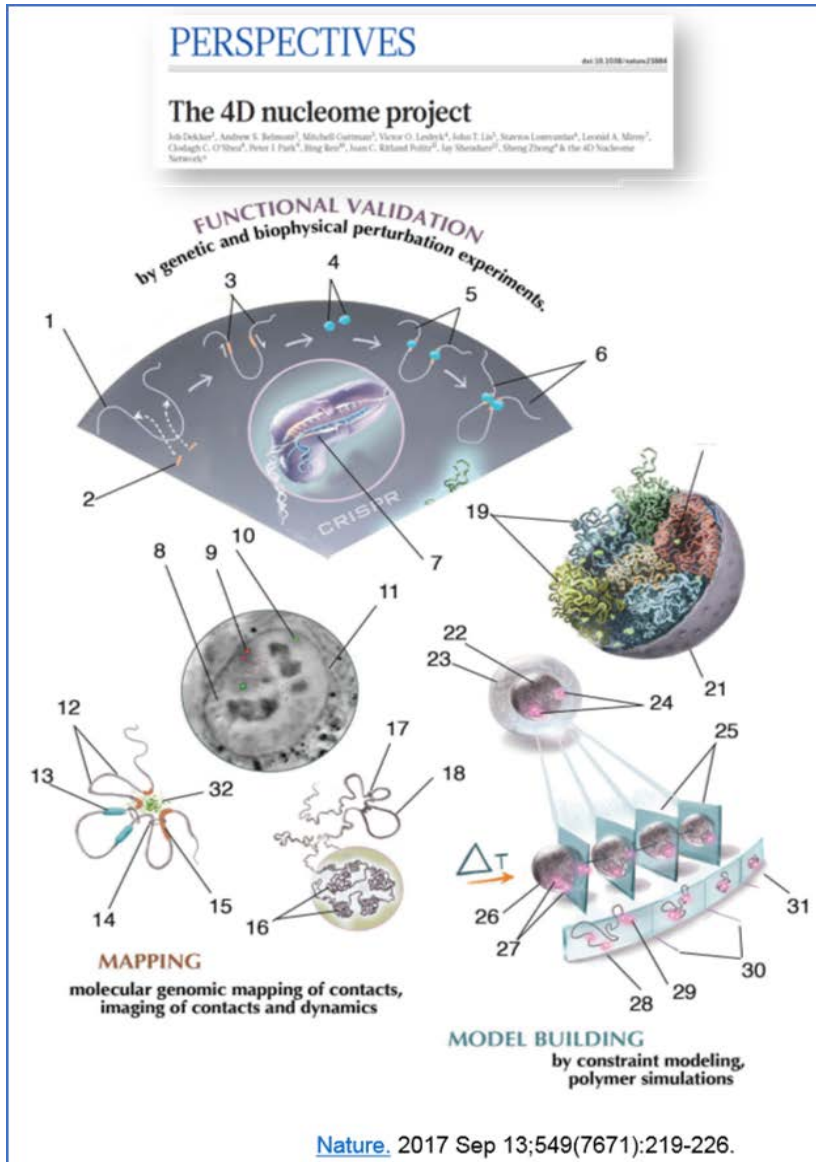
- . Next generation technologies;
- . Computational tools;
- . 3D Genome Maps;
- . Biological validation of 3D models;
- . Community standards;
- . Greater understanding of the contribution of nuclear compartments to nuclear organization.

Exploring Genome Organization



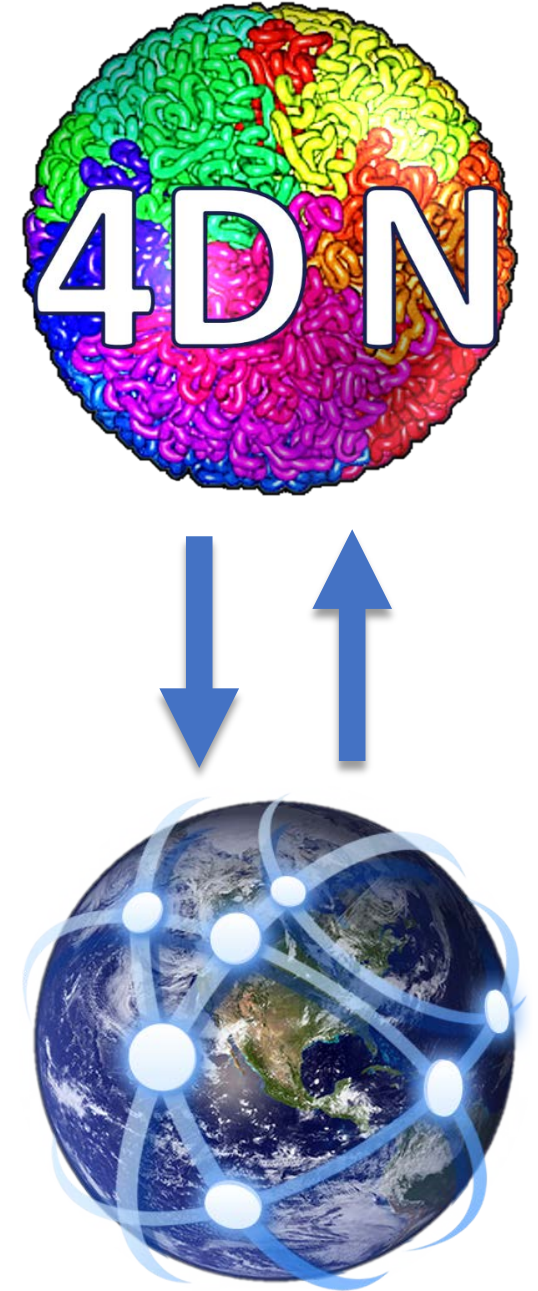
Accomplishments To Date

- . 30+ omics and 25+ imaging technologies;
- . 130+ omics datasets and 25+ protocols;
- . 60+ software packages;
- . Common cell line repository available to all;
- . Omics and Imaging data standards;
- . Consortium-wide 4DN Joint Analysis;
- . Over 160 publications and preprints.



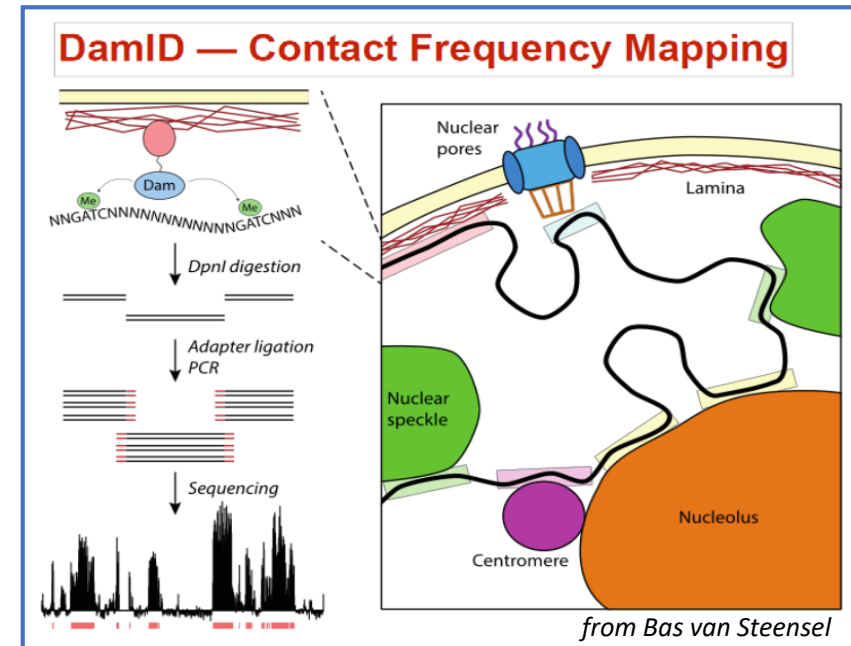
Outreach And Partnerships

- . Early sharing of pre-prints through bioRxiv ;
- . 2016 Transformative Collaborative Project Awards (TCPAs) ;
- . Joining the International Human Epigenome Consortium (IHEC) ;
- . Opening a full day of 4DN's annual meetings to the public ;
- . Implementation of 4DN Associate Membership;
- . Collaboration with ENCODE.



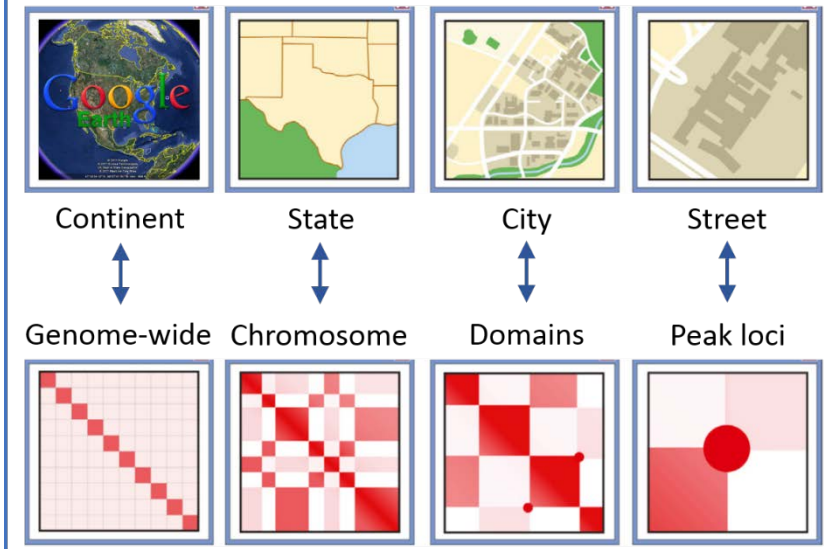
Consortium Efforts In The Next 2.5 Years

- . Benchmark and validate novel mapping and imaging technologies;
- . Combine technologies to describe principles of nuclear organizations;
- . Relate genome organization to nuclear structures using spatially-anchored sequencing-based technologies;
- . Transition omics technologies to single cell resolution, and explore the 4th dimension and cell-cell variations;
- . Produce a 1st generation of “Google Earth” 3D maps of the human nucleome in a few cell lines to define cell states.



Juicebox Provides a Visualization System for Hi-C Contact Maps with Unlimited Zoom

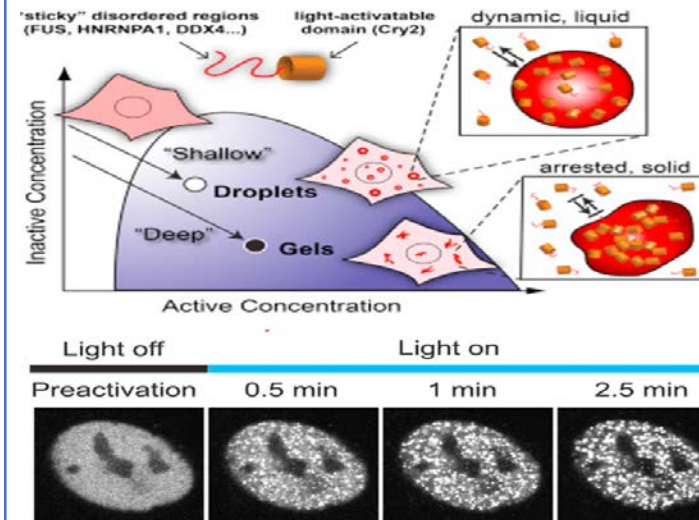
Durand NC, Robinson JT, Shamim MS, Machol I, Mesirov JP, Lander ES, Aiden EL. Cell Syst. 2016 Jul;3(1):99-101.



Envisioning the Future of 4DN

- . Establish 2nd generation of 3D maps for additional cell types and cell states;
- . Refine models of structure-function relationships in live cells using disruptors of genome architecture;
- . Transition single cell-resolution technologies from the dish to live tissues, organs and animal models;
- . Explore relationship between genetic and epigenetic background, genome organization and disease risk;
- . Make technologies, databases, analytical and visualization tools accessible and usable by the broader scientific community.

Using light to create membrane-less organelles (e.g. nuclear bodies).

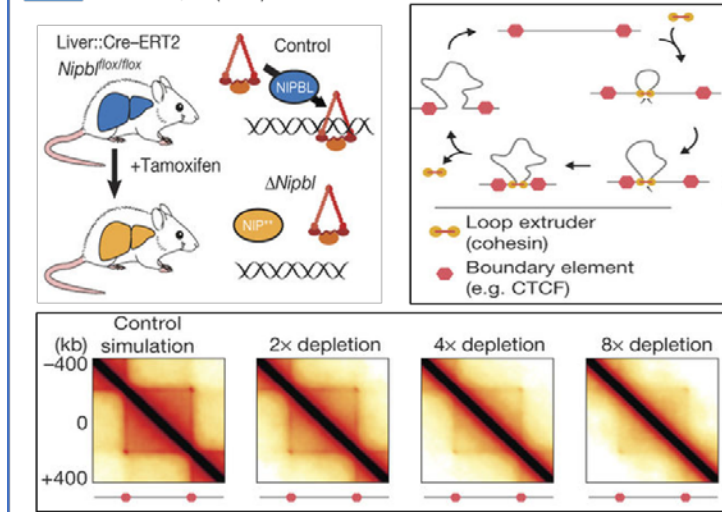


Brangwynne lab: Shin et al. 2017 Cell 168:159-171

Two independent modes of chromatin organization revealed by cohesin removal

Wibke Schwarzer^{1*}, Nezar Abdennur^{2*}, Anton Goloborodko^{3*}, Aleksandra Pekowska⁴, Geoffrey Fudenberg⁵, Yann Loe-Mie^{6,7}, Nuno A Fonseca⁸, Wolfgang Huber⁸, Christian H. Haering⁹, Leonid Mirny^{3,5} & Francois Spitz^{1,4,6,7}

Nature. 2017 Nov 2;551(7678):51-56.



Job Dekker, Ph.D.



*Professor and co-director
Program in Systems Biology
Department of Biochemistry and Molecular Pharmacology
University of Massachusetts Medical School*