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Chromatin organization in the nucleus provides a large repertoire of information in addition to that encoded genetically. Understanding how this information is established and possibly inherited through cell division is a challenge for the field. A key question is how histones, the major protein components of chromatin, as particular variants or post-translationally modified forms, can mark functional regions of the genome.

Our team is interested in understanding how chromatin organization is established, propagated, maintained, and changed during development and in response to environmental cues. Errors in these processes can lead to mis-regulation of genome functions and pathological outcomes, such as cancer.

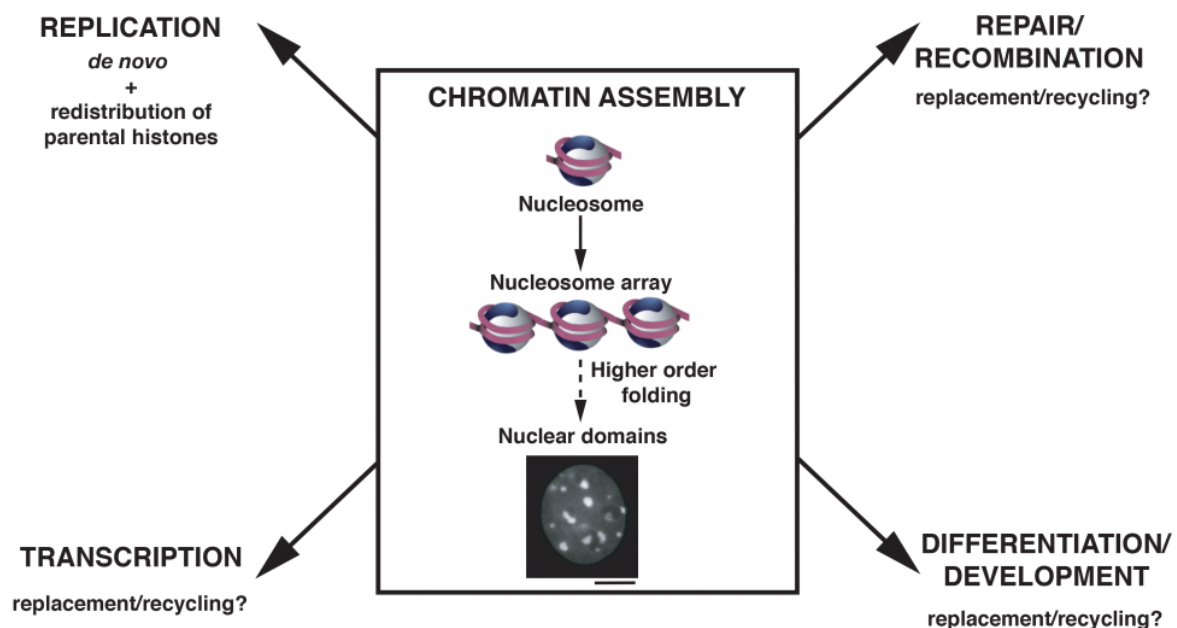


Figure 1 : Chromatin assembly during several DNA transactions in physiological contexts. To form the basic

building block of chromatin, the nucleosome, the DNA helix wraps around a central complex of histone proteins. This assembly uses both new histone deposition and recycling of parental histones from pre-existing nucleosomes.

Our general objective has been to dissect the mechanisms of chromatin assembly, from the basic structural unit, the nucleosome, up to higher-order structures in the nucleus (Fig. 1). We have characterized key chaperones involved in nucleosome assembly and defined the dynamics of new histone incorporation in chromatin. Our findings have shed light on the fundamental issues of the dynamics, fate, and inheritance of histones, with their specific marks typical of particular chromatin domains.

Our working hypothesis is that histone chaperones function in an 'assembly line' with specificity for individual histone variants to mark defined regions of the genome. Remarkably, we have found that misregulation of specific histone chaperones is a common feature of aggressive breast cancers.

Our plan is to analyze the regulatory pathways that target histone chaperones and variants to control the assembly line and its connecting network.

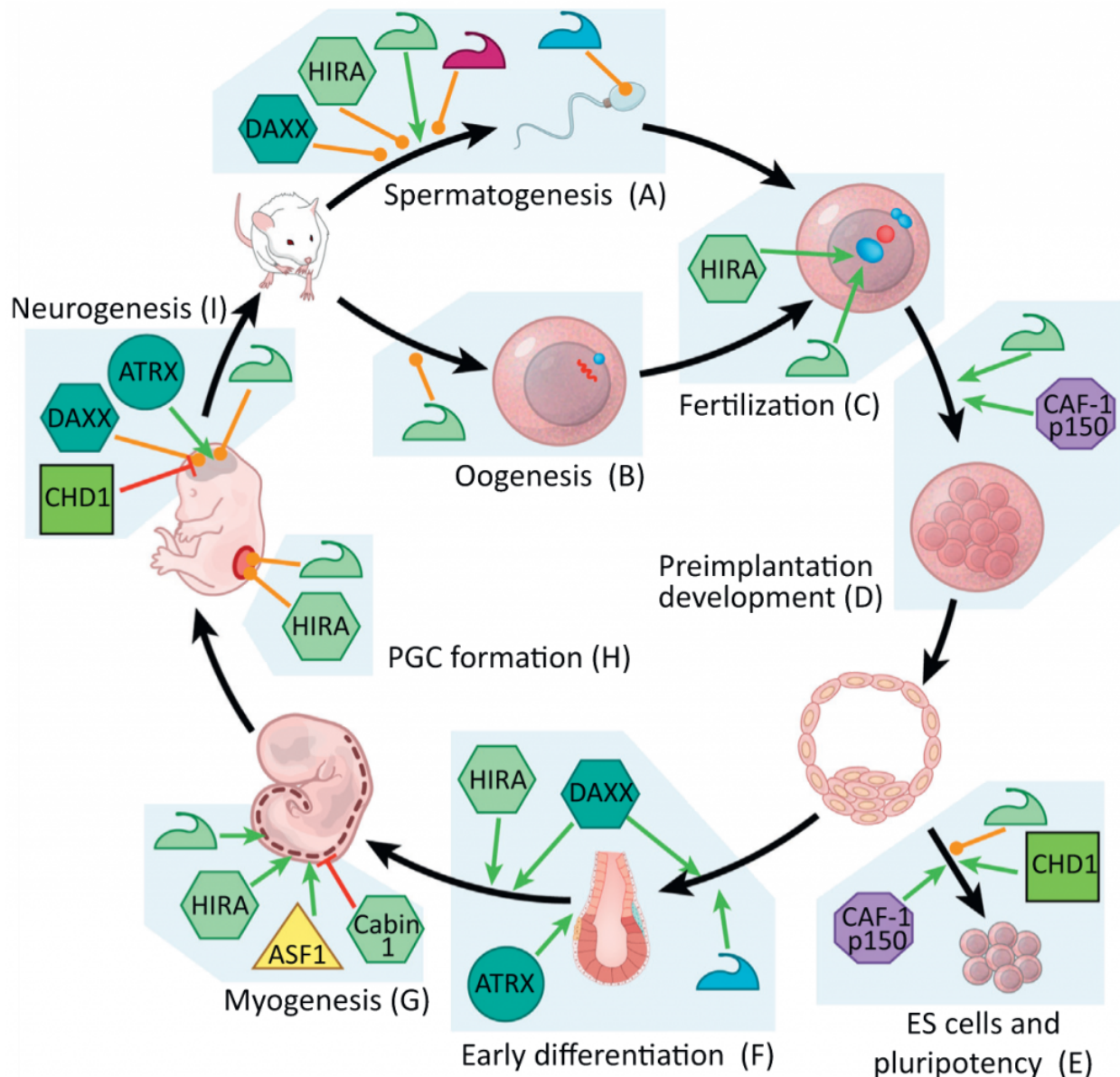


Figure 2. The importance of H3 variants and their chaperones during various stages of mouse development. The fusion of two highly differentiated gametes (A,B) into a zygote (C). This cell acquires totipotency and starts dividing (D,E), giving rise to daughter cells that will specialize progressively (F). The diverse cell lineages they establish will differentiate into the array of tissues in the adult organism (G,I). Among these lineages, primary germ cells (PGCs) undergo reprogramming to establish the germline of the adult (H), allowing it to produce either male or female gametes similar to those it originated from. H3 variants and their chaperones have been shown to contribute to the regulation of these processes (green or red arrows). For some, their contribution to developmental progression remains elusive (orange). From Filipescu D. et al., 2013.

Our specific approach to understanding all the *in vivo* functions of chromatin complexes is

based on tools and model systems (e.g. *Xenopus*, mouse) that combine biochemistry, cell biology, and developmental biology (Fig. 2). We examine specific nuclear domains: non-coding centromeric heterochromatic regions, which are of major importance for chromosome segregation.

Together these studies should ultimately help in the development of medical applications of relevance for cancer.

Key publications

Year of publication 2018

Aaron Mendez-Bermudez, Liudmyla Lototska, Serge Bauwens, Marie-Josèphe Giraud-Panis, Olivier Croce, Karine Jamet, Agurtzane Irizar, Macarena Mowinckel, Stephane Koundrioukoff, Nicolas Nottet, Genevieve Almouzni, Mare-Paule Teulade-Fichou, Michael Schertzer, Mylène Perderiset, Arturo Londoño-Vallejo, Michelle Debatisse, Eric Gilson, Jing Ye (2018 May 3)

Genome-wide Control of Heterochromatin Replication by the Telomere Capping Protein TRF2

Molecular cell : 70 : 449-461.e5 : [DOI : 10.1016/j.molcel.2018.03.036](https://doi.org/10.1016/j.molcel.2018.03.036)

Year of publication 2016

Sebastian Müller, Geneviève Almouzni (2016 Dec 1)

Chromatin dynamics during the cell cycle at centromeres.

Nature Reviews Genetics : 192-208 : [DOI : 10.1038/nrg.2016.157](https://doi.org/10.1038/nrg.2016.157)

Christèle Maison, Delphine Bailly, Jean-Pierre Quivy, Geneviève Almouzni (2016 Jul 19)

The methyltransferase Suv39h1 links the SUMO pathway to HP1 α marking at pericentric heterochromatin.

Nature communications : 12224 : [DOI : 10.1038/ncomms12224](https://doi.org/10.1038/ncomms12224)

Lisa Prendergast, Sebastian Müller, Yiwei Liu, Hongda Huang, Florent Dingli, Damaris Loew, Isabelle Vassias, Dinshaw J Patel, Kevin F Sullivan, Geneviève Almouzni (2016 Jun 11)

The CENP-T/-W complex is a binding partner of the histone chaperone FACT.

Genes & development : 1313-26 : [DOI : 10.1101/gad.275073.115](https://doi.org/10.1101/gad.275073.115)

Year of publication 2015

Hiroaki Tachiwana, Sebastian Müller, Julia Blümer, Kerstin Klare, Andrea Musacchio, Geneviève Almouzni (2015 Apr 1)

HJURP involvement in de novo CenH3(CENP-A) and CENP-C recruitment.

Cell reports : 22-32 : [DOI : 10.1016/j.celrep.2015.03.013](https://doi.org/10.1016/j.celrep.2015.03.013)

Year of publication 2014

Dan Filipescu, Sebastian Müller, Geneviève Almouzni (2014 Oct 8)

Histone H3 variants and their chaperones during development and disease: contributing to epigenetic control.

Annual review of cell and developmental biology : 615-46 : [DOI : 10.1146/annurev-cellbio-100913-013311](https://doi.org/10.1146/annurev-cellbio-100913-013311)