Katherine Duval

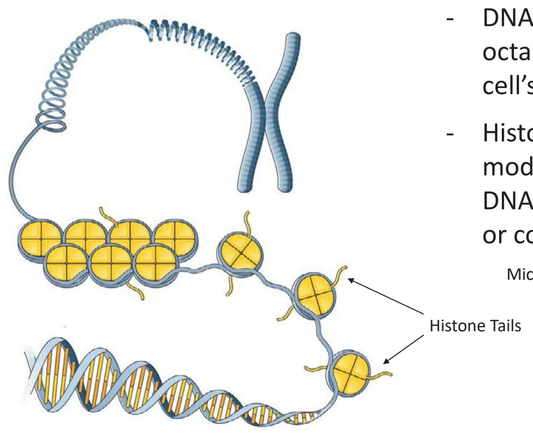
Ph.D. Candidate, Genetics
Third Year ARCS Scholar
Leake/ARCS Award

UNIVERSITY OF GEORGIA

Investigating Chromatin Organization in the Early Embryo

The human genome is massive – in fact, when stretched end-to-end, the DNA molecule from a single cell measures nearly five feet long! How does all of that DNA fit into a tiny cell in a way that still enables organisms to develop? The simple answer is chromatin, a scaffolding structure that packages DNA. Chromatin regulates gene expression by loosely packaging DNA at genes that need to be turned on and tightly packaging silenced regions. The initial fractionation of genomes into relaxed or compact chromatin regions occurs very early in embryo development, but the mechanisms that control this process remain almost completely unknown. Dysregulation of chromatin underlies many cancers and developmental disorders such as ATR-X, CHARGE, and ICF syndromes. Understanding how different chromatin states are established is the first step towards reinstating healthy chromatin regulation in disease.

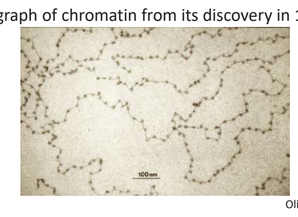
DNA is Packaged into Distinct Chromatin States



Institut Pasteur

- DNA is wrapped around histone octamers to organize it within the cell's nucleus
- Histone tails can be biochemically modified to signal that a region of DNA should be loosely packaged or compacted

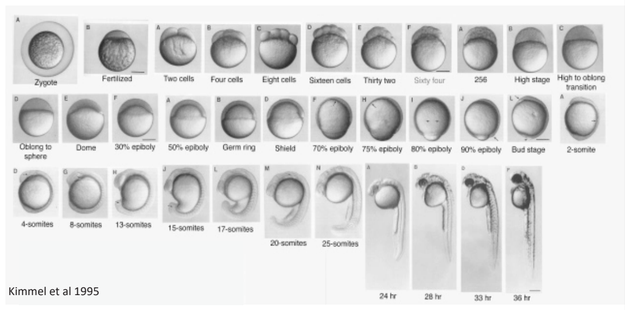
Micrograph of chromatin from its discovery in 1974



Olins & Olins 1974

Zebrafish as a Model for Embryonic Chromatin Regulation

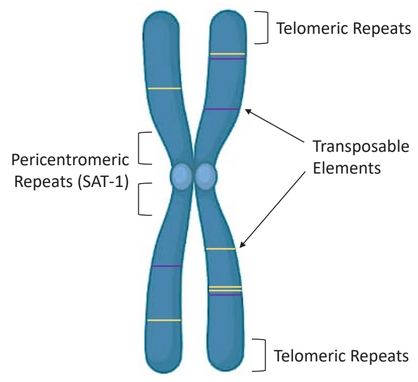
- Around 200 clear, synchronously developing embryos per cross
- One-cell embryos can be manipulated using microinjection



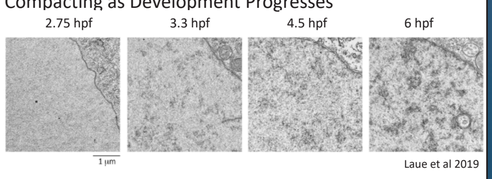
Kimmel et al 1995

Heterochromatin is Established at Repetitive DNA Sequences During Early Development

Types of Repetitive Sequences and Their Locations

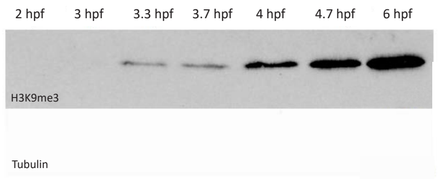


Transmission Electron Microscopy Reveals Chromatin Compacting as Development Progresses

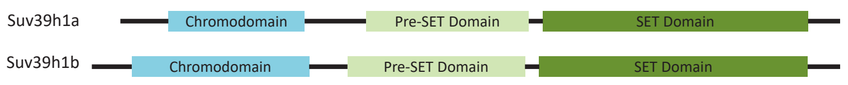


Laue et al 2019

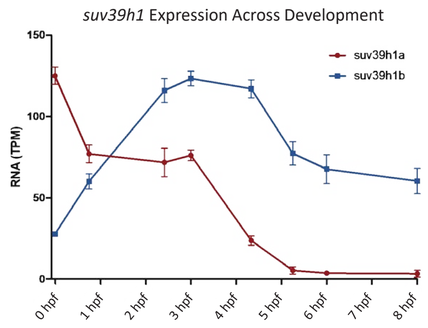
H3K9me3, a Biochemical Marker of Heterochromatin, Increases Over Embryogenesis



Suv39h1b is Necessary for Bulk H3K9me3 in the Early Embryo

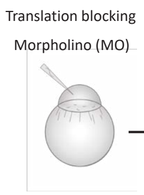


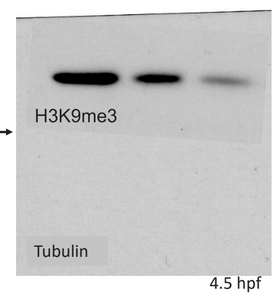
suv39h1 Expression Across Development



RNA-seq Data from White et al 2017

Translation blocking Morpholino (MO)

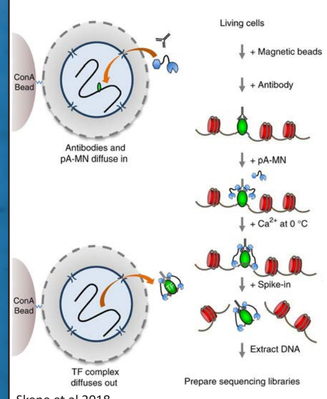




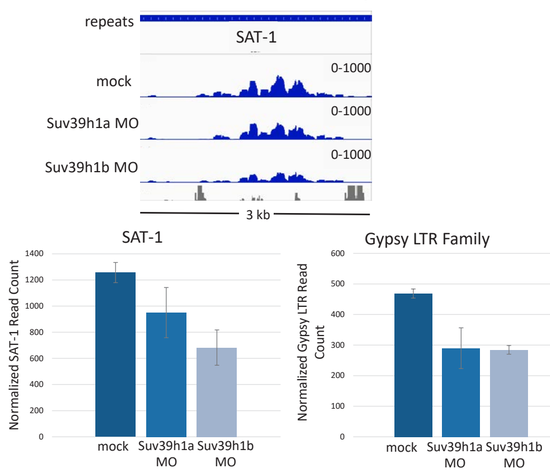
4.5 hpf

CUT&RUN Shows H3K9me3 Loss at Pericentromeric SAT-1 Repeats more Pronounced in Suv39h1b Morphants

CUT&RUN Workflow

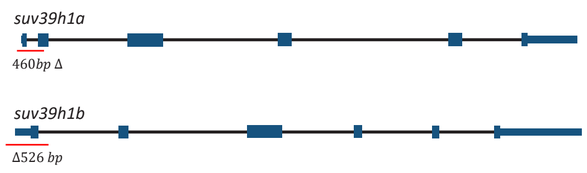


Skene et al 2018
Akdogan-Ozdilek* & Duval* et al 2021

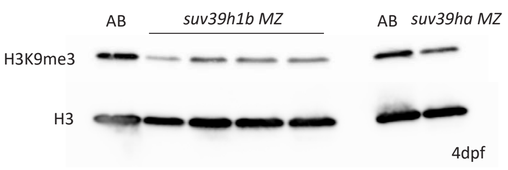


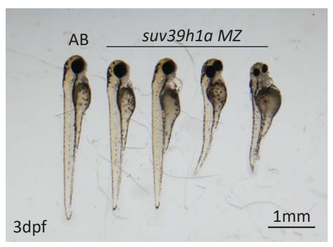
suv39h1 Mutants have Developmental and Molecular Phenotypes

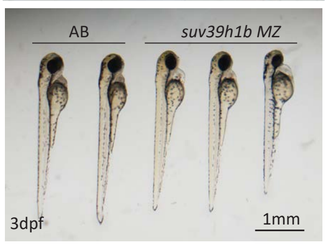
Mutations Generated Using CRISPR



Mutants Have Depleted H3K9me3 at 4 Days Post Fertilization







FOCUS ON THE FUTURE 2022

Scholar Awards Celebration
November 17, 2022