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# Epigenetic aging in oocytes



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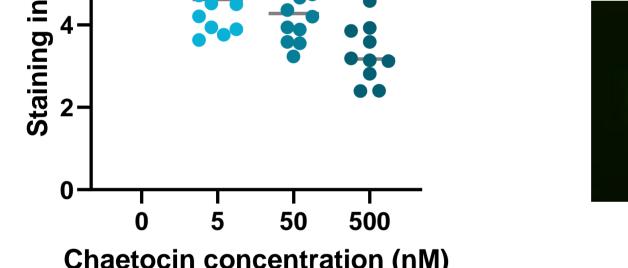
## Introduction

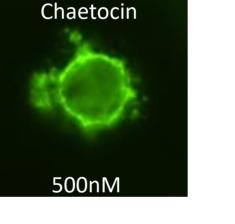
Aging oocytes significantly affect female fertility, particularly in advanced maternal age, leading to increased rates of aneuploidy and related syndromes such as Down syndrome. A key factor in this process is heterochromatin loss, which affects chromosomal stability during meiosis. This study investigates the link between heterochromatin loss and chromosomal instability, focusing on kinetochore function, sister chromatid cohesion and telomeric damage-induced foci (TIFs). Using Chaetocin as a model to induce heterochromatin loss, we analyze its effects on key chromosomal markers. Additionally, we evaluate the potential of Curcumin to restore heterochromatin levels, improve oocyte maturation, and enhance embryo viability. Understanding these mechanisms may contribute to strategies for reducing aneuploidy and enhancing in-vitro maturation (IVM) techniques.

#### Aims

- Investigating the mechanisms by which loss of heterochromatin in oocytes contributes to chromosomal instability and aneuploidy.
- Examining whether increasing heterochromatin levels can improve embryo development in IVF.

Experiment 1	<b>Methods &amp; Results</b> Experiment 2	
H3K9me2 N=7 N=14 N=12 N=10 ** *** **** **** H3K9me2	Curcumin 50 () 40 () 30 20 20 () 20 () 40 () 20 () 40 () 20 () 40 () 20 () 40 () 40 (	<b>Figure 2. Fertilization Rates (%) in Young (2M) and Old (9M) Mice.</b> Fertilization percentages on days 1 and 3 after fertilization under control and Curcumin treatments, comparing age groups.





Chaetocin concentration (nM)

Figure 1. Chaetocin Treatment Reduces H3K9me2 Levels in a Dose-Dependent Manner. Chaetocin treatment leads to a dose-dependent decrease in H3K9me2 levels, reflecting the reduction in heterochromatin. Statistical significance is indicated (\*\*p < 0.01, \*\*\*p < 0.001, \*\*\*\*p < 0.0001).

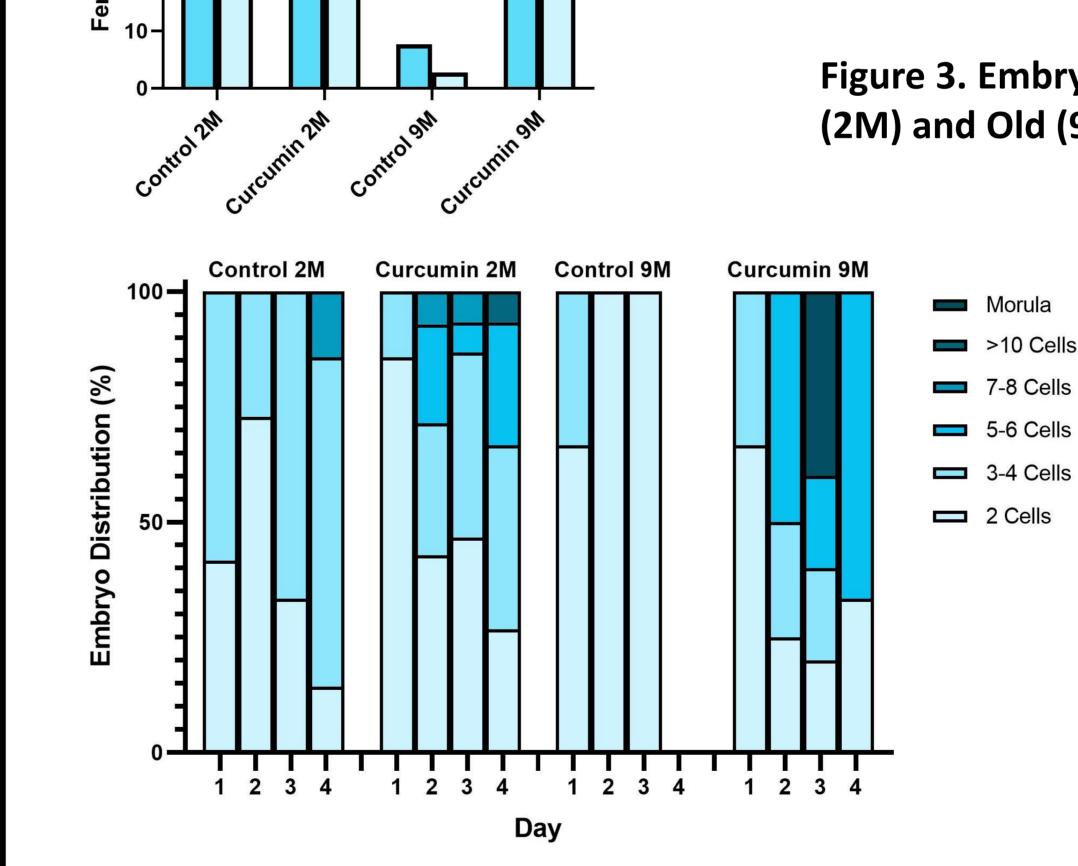


Figure 3. Embryo Development Distribution (%) in Young (2M) and Old (9M) Mice. The percentage distribution of embryos at various developmental stages over days 1-4 in young (2M) and old (9M) mice under control and Curcumin treatments.

#### Conclusions

Our research highlights the critical role of heterochromatin in maintaining chromosomal stability during meiosis. Understanding these epigenetic changes can provide valuable insights for improving fertility treatments and reducing aneuploidy risks in assisted reproductive technologies. These findings support the development of targeted interventions, such as curcumin supplementation, to enhance oocyte quality and embryo viability in aging individuals.

### **Future plans**

Sinetochore, cohesin and telomere components staining

Retrotransposons levels 0.

Chromosome spreads Maturation+aneuploidity

#### **References**:

[1] Wasserzug-Pash, P., & Klutstein, M. (2023). Epigenetic aging in oocytes. Aging (Albany NY), 15(15), 7334-7335. [2] Bricarelli, D., et al. (1989). Parental age and the origin of trisomy 21: A study of 302 families. Human Genetics, 82(1), 20-26. [3] Wasserzug-Pash, P., et al. (2022). Loss of heterochromatin and retrotransposon silencing as determinants in oocyte aging. *Aging Cell, 21*(3), e13568.

[4] Sun, H., et al. (2010). Inhibition of p300-HAT results in reduced histone acetylation and down-regulation of gene expression in cardiac myocytes. Life Sciences, 87(23-26), 707-714.





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