

# IMEG Seminar Series

## The road to global science

**Dr. Xin Chen** Professor, Department of Biology, Johns Hopkins University, Investigator, Howard Hughes Medical Institute, USA



**November 19 th, 2021, 9:00~10:00**

### Breaking symmetry: asymmetric histone inheritance

This seminar series is for all students and researchers in Kumamoto University. The seminar is jointly hosted by Grant-in-Aid for Scientific Research on Innovative Areas, "**Replication of non Genome**". Check your email and find the Zoom ID and passcode.

Most of the cells within a multicellular organism carry identical DNA sequences but take on a wide variety of fates by differential gene expression. This process is regulated through the epigenome, particularly the post-translational modifications of histones, which inform gene expression in a temporo-spatially specific manner. Considering that all cells in a multicellular animal originate from a single zygote, one key question is how different epigenomes are established to regulate distinct fates of the daughter cells resulting from divisions of their mother cell. Our previous and current work has led to the discoveries that during asymmetric division of stem cells, preexisting old histones are selectively retained in the stem cell, whereas newly synthesized histones are enriched in the daughter cell that is committed to differentiation. This process provides an important mechanism that allows the two daughter cells to each inherit different epigenetic information from a single cell division. These intriguing findings urge us to better understand how cells maintain their epigenetic memories or reset their epigenome. We found that the mechanism and readout of asymmetric histone inheritance is at least a three-step process, wherein old and new histones are asymmetrically incorporated during DNA replication (Step 1) and are segregated in a biased manner during mitosis (Step 2), driving differential inheritance of key factors to define distinct cell fates (Step 3). Our recent studies on all three steps will be discussed. The generality of these mechanisms used in other stem cell systems or asymmetrically dividing cells will also be discussed.

#### References

1. Zion, E. and Chen, X. Asymmetric histone inheritance regulates stem cell fate in *Drosophila* midgut, biorxiv doi: <https://doi.org/10.1101/2020.08.15.252403>.
2. Ranjan, R.<sup>#</sup>, Snedeker, J.<sup>#</sup>, Wooten, M.<sup>#</sup> et. al., and Chen, X.\* Differential condensation of sister chromatids coordinates with Cdc6 to ensure distinct cell cycle progression in *Drosophila* male germline stem cell lineage, biorxiv, doi: 10.1101/2021.03.08.434490
3. Ranjan, R., Snedeker, J., and Chen, X. (2019) Asymmetric centromeres differentially coordinate with mitotic machinery to ensure biased sister chromatid segregation in germline stem cells, *Cell Stem Cell*.
4. Wooten, M. et. al., and Chen, X. (2019) Asymmetric histone inheritance via strand specific incorporation and biased replication fork movement, *Nature Structural & Molecular Biology*.
5. Xie, J. et. al., and Chen, X. (2015) Histone H3 Threonine phosphorylation regulates asymmetric histone inheritance in the *Drosophila* male germline, *Cell*.
6. Tran, V.<sup>#</sup>, Lim, C.<sup>#</sup>, Xie, J. and Chen, X. (2012) Asymmetric division of *Drosophila* male germline stem cell shows asymmetric histone distribution. *Science*.  
(#: equal contribution)