

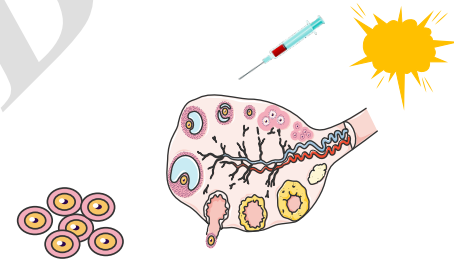
***Cite this as:*** Quanmin KANG, Fang LE, Xiayuan XU, Lifang CHEN, Shi ZHENG, Lijun LOU, Nan JIANG, Ruimin ZHAO, Yuanyuan ZHOU, Juan SHEN, Minhao HU, Ning WANG, Qiongxiao HUANG, Fan JIN, 2025. High-dose estrogen impairs demethylation of H3K27me3 by decreasing Kdm6b expression during ovarian hyperstimulation in mice. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 26(3):269-285. <http://doi.org/10.1631/jzus.B2300681>

# High-dose estrogen impairs demethylation of H3K27me3 by decreasing Kdm6b expression during ovarian hyperstimulation in mice

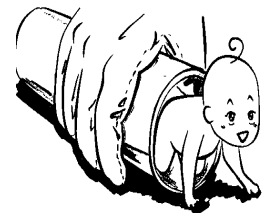
**Key words:** Ovarian stimulation; Histone methylation; Assisted reproductive technology (ART)

# Research Summary

This article revealed that hyperstimulation-induced high-dose estrogen could impair the demethylation of H3K27me3 by reducing Kdm6b expression, and explored the key pathway in the following aspects:

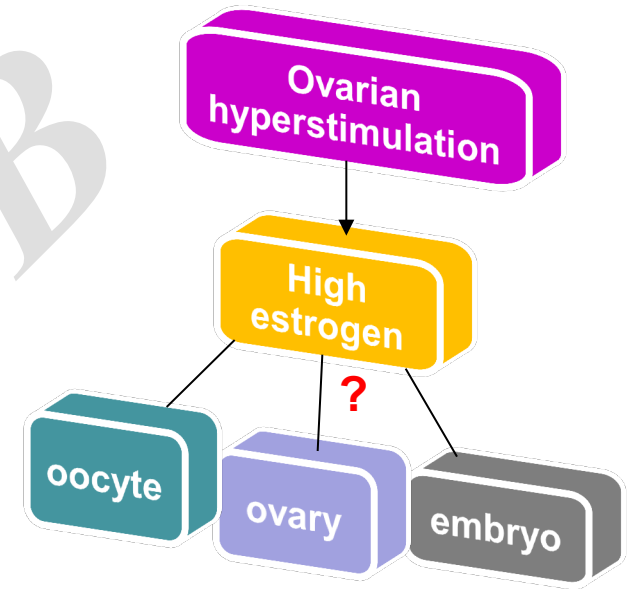


- Different ovarian stimulation mouse models
- Gene transcription sequencing of oocytes
- Estrogen treated mouse embryonic stem cells (mESCs)
- Kdm6b gene knockdown in mESCs

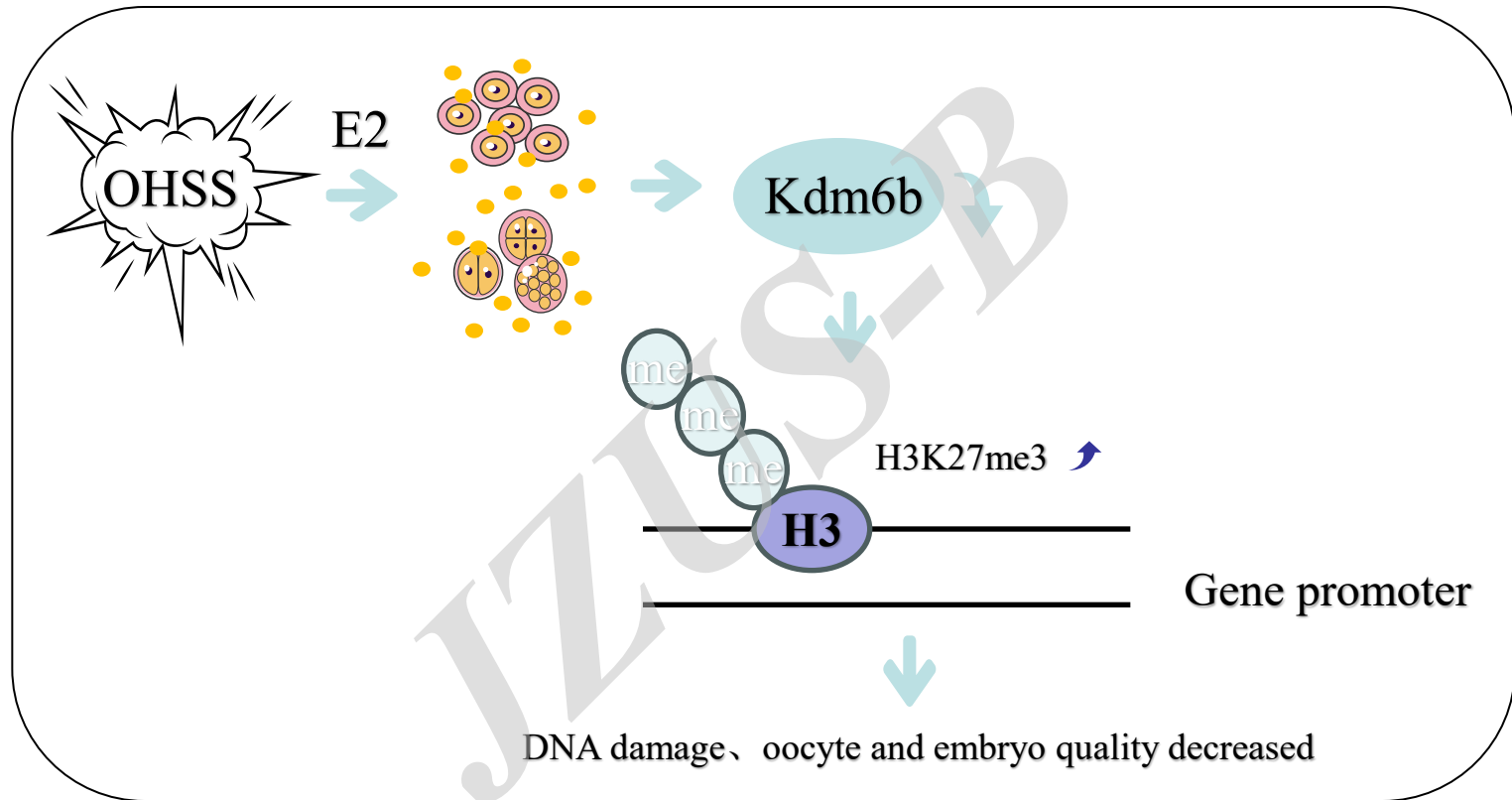


# *Innovation points*

- **Introduction** of the hyperstimulation resulted in high serum estrogen levels, enlarged ovaries, an increased number of aberrant oocytes, and decreased embryo formation.
- **Exploration** of the Kdm6b expression was downregulated in ovarian hyperstimulation oocytes and in mESCs treated with high-dose estrogen.
- **Hypothesis** of the Kdm6b may be a key factor indicating hyperstimulation-induced aberrant oocytes and embryos.



# *Innovation points*



# ***Innovation points***

**A series of comprehensive figures and tables were generated to elucidate the pathway.**

**figure 1 | Effects of ovarian stimulation on ovary morphology.**

**figure 2 | Effects of ovarian stimulation on oocytes.**

**figure 3 | Analysis of differentially expressed genes of oocytes obtained from different ovarian stimulation treatments.**

**figure 4 | Expression of Kdm6b at early embryo stages and H3K27 methylation levels.**

**figure 5 | High estrogen concentrations affect growth and histone methylation levels of mESCs.**

**figure 6 | Inhibition of Kdm6b alters histone methylation levels and  $\gamma$ -H2AX expression.**

# ***Innovation points***

**A series of comprehensive figures and tables were generated to elucidate the pathway.**

**table S1 | Primer sequences.**

**table S2 | Antibodies.**

**table S3 | The ovarian weight of each mouse.**

**table S4 | Average numbers of retrieved oocytes, 2-cell embryos, and blastocysts from the four groups.**

**table S5 | Differentially expressed genes associated with gene stability.**