BDR SEMINAR in Kobe

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14:00-15:00, 7F Seminar Room, DB Building A

The role of DUX4 in the early human embryo

Summary

Human embryo development starts after the fertilization of the oocyte with a rapid succession of parallel processes, each critical for the progression of development. The earliest alterations in the transcriptome include the rapid but transient appearance of transcripts of the DUX4 gene in the zygotes, but not oocytes; the fourfold degradation of a large number of oocyte-specific mRNAs until the 4-cell stage; and the early embryo genome activation (EGA) at the 4-cell stage, involving the significant accumulation of 32 mRNAs, followed by 129 additional genes at the 8-cell stage (1).

Following up on our earlier studies to understand human EGA by single-cell transcriptome sequencing (1), we have now focused on the role of DUX4 in regulating the transition from the oocyte to totipotent blastomeres. We examined its expression, DUX4 protein-protein interactions using the MAC-TAG method (2) and effects of DUX4 down-regulation on the chromatin and transcriptome.

Our findings indicate that the DUX4 protein localizes in zygotes and 2- and 4-cell blastomeres in the cytoplasm and nuclei. At the 8-cell stage, virtually no DUX4 protein remains in cells. Downregulation of DUX4 in zygotes does not affect cell divisions, but the analysis of the transcriptomes of blastomeres indicates delayed oocyte mRNA degradation. The DUX4 protein interacts with several major chromatin and transcription regulators. In the hESC model, DUX4 exerts a major effect on the opening of chromatin. Our results reveal multiple roles for DUX4 in early human development, including regulation of the chromatin, transcription and reprogramming the oocyte transcriptome.

References

1) Töhönen V, Katayama S, & al. Novel PRD-like homeodomain transcription factors and retrotransposon elements in early human development. Nature Commun 6:8207 (2015)

2) Liu X, Salokas K, & al. An AP-MS- and BioID-compatible MAC-tag enables comprehensive mapping of protein interactions and subcellular localizations. Nature Commun 9:1188 (2018)

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