CDB SEMINAR

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16:00~17:00 A7F Seminar Room

Reprogramming and nuclear dynamics

Summary

Pluripotency is established through genome-wide reprogramming during mammalian pre-implantation development, resulting in the formation of the naive epiblast. Reprogramming involves both the resetting of epigenetic marks and the activation of pluripotent-cell-specific genes such as Nanog and Oct4 . The tight regulation of these genes is crucial for reprogramming, but the mechanisms that regulate their expression in vivo have not been uncovered. We found that Nanog is initially expressed monoallelicaly in early preimplantation embryos and then undergoes a progressive switch to biallelic expression coinciding with the transition towards ground-state pluripotency in the naive epiblast. Our data highlight an unexpected role for allelic expression in controlling the dose of pluripotency factors in vivo, adding an extra level to the regulation of reprogramming.

The activation of Nanog is accompanied by formation of enhancer-promoter looping in ES cells. 3D nuclear architecture is emerging as a key player in gene regulation. Although the nuclear organization is drastically restructured during mammalian development, its role in genomic reprogramming remains largely unexplored, possibly due to technical difficulties to study "nuclear dynamics". The live imaging of nuclear architecture is inaccessible by existing approaches such as DNA-FISH and chromosome conformation capture (3C). We integrated TAL effectors to overcome the technical limitation and developed a novel technique which allows the spatiotemporal organization of target sequences to be monitored in living cells. Our findings extend the applications of TAL effector as a flexible scaffold for studying nuclear dynamics.

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