

## Reprogramming and nuclear dynamics

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(in English)

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### 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 transcription in vivo have not been uncovered. We found that Nanog is initially transcribed monoallelically in early preimplantation mouse embryos and then undergoes a progressive switch to biallelic transcription coinciding with the transition towards ground-state pluripotency in the naive epiblast. Our data highlight an unexpected role for allelic transcription in controlling the dose of pluripotency factors in vivo, adding an extra level to the regulation of reprogramming (Nature, 2012). We are currently studying molecular mechanism underlying the allelic regulation of Nanog, especially by dissecting through subnuclear positioning of Nanog loci (unpublished).

The spatiotemporal organization of genomes in the nucleus is an emerging key player to regulate genome function. Live imaging of nuclear organization dynamics would be a breakthrough towards uncovering the functional relevance and mechanisms regulating genome architecture. We established TAL effector-mediated Genome Visualization (TGV) to monitor nuclear positioning and chromatin dynamics in cultured cells and the living organism. TGV is highly specific, allowing differential labeling of parental chromosomes by distinction of single-nucleotide polymorphisms (SNPs). Our findings provide a framework to address the function of genome architecture through visualization of nuclear dynamics in vivo (Nature Structural & Molecular Biology, in press, 2013)

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