Reversing back to totipotency through chromocenter and 3D genome remodeling

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Abstract： Chromocenters emerge upon exit from the 2C totipotent state in mice. How chromocenters form and regulate early cell fate decisions remains largely unknown. Here, we show that Spalt-like transcription factor 4 (SALL4) is highly enriched in chromocenters and its depletion dissolves chromocenters in mouse embryonic stem cells (mESCs). Dissolved chromocenters de-compact the genome and re-establish the totipotency-like nuclear architecture. This leads to the de-repression of the totipotent program, reprograming mESCs back to the totipotent fate. Our results illuminate that SALL4 safeguards the pluripotent fate through maintaining chromocenters and chromocenters function as an organization core of the 3D genome architecture during toti- to pluri-potency transition.