

Oct4 kinetics predict cell lineage patterning in the early mammalian embryo.

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Public Summary:

Scientific Abstract:

Transcription factors are central to sustaining pluripotency, yet little is known about transcription factor dynamics in defining pluripotency in the early mammalian embryo. Here, we establish a fluorescence decay after photoactivation (FDAP) assay to quantitatively study the kinetic behaviour of Oct4, a key transcription factor controlling pre-implantation development in the mouse embryo. FDAP measurements reveal that each cell in a developing embryo shows one of two distinct Oct4 kinetics, before there are any morphologically distinguishable differences or outward signs of lineage patterning. The differences revealed by FDAP are due to differences in the accessibility of Oct4 to its DNA binding sites in the nucleus. Lineage tracing of the cells in the two distinct sub-populations demonstrates that the Oct4 kinetics predict lineages of the early embryo. Cells with slower Oct4 kinetics are more likely to give rise to the pluripotent cell lineage that contributes to the inner cell mass. Those with faster Oct4 kinetics contribute mostly to the extra-embryonic lineage. Our findings identify Oct4 kinetics, rather than differences in total transcription factor expression levels, as a predictive measure of developmental cell lineage patterning in the early mouse embryo.

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