Imaging transcription factors in the living mouse embryo

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Transcription factors (TFs) are essential to control cell fate decisions during embryonic development. While the biological functions of these proteins directly rely on their dynamic mobility within the cell, few tools permit to study TF dynamics in intact developing mammalian organisms.

We have recently developed tools to study TF dynamics within individual cell nuclei of living mouse embryos. By combining selective, multiphoton-based photoactivation of TFs fused to the photo-activatable protein paGFP, and quantitative imaging of the photoactivated TF-paGFP fusion proteins in 4-dimensions (x, y, z and time), we can measure the kinetics of TFs as the embryos develop and the cells undergo the earliest lineage differentiation events.

Applying these tools reveals that the 8–cell stage embryo is composed of two cell populations displaying distinct kinetics of the TF Oct4, a protein essential to support pluripotency. Different Oct4 kinetics result from differential binding to nuclear targets and predict the differentiation of cells to the pluripotent or extraembryonic lineages.

We propose that studying the kinetics of TFs controlling cell fate decisions will help revealing some of the earliest forms of cell-to-cell variability in mammals.