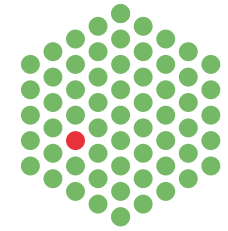


EMBL
Australia



Partner Laboratory Group Leader Applicant

Nicolas Plachta – 1:15pm

*California Institute of Technology, Pasadena, USA
Professor Scott E. Fraser Laboratory*

Transcription factor dynamics in the early mouse embryo

Discovering the dynamic mechanisms that pattern mammalian development is key to understanding human biology and disease. However, few experimental systems currently permit to study single cells and molecules in live mammalian embryos. In my talk, I will present our recent findings studying the kinetic behaviour of the transcription factor (TF) Oct4, a key protein controlling pre-implantation development in mammals. Like most regulatory proteins trafficking between the nucleus and cytoplasm, the kinetic behaviours of Oct4 should be central to its biological functions inside cells, yet little is known about such protein kinetic behaviours in intact embryos. To study Oct4 kinetics in single cells of live mouse embryos, we have established a new experimental assay called fluorescence decay after photoactivation (FDAP). Using FDAP, we quantified the rates of Oct4 nuclear export, import, degradation and the immobile fraction. Independently of the total level of protein expression, distinct Oct4 kinetics identified two morphologically indistinguishable cell populations before the earliest signs of lineage patterning. Tracing the lineage of these populations revealed that Oct4 kinetics predict whether cells divide symmetrically, contributing cells only to the extra-embryonic cell lineage, or asymmetrically, contributing cells to the extra-embryonic and pluripotent cell lineage. Thus, our findings identify TF kinetics as a measure of developmental heterogeneities in the early mouse embryo. Furthermore, this new form of cell-to-cell variability predicts lineage-patterning events.

Finally, I will briefly discuss my future research plans to investigate the kinetic behaviours of other proteins with key functions in the early embryo and in cultured pluripotent stem cells, and the use of multiphoton imaging tools to study single cell dynamics during mouse gastrulation.

Wednesday
4 August
1:15pm
Meeting Room G19
Ground Floor
STRIP (Building 75)
Monash University
Clayton