BDR SEMINAR (Kobe & online hybrid)

Masaki Kinoshita

School of Biosciences, University of Nottingham

Thursday, July 6, 2023

14:00-15:00

1F Auditorium, DB Building C, Kobe / Broadcast online via Zoom

Zoom meeting URL will be announced on the event day by e-mail.

※Non-BDR members: Please register from the following link.
https://krs1.riken.jp/m/bdrseminarregistration (Registration deadline: July 4)

Formative Pluripotency: Dissection of a pluripotency continuum

Summary

Pluripotency exists during early mouse development but transiently. This short period is further dissected into three phases such as "naïve", "formative" and "primed". In mice, cells in the naïve state are equivalent to pre-implantation epiblast cells as well as embryonic stem (ES) cells. Formative phase starts after implantation and ends at the onset of gastrulation and recently captured as formative stem (FS) cells by us. Primed cells are represented by gastrulation stage cells, which still have the plasticity in embryos and their in vitro counterpart is EpiSCs.

ES cells differentiate into any lineages however they don't respond to differentiation signals. To do so, they need to exit from naïve state, and transit to formative state. Primed EpiSCs are known to lose germ cell competency. Unlike these cells, FS cells have a good responsiveness to the growth factor signals and differentiate into all three germ layer cell types and germline cells. FS cells are capable of making blastocyst chimaera. In mice, we found these three pluripotent states have different growth factor signal requirements, transcriptomes and chromatin landscapes. We identified Otx2 is uniquely required for the FS cell maintenance but de novo DNA methylation enzymes are dispensable for it.

Most recently, we have established the pluripotent stem cell lines from livestock species (pig, sheep and cattle) and termed as Embryonic Disc Stem Cells (EDSCs). We maintain them under chemically defined culture condition and they self-renew robustly. They differentiate into three germ layers and share transcriptome similarities to the formative epiblast cells of embryonic disc stage embryos. We successfully produced transgenic foetus by nuclear transfer using gene targeted EDSCs. Therefore, our EDSCs open the door of stem cell biology for the first time to these species.