IMEG mini symposium

“Stem cells and early development”

December 1 Fri, 2023, 14:00-16:00

IMEG 1F Conference room

14:00-14:30

Formative pluripotency in livestock species

Masaki Kinoshita, School of Biosciences, University of Nottingham
Centre for Large Animal Biotechnology, University of Nottingham

Pluripotency emerges as naïve state in the blastocyst stage embryo and ended at the gastrulation in the primed state. Naïve cells are incompetent to respond to the differentiation signals, so they need to exit their state and capacitate themselves towards the next ‘formative’ phase. In the formative state, cells are competent to differentiate into any lineage including germlines. Formative cells move to primed state when embryo receives gastrulation signals. Primed cells are still pluripotent however, they start to have a biased differentiation potency depends on the positions in the embryo. These three phases are commonly observed across mammalian embryos. We previously established formative stem cells from mouse and human embryos and now we ask whether formative stem cells can be derived from other mammalian species.

14:30-15:00

Distinct phospho-variants of STAT3 regulate developmental pace in mouse development

Takuya Azami, MRC Human Genetics Unit, Institute of Genetics and Cancer, The University of Edinburgh

STAT3 has been studied extensively in the context of self-renewal of naïve pluripotent mouse embryonic stem cells (mESCs). Although STAT3 is required to maintain inner cell mass lineages when maternal-zygotically eliminated, the role of STAT3 during gastrulation is unclear as the original knockout of Stat3 develops until E6.5. In this study, we observed that on CD1 genetic background zygotic loss of Stat3 leads to consistent developmental retardation from implantation to mid-gestation, beginning with a significant reduction in the number of epiblast cells by the time of implantation. Remarkably, mutants appear to scale normally and resemble non-affected embryos from the previous day at all postimplantation stages examined. We attribute this phenotype to loss of the active serine phosphorylated (pS727) form of STAT3, required for neural differentiation of mESCs, which is also implicated in growth defects during organ expansion in mice and humans. Bulk RNA-seq analysis showed transcriptional developmental retardation in Stat3 null embryos. Single cell chimera RNA-sequence analysis revealed specific exclusion of Stat3 null cells in rapidly proliferating erythroid lineage. Our study demonstrates the role of the STAT3 in the temporal control of embryonic progression and metabolic mechanisms.

15:00-16:00

Investigation formation of trophoblast in mice and humans

Jennifer Nichols, University of Edinburgh

Methods of embryo implantation vary between mammalian species. The human blastocyst attaches directly to the uterine wall, via polar trophectoderm. This tissue becomes multi-layered from around the mid blastocyst stage, sometimes occupying most of the embryo. Naïve pluripotent embryonic stem cells or epiblasts dissected from human blastocysts readily convert to trophoblast when exposed to simple culture conditions. However, fluorescent labelling experiments imply that inner cells do not migrate into the trophectoderm of intact blastocysts, but polar trophectoderm appears to move inwards. There is no multi-layering of this tissue in mouse blastocysts, but the entire mouse embryo converts to trophoblast if Oct3/4 is deleted. The sequence of transcriptional events leading to this involve upregulation of some trophectoderm-associated genes prior to downregulation of other pluripotency factors. The STAT3 signalling pathway is the first to be affected, which is required to maintain naïve pluripotency during embryonic diapause and also associated with developmental pace.

Organizer: Hitoshi Niwa (Ext. 6620)