CDB
RIKEN Kobe since 2000

CDB SEMINAR

Micha Drukker & Yoav Soen

Stanford Institute for Stem Cell Biology & Weizmann Institute of Science

Monday, June 8, 2009
14:30~15:20/15:30~16:10 A7F Seminar Room

Prospective Isolation of Blastocyst- and Epiblast-Stage Precursors from Human Embryonic Stem Cells (Dr. Drukker)

To explore the landscape and properties of the earliest precursors derived from hESCs we conducted a flow cytometry screen with over 400 monoclonal antibodies against cell surface markers. This screen identified distinct subsets of putative precursors that are either present in undifferentiated cultures, or that emerge following 3 days of differentiation in response to BMP4 and retinoic acid. By isolating over 30 cell subpopulations and analyzing the expression of developmental genes, we identified 4 distinct candidate precursor populations corresponding respectively, to embryonic primitive endoderm precursors of the pre-gastrulation stage and to gastrulation-stage precursors of the primitive streak (meso-endoderm), allantois and chorion. Single cell analysis revealed a surprising transcriptional state of the visceral endoderm-like cells, characterized by strong induction of a wide range of differentiation associated genes but only a relatively marginal decrease in pluripotency genes. In addition, a small portion of the meso-endoderm-like cells co-expressed pan-mesoderm and endoderm genes, suggesting the existence of human bi-potent meso-endoderm precursors. Prospective isolation of cell populations with striking similarities to pre-gastrulation and gastrulation-stage precursors provides an important platform for studying human development with unprecedented resolution, and may facilitate production of tissue progenitors for therapeutic applications from hES and induced pluripotent (iPS) cell lines.

Induction and trans-generational inheritance of responses to a novel challenge presented to developing flies (Dr. Soen)

It is widely accepted that many of the regulatory networks of development were shaped by evolution to support robust processes of development. How these networks cope with evolutionary unforeseen challenges is, however, largely unknown. While the ability to adapt to novel challenges may be crucial for the organism to evolve, direct experimental studies of it have been lacking. To address this gap we have developed an experimental framework to investigate the capacity of a multi-cellular organism to cope with an unforeseen challenge. The experimental framework is based on confronting the developmental network of the fly, D. melanogaster, with a (synthetically engineered) challenge for which no specific response was likely been selected during the evolutionary history of the fly. Analysis of responses to the challenge revealed a surprising ability of the larva to modify its course of development within the first generation of exposure. This modification coincided with complete tolerance to an otherwise lethal challenge and occurred, without selection, in every single larva. Importantly, the induced phenotypes were transmitted to every single offspring in subsequent generations that were not exposed to the challenge. We provide initial molecular characterization of the response and propose a conceptual model for its inheritance.

Host:
Shinichi Nishikawa
Stem Cell Biology, CDB
nishikawa@cdb.riken.jp
Tel:078-306-1893
(ext : 5301)