ASHBi SEMINAR

A cell model to study embryonic genome activation

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Venue Hybrid*
Conference Room / Zoom online
B1F, Faculty of Medicine Bldg. B

*Register via the right QR code

Abstract

In human, Embryonic Genome Activation (EGA) occurs during days 2-3 after fertilization, at 4-8 cell stages, when the combined genome of the zygote start to be transcribed. EGA coincides with the reprogramming of the oocyte transcriptome to the totipotent cell phenotype of the 4-8 cell stage cells. We have earlier studied human EGA by single-cell RNA sequencing of oocytes, zygotes, and single cells from 4- and 8-cell stage embryos[1]. This study allowed us to list 32 genes activated at 4-cell stage compared to oocytes (minor EGA), 129 genes activated at 8-cell stage compared to 4-cell stage (major EGA), and thousands of specifically degraded mRNAs until the 4-cell stage, corresponding to ≈75% of oocyte mRNA content. We cloned new paired-like (PRDL) homeobox family genes not detected earlier active in any human tissues[2] . Recently, we have continued to characterize the roles of key genes[3]. Our results implicated DUX4 functions to include chromatin modification, enhancer activation, transcriptional activation, and regulation of oocyte mRNA degradation. However, work to understand human EGA in detail has been hampered not only by technical aspects, but also by that work destroying human embryos is not allowed in all legislations. Therefore, cell models to study human EGA and the genes involved in it are badly needed. Toward this aim, we succeeded in reprogramming human embryonic stem cells (hESCs) to 8-cell-like cells (8CLC, called by us as induced blastomeres, iBM) by a brief pulse of DUX4 expression[4]. Human 8CLCs had recently been derived also by chemical induction[5]. The cell models now also open up new routes to study human EGA without harming human embryos, allowing manipulations such as inactivation of selected genes, studying effects of chemical compounds and biochemical changes, and drawing the complete landscape of human EGA.

[1] Töhönen & al. 2015; DOI: 10.1038/ncomms9207)
[2] Töhönen & al. 2015; Jouhilahti & al. 2016; DOI: 10.1242/dev.134510; Madissoon & al. 2016; DOI:10.1038/srep28995)
[3] Vuoristo & al. 2022; DOI: 10.1016/j.isci.2022.104137
[4] Yoshihara & al. 2022; DOI: 10.1016/j.stemcr.2022.06.002
[5] Mazid & al. 2022; DOI: 10.1038/s41586-022-04625-0

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