CDB SEMINAR

Juha Kere

Department of Biosciences and Nutrition, Karolinska Institutet, Sweden

Tuesday, August 22, 2017
14:00~15:30 Auditorium C1F

Transcriptional control of human embryo genome activation

Summary

After fertilization of the egg cell, the embryonal development starts with its individual transcriptome activation (Embryo Genome Activation, EGA) accompanied by the degradation of maternal transcripts, to be followed later with new waves of transcriptional activation. These steps are especially amenable to transcriptomic analysis, but pose also challenges, such as ≈30-fold changes in cellular mRNA content. To understand human EGA, we performed single-cell transcriptome sequencing of over 340 cells, including oocytes, zyogtes and single blastomeres from 4-cell and 8-cell embryos, obtained by informed consent as donations after in vitro fertilization treatments1. The total content of mRNA molecules remained essentially unchanged between oocytes and zygotes, but revealed an increase of *DUX4* repeat-sequence transcripts[2]. Comparison of the transcriptomes of oocytes and 4-cell stage blastomeres identified the first 32 embryonally transcribed genes, including previously uncharacterized Paired-like (PRDL) homeobox domain genes, as well as the significant reduction of thousands of maternal transcripts[1]. At the 8-cell stage, 129 additional genes were upregulated compared to the 4-cell stage. Our transcription start site targeted data allowed also the identification of critical regulators of EGA as 36 bp and 35 bp conserved promoter elements at the two stages of EGA, respectively. We cloned and confirmed the genomic structures of seven new PRDL genes expressed only during EGA. Their functional analysis confirmed their roles as transcriptional regulators, ranging from *LEUTX* as a strong transcriptional activator to *DPRX* with a strong downregulatory profile. These data constitute a resource for understanding the earliest steps of human embryonal development and provide new genes of interest for study of pluripotency and stem cell technologies.

References

1) Töhönen V, Katayama S, Vesterlund L, Jouhilahti E-M, Sheikhi M, Madissoon E, Filippini-Cattaneo G, Jaconi M, Johnsson A, Bürglin TR, Linnarsson S, Hovatta O, Kere J. Novel PRD-like homeodomain transcription factors and retrotransposon elements in early human development. *Nature Commun* 6:8207 (2015)

2) Töhönen V, Katayama S, Vesterlund L, Jouhilahti E-M, Sheikhi M, Madissoon E, Filippini-Cattaneo G, Jaconi M, Johnsson A, Bürglin TR, Linnarsson S, Hovatta O, Kere J. Transcription activation of early human development suggests DUX4 as an embryonic regulator. Biorxiv.org. doi: https://doi.org/10.1101/123208

Host:
Hiroshi Hamada
Organismal Patterning, CDB
hiroshi.hamada@riken.jp
Tel:078-306-3002
(ext:3325)