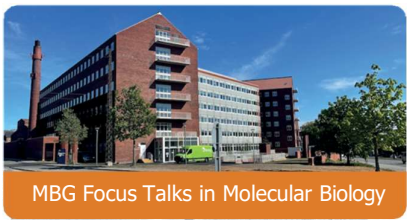
MBG FOCUS TALK

Hosted by Peter Ebert Andersen



Wednesday 18 September 2024 @ 09:00-09:45
Faculty Club (1870-816)

Peter Zeller, PhD

Hubrecht Institute

Utrecht, NL

Understanding epigenetic gene regulation at single cell resolution

Cells share the same genetic code but utilize it differently based on their type and context. Epigenetic changes, such as post-translational histone modifications (PTHMs), regulate DNA interactions. As cells differentiate, PTHMs are reorganized to support their new functions. For a long time there existed only a few cell types we could purify clean and abundant enough to analyse their cell type specific epigenome. During my postdoc I developed multiple single cell multi-omics techniques including T-ChIC (Transcriptome + Chromatin ImmunoCleavage), a method allowing for acquisition of full-length transcripts and histone mark positions of the same single cell.
We applied this technique to an in vitro model of gastrulation, termed gastruloids. These are aggregates of (mouse) embryonic stem cells, which over the course of several days differentiate into polarised structures with an anteroposterior axis and cell types derived from all three germ layers. Our analysis of H3K27me3 (repressed regions) and H3K4me3 (active promoters) distributions revealed global restructuring of chromatin states. The first phase of development is characterised by a genome wide restriction of repressive H3K27me3 and the de-repression of bivalently marked genes (H3K27me3 + H3K4me3 positive). Afterwards changes become germlayer specific, which includes the sequential de-repression of lineage specific gene sets in uncommitted cells. A process that starts with the exclusive de-repression of Endodermal genes, followed by an additional de-repression of Mesodermal and finally Ectodermal genes.
These results extend the Ectodermal focused knowledge about early epigenetic changes and suggest a de-repression-based default Ectodermal trajectory, that allows induction of other germlayers during defined developmental time windows.

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