Pre-patterning developmental gene expression by modified histones and DNA hypomethylation

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Venue: GIS Seminar Area, Level 2

Abstract:

A hallmark of anamniote vertebrate development is a window of embryonic transcription-independent cell divisions before onset of zygotic genome activation (ZGA)(1). Chromatin determinants of ZGA are unexplored. However, marking of developmental genes by modified histones over a hypomethylated DNA background in sperm suggests a predictive role of histone marks and DNA hypomethylation for ZGA (2). In zebrafish, pre-ZGA development for ten cell cycles provides an opportunity to examine whether genomic enrichment in modified histones is present before initiation of transcription. By profiling histone H3 trimethylation and DNA methylation on zebrafish promoters before and after ZGA, we show an epigenetic pre-patterning of developmental gene expression (3). This involves, before onset of ZGA, marking of transcriptionally inactive genes involved in homeostatic and developmental regulation, by permissive H3K4me3 with or without repressive H3K9me3 or H3K27me3. We also show the DNA methylation of thousands of promoters before ZGA and additional methylation during ZGA without marked demethylation. We identify developmentally regulated hypomethylated promoters that are CG-rich, remain hypomethylated through the MBT and constitute a platform for H3K4me3. Genes differentially expressed through the MBT display distinct methylation patterns. Methylation states in sperm largely overlap those of pre-MBT embryos, supporting a model of transgenerational inheritance of epigenetic marks. Our data suggest that histone modifications are instructive for the developmental gene expression program. This work was done in collaboration with GIS (Dr.Mathavan)

Aanes et al. 2011. Genome Res. 21, 1328-1338
Wu SF, Zhang, H, Cairns, B.R, 2011. Genome Res. 21, 578-589.
Lindeman et al., 2011. Dev. Cell, in press.

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