CDB SEMINAR

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16:00~17:00 C1F CDB Auditorium

Novel roles for mouse Polycomb Group proteins in pericentric heterochromatin formation and genomic imprinting

Summary

Polycomb group (PcG) proteins are part of an evolutionarily conserved memory system required for the maintenance of cell identity. PcG proteins function in two distinct multi-protein complexes, Polycomb Repressive Complex (PRC1) 1 and 2. Genome-wide ChIP and functional assays indicate that PRC1 and PRC2 cooperate to repress key developmental regulators. Here we report novel roles for PRCs during mouse pre-implantation development.

In eukaryotes, homologues of the Suv39h H3K9 tri-methyltransferases are required for pericentric heterochromatin formation and function. In one to 8-cell stage pre-implantation embryos, however, paternal pericentric heterochromatin lacks *Suv39h*-dependent H3K9me3 and downstream marks. Instead, maternally provided PRC1 components are targeted to paternal heterochromatin in a PRC2 (*Ezh2*)-independent manner. In *Suv39h2* maternally deficient zygotes, PRC1 also associates with maternal heterochromatin lacking H3K9me3, thereby revealing hierarchy between repressive pathways. We conclude that in early embryos PRC1 functions as the default repressive back-up mechanism in absence of H3K9me3, that constitutes the dominant maternal trans-generational signal for pericentric heterochromatin formation.

In placental mammals, certain genes are mono-allelically expressed in a parent-of-origin dependent manner. At the *Kcnq1* imprinted cluster, mono-allelic silencing of paternal genes depends on expression of the *Kcnq1ot1* non-coding RNA *in-cis*. We detect by immuno-FISH PRC1 and PRC2 proteins, and related histone modifications associated with *Kcnq1ot1*, forming a distinct repressive nuclear compartment devoid of active marks and RNA polymerase II. In *Ezh2-/-* embryos, mono-allelic repression of several genes in the *Kcnq1* cluster is impaired, revealing an essential role for PRC2 in imprinted silencing during embryogenesis.

Host:

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