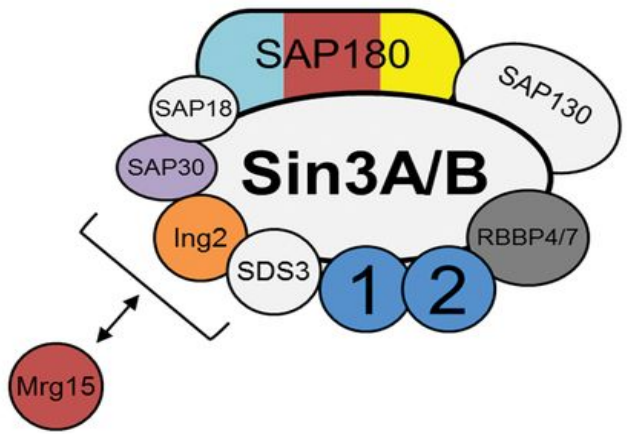
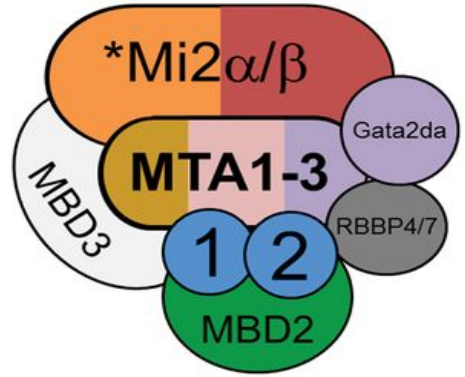
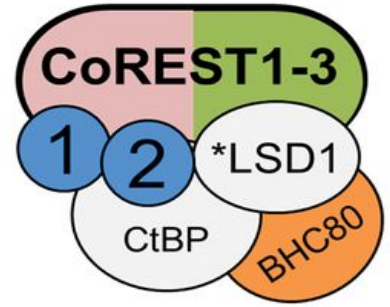
How epigenetics can affect expression of genes







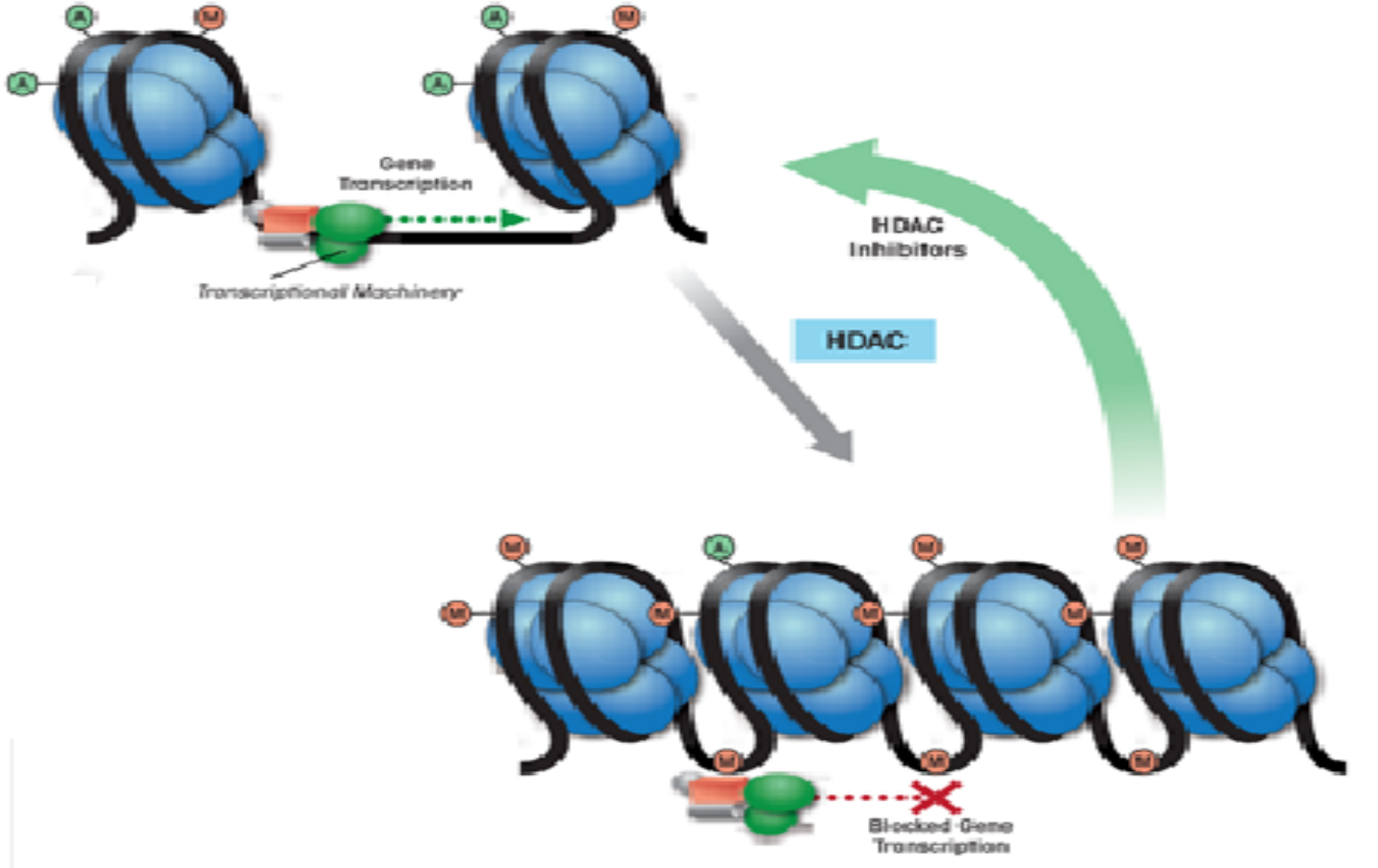
Sin3 *NuRD* *CoREST*

**helicase-deacetylase* **demethylase-deacetylase*

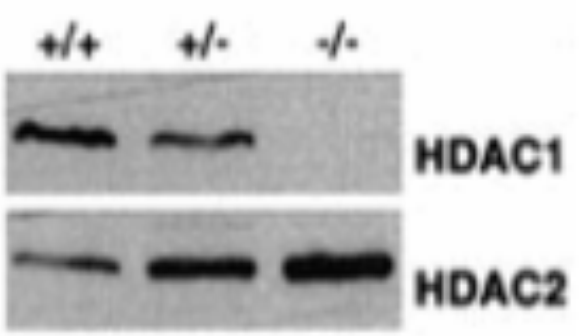
DNA / Chromatin Binding Motif

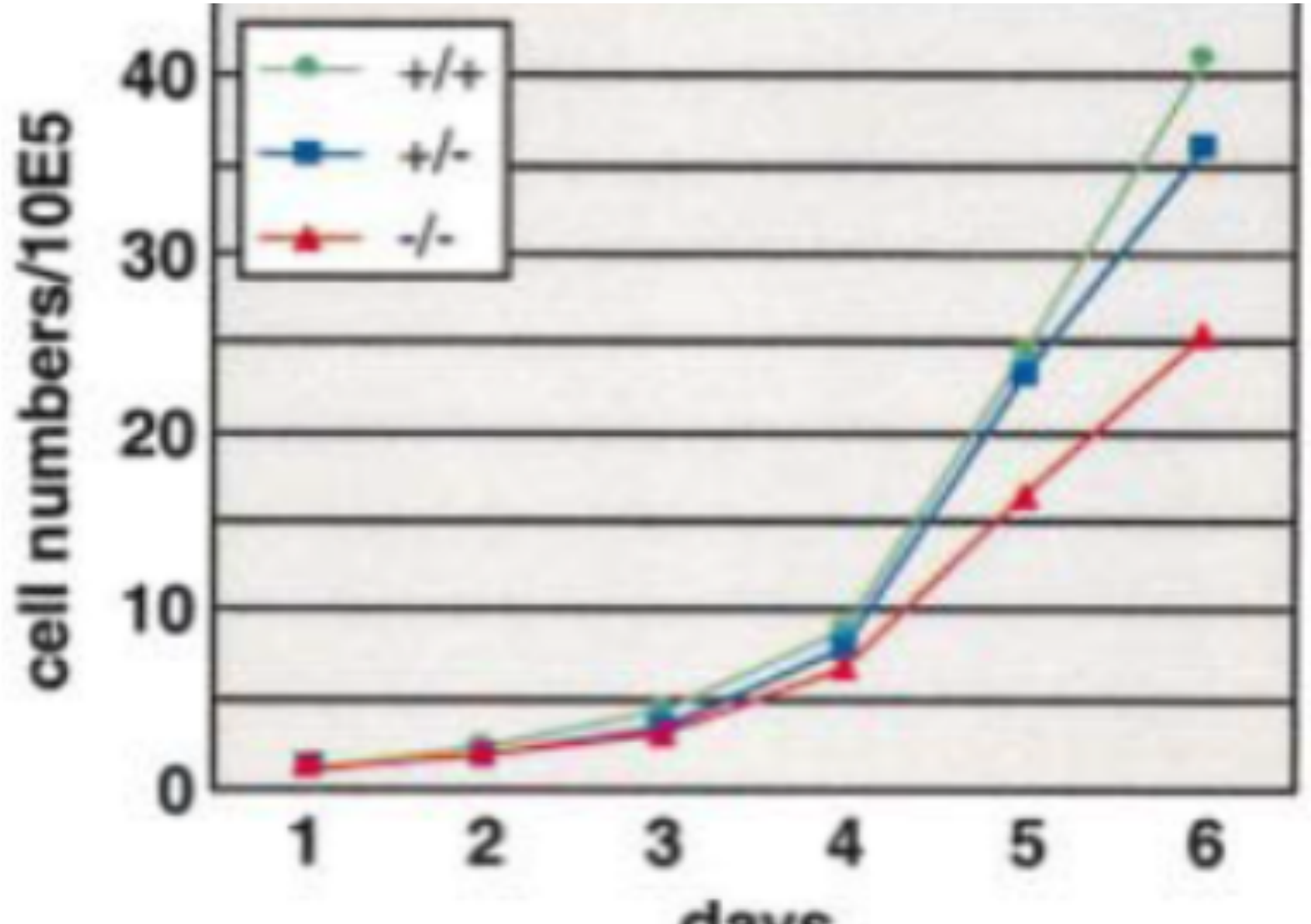
SANT domain	WD40 repeats	Methyl-DNA binding
Chromodomain	PhD Finger	Zn-finger
Tudor domain	ARID domain	BAH domain

Deacetylase ELM2/SANT


Gene
Transcription
Transcriptional Machinery
HDAC
Inhibitors
HDAC
Blocked Gene
Transcription

- ESC proliferation in embryogenesis
- Silencing of genes which inhibit cell cycle
- p21





EMBO J. 2002 Jun 3; 21(11): 2672–2681.
doi: 10.1093/emboj/21.11.2672
PMCID: PMC126040

Essential function of histone deacetylase 1 in proliferation control and CDK inhibitor repression

Gerda Lagger, Dónal O'Carroll,[1,2] Martina Rembold, Harald Khier, Julia Tischler, Georg Weitzer,[3] Bernd Schuettengruber, Christoph Hauser, Reinhard Brunmeir, Thomas Jenuwein,[1] and Christian Seiser[4]

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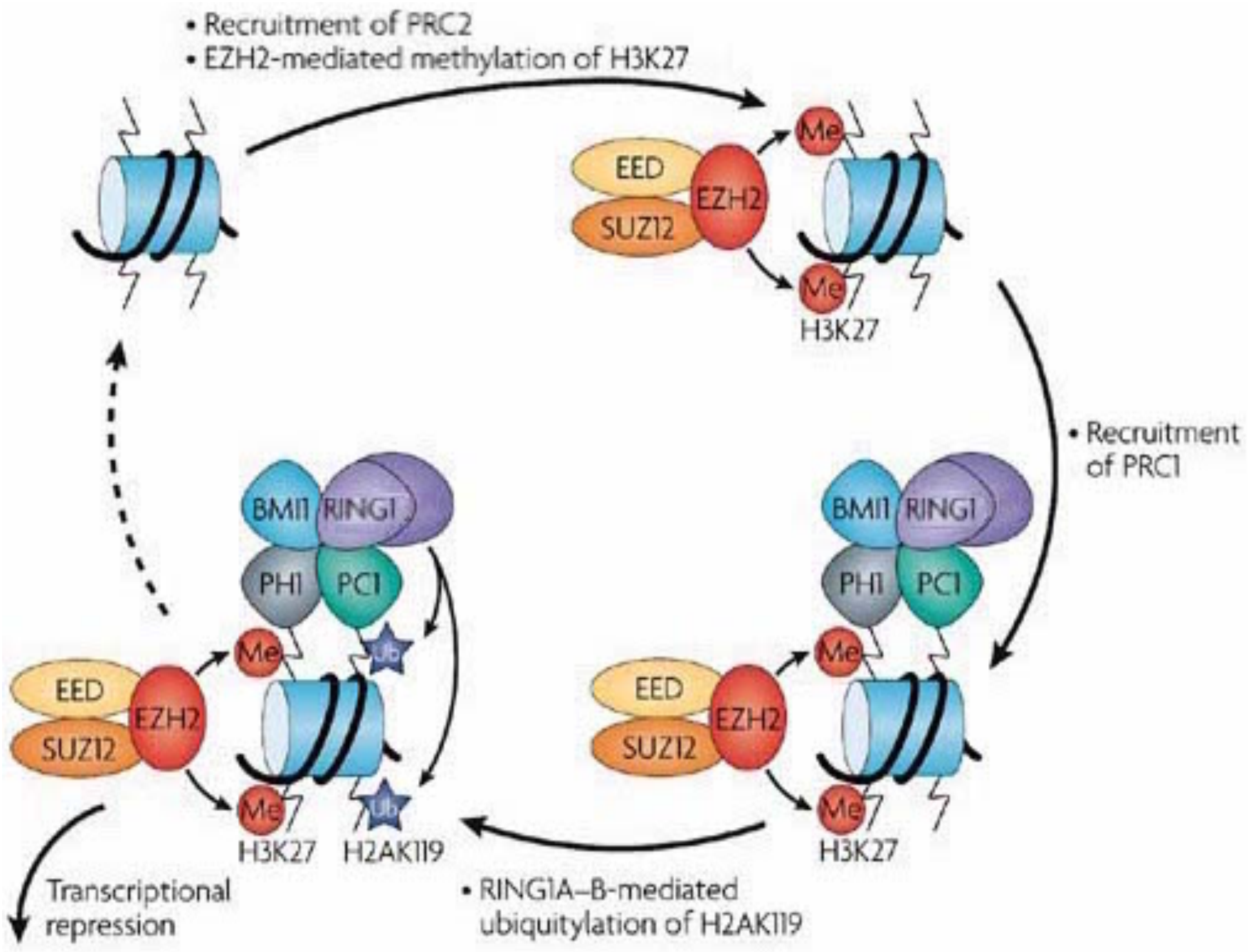
Abstract

Go to:

Histone deacetylases (HDACs) modulate chromatin structure and transcription, but little is known about their function in mammalian development. HDAC1 was implicated previously in the repression of genes required for cell proliferation and differentiation. Here we show that targeted disruption of both HDAC1 alleles results in embryonic lethality before E10.5 due to severe proliferation defects and retardation in development. HDAC1-deficient embryonic stem cells show reduced proliferation rates, which correlate with decreased cyclin-associated kinase activities and elevated levels of the cyclin-dependent kinase inhibitors p21$^{WAF1/CIP1}$ and p27^{KIP1}. Similarly, expression of p21 and p27 is up-regulated in HDAC1-null embryos. In addition, loss of HDAC1 leads to significantly reduced overall deacetylase activity, hyperacetylation of a subset of histones H3 and H4 and concomitant changes in other histone modifications. The expression of HDAC2 and HDAC3 is induced in HDAC1-deficient cells, but cannot compensate for loss of the enzyme, suggesting a unique function for HDAC1. Our study provides the first

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC126040/

- Polycomb group gene silencing
- Hox gene repression



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PMCID: PMC3019975

Mammalian Polycomb-Like Pcl2/Mtf2 Is a Novel Regulatory Component of PRC2 That Can Differentially Modulate Polycomb Activity both at the *Hox* Gene Cluster and at *Cdkn2a* Genes

Xiangzhi Li,[1] Kyo-ichi Isono,[1,†] Daisuke Yamada,[1,†] Takaho A. Endo,[2] Mitsuhiro Endoh,[1,3] Jun Shinga,[1] Yoko Mizutani-Koseki,[1] Arie P. Otte,[4] Miguel Casanova,[5] Hiroshi Kitamura,[1] Takehiko Kamijo,[6] Jafar Sharif,[1] Osamu Ohara,[1] Tetsuro Toyada,[2] Bradley E. Bernstein,[7] Neil Brockdorff,[5] and Haruhiko Koseki[1,3,*]

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This article has been corrected. See Mol Cell Biol. 2014 July; 34(14): 2773.

This article has been cited by other articles in PMC.

ABSTRACT

Go to:

The Polycomb group of proteins forms at least two distinct complexes designated the Polycomb repressive complex-1 (PRC1) and PRC2. These complexes cooperate to mediate transcriptional repression of their target genes, including the *Hox* gene cluster and the *Cdkn2a* genes. Mammalian Polycomb-like gene Pcl2/Mtf2 is expressed as four different isoforms, and the longest one contains a Tudor domain and two plant homeodomain (PHD) fingers. Pcl2 forms a complex with PRC2 and binds to *Hox* genes in a PRC2-dependent manner. We show that Pcl2 is a functional component of PRC2 and is required for PRC2-mediated *Hox* repression. Pcl2, however, exhibits a profound synergistic effect on PRC1-mediated *Hox*

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Abstract ▾ Send to: ▾

Dev Cell. 2003 Apr;4(4):481-95.

Establishment of histone h3 methylation on the inactive X chromosome requires transient recruitment of Eed-Enx1 polycomb group complexes.

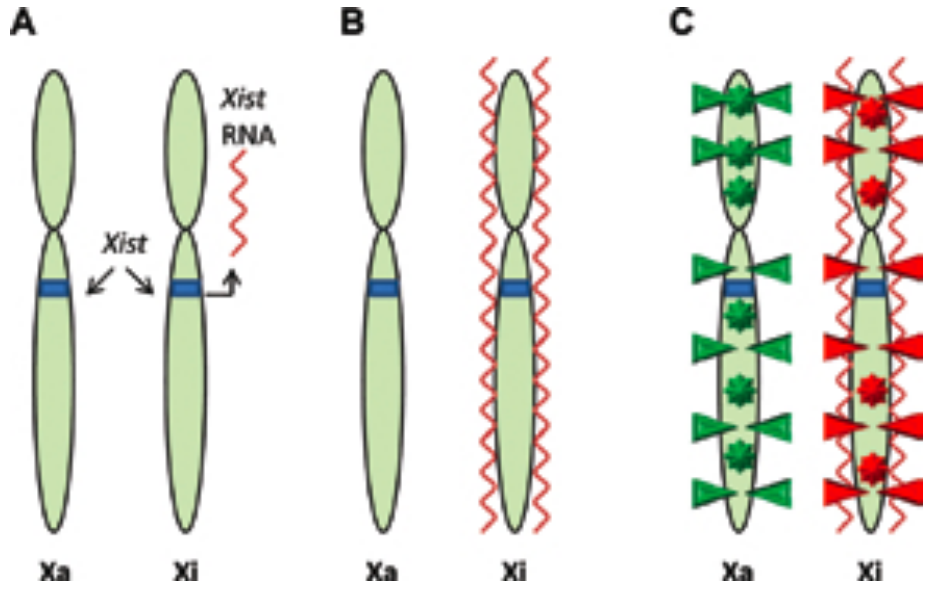
Silva J[1], Mak W, Zvetkova I, Appanah R, Nesterova TB, Webster Z, Peters AH, Jenuwein T, Otte AP, Brockdorff N.

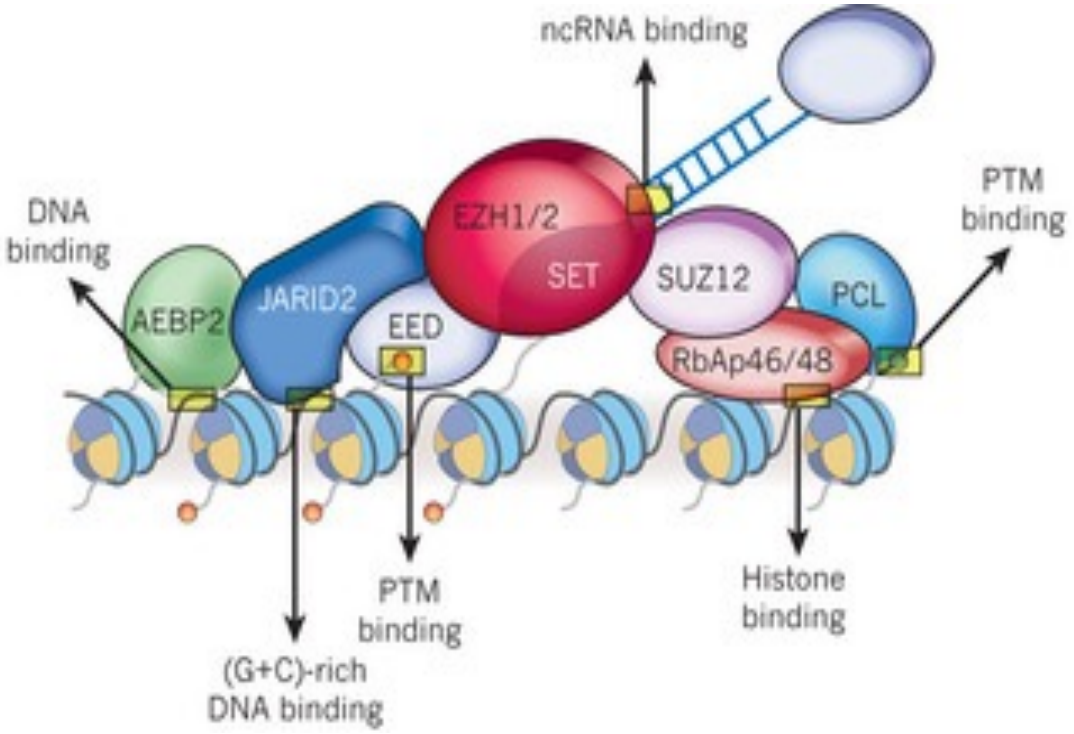
⊕ Author information

Abstract

Previous studies have implicated the Eed-Enx1 Polycomb group complex in the maintenance of imprinted X inactivation in the trophectoderm lineage in mouse. Here we show that recruitment of Eed-Enx1 to the inactive X chromosome (Xi) also occurs in random X inactivation in the embryo proper. Localization of Eed-Enx1 complexes to Xi occurs very early, at the onset of Xist expression, but then disappears as differentiation and development progress. This transient localization correlates with the presence of high levels of the complex in totipotent cells and during early differentiation stages. Functional analysis demonstrates that Eed-Enx1 is required to establish methylation of histone H3 at lysine 9 and/or lysine 27 on Xi and that this, in turn, is required to stabilize the Xi chromatin structure.

http://www.ncbi.nlm.nih.gov/pubmed/12689588





X inactive specific transcript is transcribed center of the inactive X chromosome. B) Xist binds throughout the length of Xi. C) **The silenced Xi displays suppressive histone modifications (red triangles) and DNA methylation at intragenic and promoter loci (red stars).** The active X chromosome (Xa) displays activating histone modifications (green triangles) and gene body methylation (green stars).

http://epigenie.com/epigenie-learning-center/epigenetics/epigenetic-regulation/