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► To cite this version:

Matteo Tosolini, Vincent Brochard, Pierre Adenot, Martine Chebrou, Grillo Giacomo, et al.. Contrasted regulation of pericentromeric hetero chromatin in mouse ground naive and primed pluripotent stem cells. France-Japan Epigenetics Workshop 2017, Nov 2017, Paris, France. , 2017. hal-02786601

HAL Id: hal-02786601

<https://hal.inrae.fr/hal-02786601v1>

Submitted on 5 Jun 2020

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Contrasted regulation of pericentromeric heterochromatin in mouse ground naive and primed pluripotent stem cells

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Background

The constitutive heterochromatin compartment:

- composed of telomeres, centromeres and pericentromeric (PCH) regions
- PCH = Major satellites : 234bp, ~ 10.000 repeats (3% of the mouse genome)
- Compacted and mainly silenced
- Usually enriched in H3K9me3 and DNA methylation = repressive transcriptional environment

Probst, Almouzni et al. TIG 2011

2i-ESC Naive pluripotency

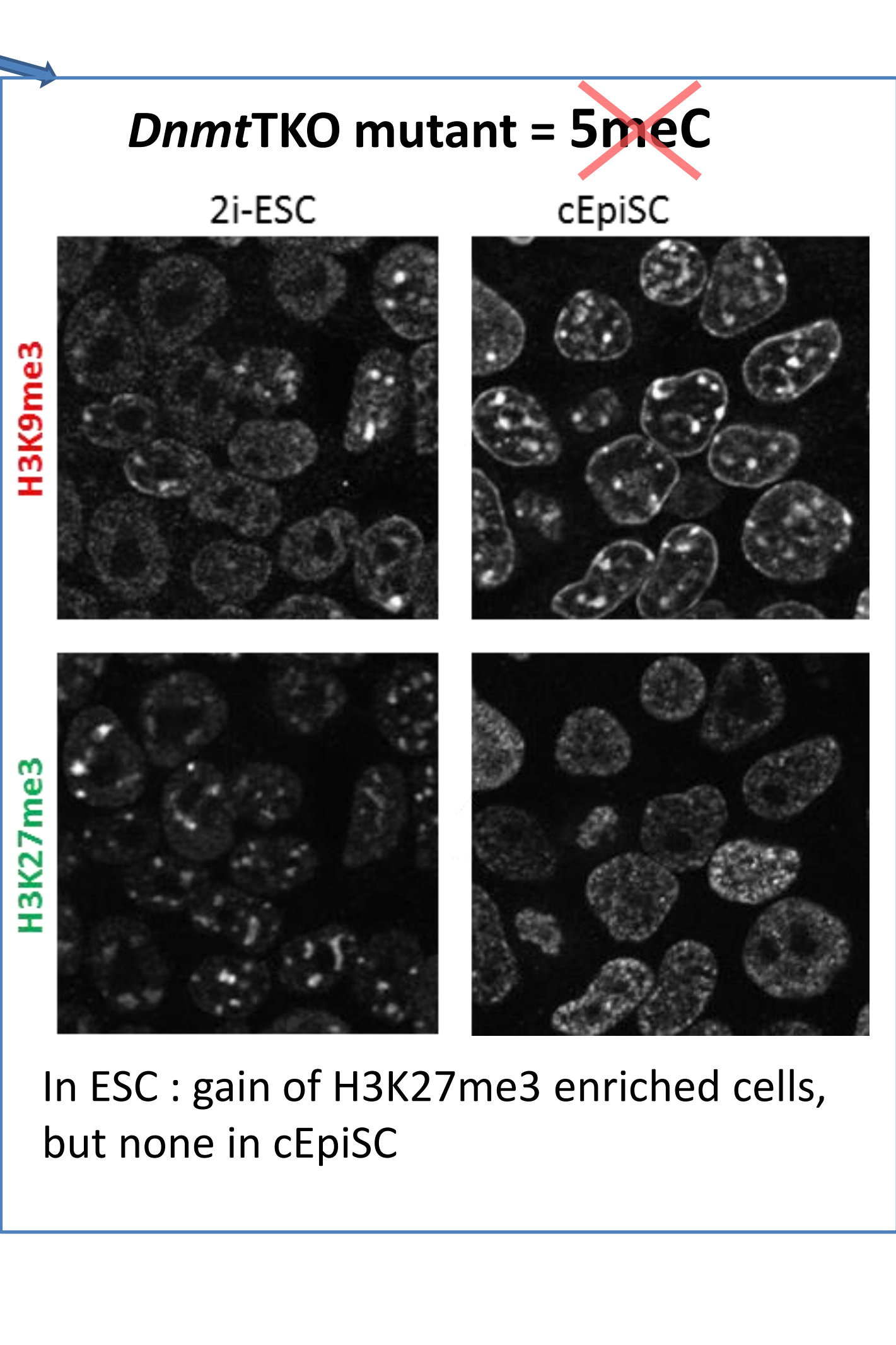
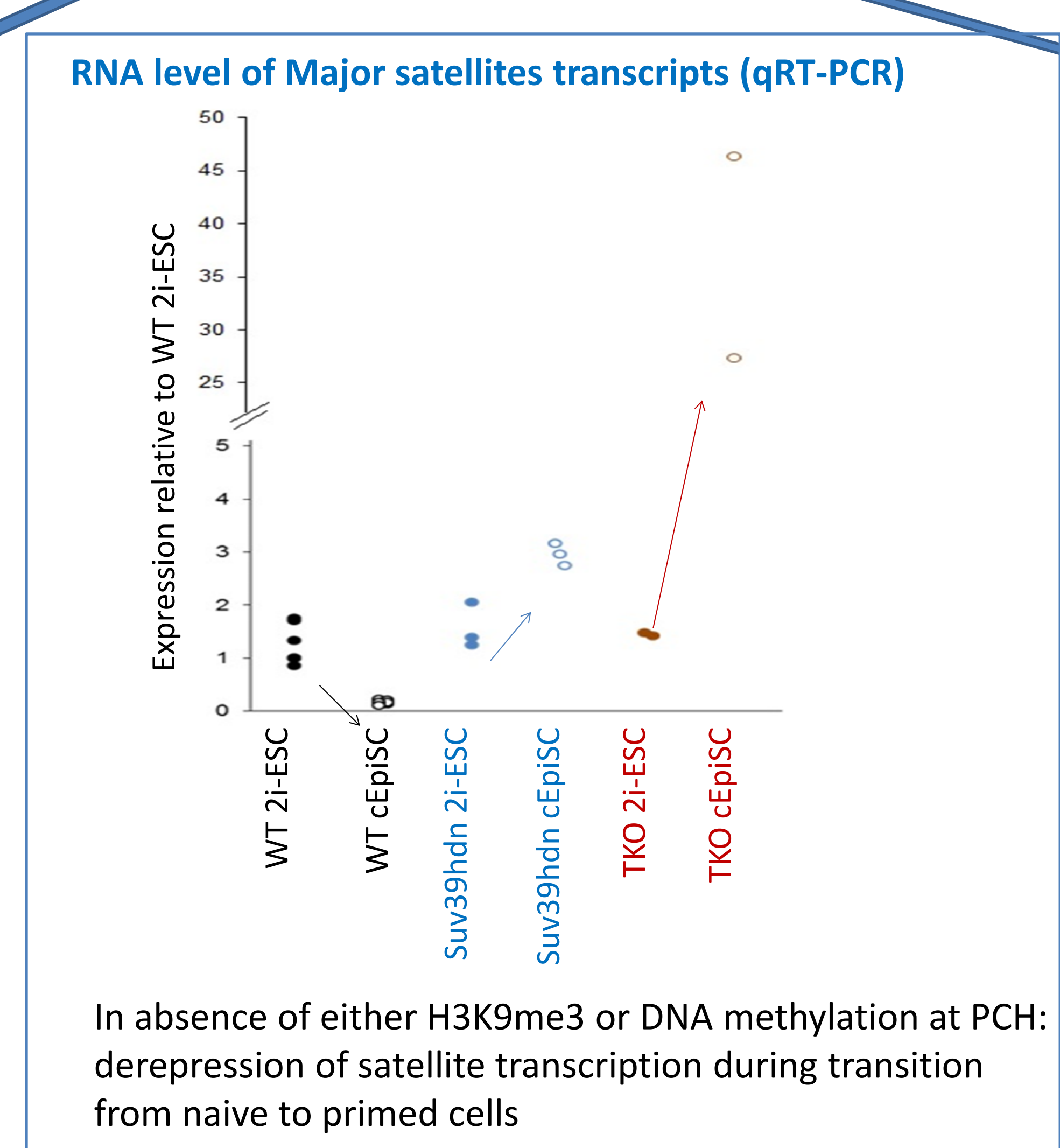
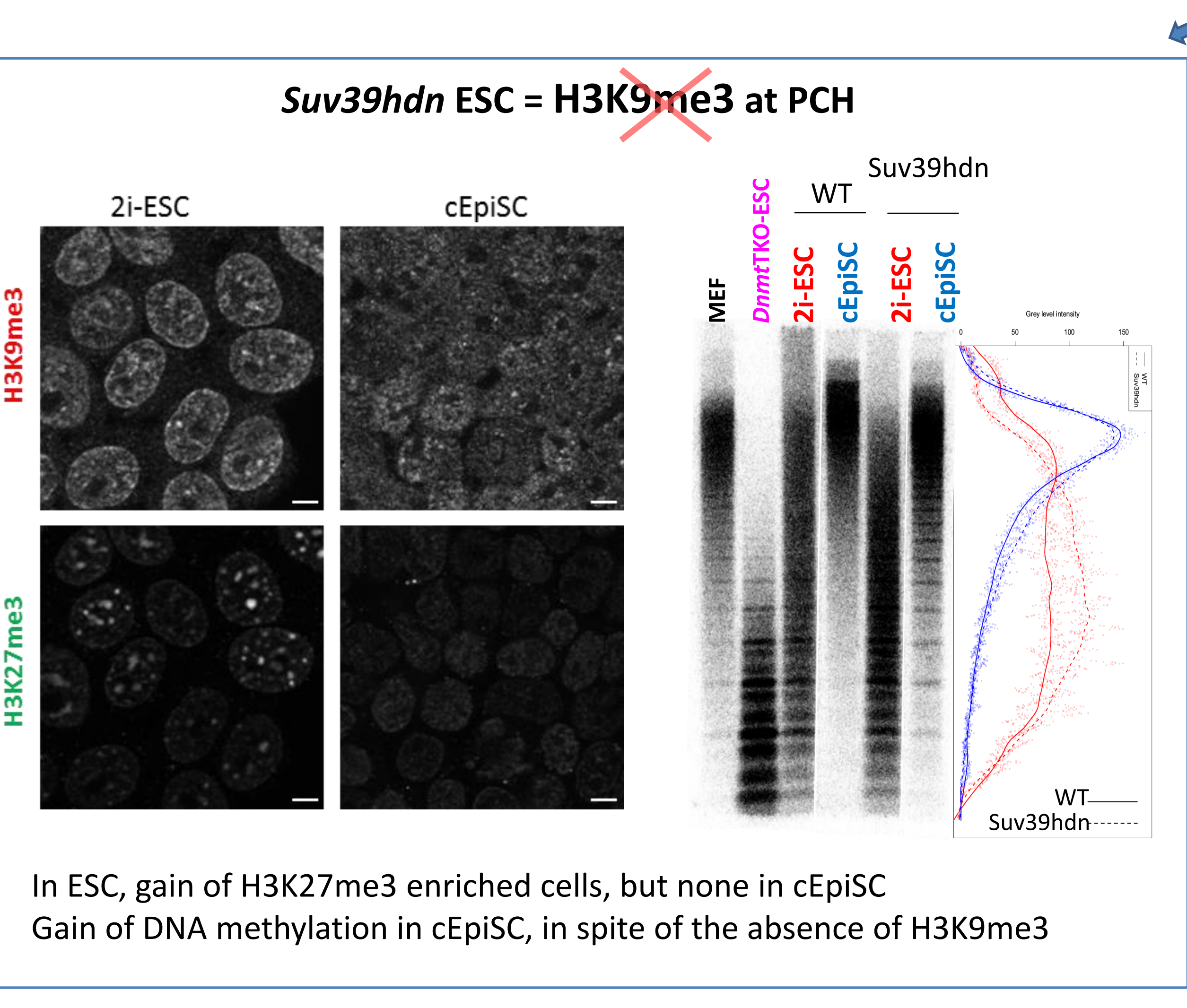
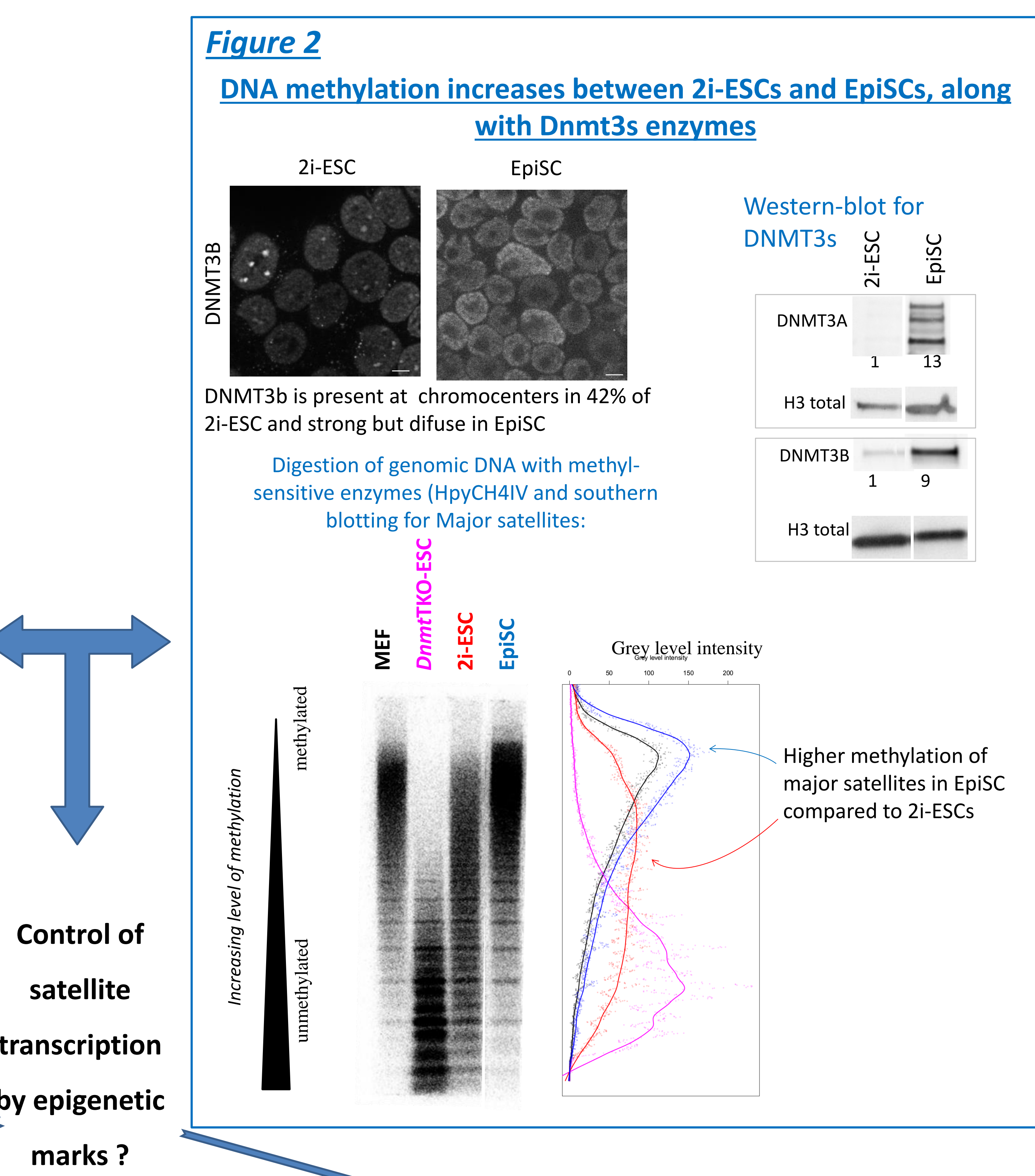
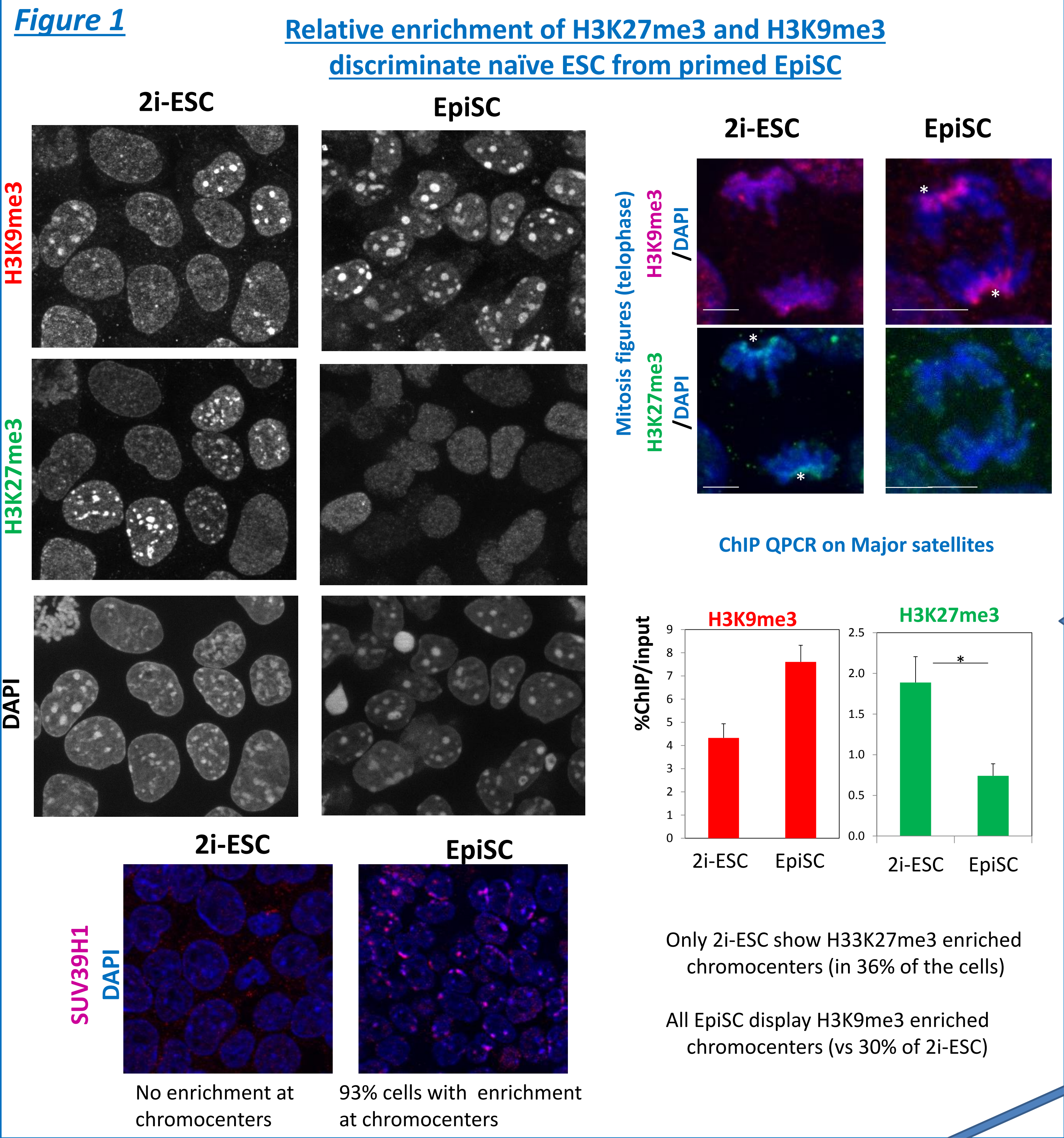
Focus on constitutive heterochromatin:

- Epigenetic constituents?
- Role in the epigenetic barrier?

EpiSC Primed pluripotency

Model: Conversion of WT and mutant ESC into cEpiSC: *Suv39hdn* : double KO of *Suv39h* enzymes that deposit H3K9me3 at PCH (Lehnertz et al, Current Biol 2003)

DnmtTKO : *dnmt1*^{-/-}; *dnmt3a*^{-/-}; *dnmt3b*^{-/-} (Tsumura et al, Genes to cell, 2006)



CONCLUSION :

Transition from naive to primed state of pluripotency is characterized by a more repressive status of PCH, with a loss of H3K27me3 and a gain of H3K9me3 and 5meC. Regulation of transcription at PCH in naive (ground) 2i-ESCs is uncoupled with their epigenetic state, while it is tightly controlled by heterochromatic marks in primed pluripotent cells.

WORKING MODEL

