La régulation épigénétique de HsMar1, un transposon d'ADN humain
The epigenetic regulation of HsMar1, a human DNA transposon

Abstract

Background - Both classes of transposable elements (DNA and RNA) are tightly regulated at the transcriptional level leading to the inactivation of transposition via epigenetic mechanisms. Due to the high copies number of these elements, the hypothesis has emerged that their regulation can coordinate a regulatory network of genes. Herein, we investigated whether transposition regulation of HsMar1, a human DNA transposon, differs in presence or absence of endogenous HsMar1 copies. In the case where HsMar1 transposition is regulated, the number of repetitive DNA sequences issued by HsMar1 and distributed in the human genome makes HsMar1 a good candidate to regulate neighboring gene expression by epigenetic mechanisms.

Results - A recombinant active HsMar1 copy was inserted in HeLa (human) and CHO (hamster) cells and its genomic excision monitored. We show that HsMar1 excision is blocked in HeLa cells, whereas CHO cells are competent to promote HsMar1 excision. We demonstrate that de novo HsMar1 insertions in HeLa cells (human) undergo rapid silencing by cytosine methylation and apposition of H3K9me3 marks, whereas de novo HsMar1 insertions in CHO cells (hamster) are not repressed and enriched in H3K4me3 modifications. The overall analysis of HsMar1 endogenous copies in HeLa cells indicates that neither full-length endogenous inactive copies nor their Inverted Terminal Repeats seem to be specifically silenced, and are, in contrast, devoid of epigenetic marks. Finally, the setmar gene, derived from HsMar1, presents H3K4me3 modifications as expected for a human housekeeping gene.

Conclusions - Our work highlights that de novo and old HsMar1 are not similarly regulated by epigenetic mechanisms. Old HsMar1 are generally detected as lacking epigenetic marks, irrespective their localisation relative to the genes. Considering the putative existence of a network associating HsMar1 old copies and SETMAR, two non-mutually exclusive hypotheses are proposed: active and inactive HsMar1 copies are not similarly regulated or/and regulations concern only few loci (and few genes) that cannot be detected at the whole genome level.

Keywords
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geneic regulation of *HsMar1*, a DNA transposon

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Both classes of transposable elements (DNA and RNA) are tightly regulated at the transcription level via epigenetic mechanisms. Due to the high copies number hypothesis has emerged that their regulation can coordinate a regulatory network of genes.

Whether transposition regulation of *HsMar1*, a human DNA transposon, differs in endogenous *HsMar1* copies. In the case where *HsMar1* transposition is regulated, the number of sequences issued by *HsMar1* and distributed in the human genome makes *HsMar1* a major player in regulating neighboring gene expression by epigenetic mechanisms.

A recombinant active *HsMar1* copy was inserted in HeLa (human) and CHO (hamster) cells and monitored. We show that *HsMar1* excision is blocked in HeLa cells, whereas CHO cells promote *HsMar1* excision. We demonstrate that de novo *HsMar1* insertions in HeLa cells differ from silencing by cytosine methylation and apposition of H3K9me3 marks, whereas de novo inserts in CHO cells (hamster) are not repressed and enriched in H3K4me3 modifications. The overexpression copies in HeLa cells indicates that neither full-length endogenous inactive copies nor transposon *HsMar1* repeats seem to be specifically silenced, and are, in contrast, devoid of epigenetic marks. Derived from *HsMar1*, presents H3K4me3 modifications as expected for a human host cell.

Our work highlights that de novo and old *HsMar1* are not similarly regulated by epigenetic mechanisms, and that *HsMar1* are generally detected as lacking epigenetic marks, irrespective of their localization within the genome. Considering the putative existence of a network associating *HsMar1* old copies and SE exclusive hypotheses are proposed: active and inactive *HsMar1* copies are not similarly regulated.

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elements (TEs) are mobile genetic elements, a prevalent part of eukaryotic genes. They are known to display various consequences, promoting various effects such as disrupting genes (upon or inducing recombination between genes at divergent loci. Beyond these foreseeable consequences in view of their occurrence, other more uncertain sequences, and then could alter the genetic regulatory network of several TEs is believed to be a genetic innovation [2].

The genetic consequences of TEs monomeric via an RNA intermediate (also known as sponrons) were widely illustrated in human genetics.

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