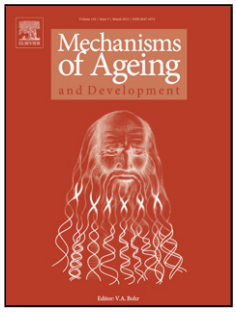

Title: The epigenetic alterations of endogenous retroelements in aging

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PII: S0047-6374(17)30291-9
DOI: https://doi.org/10.1016/j.mad.2018.02.002
Reference: MAD 11027

To appear in: *Mechanisms of Ageing and Development*

Received date: 30-11-2017
Revised date: 5-2-2018
Accepted date: 8-2-2018

Please cite this article as: Cardelli, Maurizio, The epigenetic alterations of endogenous retroelements in aging.Mechanisms of Ageing and Development https://doi.org/10.1016/j.mad.2018.02.002

The epigenetic alterations of endogenous retroelements in aging

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Highlights

- Endogenous retroelements host most of the CpG sites in the human genome
- Various epigenetic alterations involving endogenous retroelements are observed in aging
- Tumours are strongly associated with an epigenetic alteration of endogenous retroelements
- Various environmental stressors and age-related physiological modification can trigger an epigenetic alteration of endogenous retroelements
- An altered epigenetic status of endogenous retroelements can affect gene expression in several ways

Abstract

Endogenous retroelements, transposons that mobilize through RNA intermediates, include some of the most abundant repetitive sequences of the human genome, such as Alu and LINE-1 sequences, and human endogenous retroviruses. Recent discoveries demonstrate that these mobile genetic elements not only act as intragenomic parasites, but also exert regulatory roles in living cells. The risk of genomic instability represented by endogenous retroelements is normally counteracted by a series of epigenetic control mechanisms which include, among the most important, CpG DNA methylation. Indeed, most of the genomic CpG sites subjected to DNA methylation in the nuclear DNA are carried by these repetitive elements. As other parts of the genome, endogenous retroelements and other transposable elements are subjected to deep epigenetic alterations during aging, repeatedly observed in the context of organismal and cellular senescence, in human and other species. This review summarizes the current status of knowledge about the epigenetic alterations occurring in this large, non-genic portion of the genome in aging and age-related conditions, with a focus on the causes and the possible functional consequences of these alterations.

Keywords

Transposons; Endogenous Retroelements; DNA methylation; Epigenetics; Aging; Age-related diseases.

Abbreviations:

5mC: 5-methylcytosine; a-DMR: age-differentially methylated region; *Avy*: Agouti viable yellow; cfDNAs: cell-free DNA; COBRA: combined bisulfite restriction analysis; ERE: Endogenous Retroelement; early transposons: ETns; hADSC : human adipose derived mesenchymal stem cells; HERV: human endogenous retrovirus; HNSCC: head and neck squamous cell carcinoma; IAP: intracisternal A-particle; LINE: long interspersed nuclear element; LMNB1: Lamin B1; lncRNA: long non coding RNA; LTR: long terminal repeat; mammalian apparent LTR retrotransposons: MaLR; MeCP2: methyl-CpG-binding protein 2; meDIP: Methylated