Original article

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Genome-wide hypomethylation of LINE-1 and Alu retroelements in cell-free DNA of blood is an epigenetic biomarker of human aging

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Epigenetics, DNA methylation, cell-free DNA, retroelements, LINE-1

Abstract

Aging associated DNA hypomethylation of LINE-1 and Alu retroelements may be a crucial determinant of loss of genomic integrity, deterioration and cancer. In peripheral blood LINE-1 hypomethylation has been reported to increase during aging, but other studies did not observe significant changes. We hypothesized that these apparently inconsistent reports might relate to differences between cellular and cell-free DNA. Using the technique of idiolocal normalization of real-time methylation-specific PCR (IDLN-MSP) for genetic imbalanced DNA specimens we obtained evidence that LINE-1 hypomethylation in cell-free DNA, but not cellular DNA from peripheral blood is an epigenetic biomarker for human aging. Furthermore, hypomethylation of cell-free DNA is more extensive in smokers, suggesting that it might be used as a surrogate marker for monitoring the improvement of smoking-induced adverse effects after cancelling smoking.

1. Introduction

Long Interspersed Nuclear Elements (LINEs) and Short Interspersed Nuclear Elements (SINEs) are crucial contributors to the dynamics, plasticity and integrity of the human genome. LINE-1s are the only currently active autonomous mobile DNA elements in humans with at least 100 potential mobile copies in any individual diploid genome (Goodier, 2016). They have massively expanded throughout evolution with roughly 500,000 copies occupying about 17 % of the human DNA; all but around hundred copies are inactivated by truncations or mutations (Goodier, 2016). Alu elements are small dimeric SINE retroelements with almost one million genomic copies. They lack a coding sequence and hence depend on an active LINE-1 retrotransposition machinery to become mobile (Dewannieux et al., 2003). Noteworthy active LINE-1s are able to mediate high rate Alu transposition (Dewannieux