Francesco Neri, J Stem Cell Res Ther 2017, 7:8(Suppl)
DOI: 10.4172/2157-7633-C1-026

Intragenic DNA methylation prevents spurious transcription initiation

Francesco Neri
Leibniz Institute on Aging – Fritz Lipmann Institute, Germany

DNA methylation is a heritable epigenetic modification required for embryonic development, which causes transcriptional repression when established on gene promoters. Recent studies have reported that Dnmt3b binds preferentially to the gene bodies by interacting with the histone modification H3K36me3. While the molecular and biological functions of intragenic DNA methylation are still unknown, the deregulation of this epigenetic feature has been associated with several diseases. Here, we show that the Dnmt3b-dependent intragenic DNA methylation protects the gene body from RNA Polymerase II (RNA Pol II) spurious entry and cryptic transcription initiations. Using different genome-wide approaches, we demonstrate that loss of Dnmt3b leads to an increase of the RNA Pol II engagement within gene bodies resulting in the onset of spurious intragenic transcription initiations. Finally, we demonstrate that inhibition of RNA Pol II spurious entry depends on the enzymatic activity of the Dnmt3b recruited by H3K36me3. Our results elucidate the functional role of the Dnmt3b-dependent intragenic DNA methylation and the existence of a RNA Pol II-triggered epigenetic crosstalk involving SetD2, H3K36me3, Dnmt3b and DNA methylation, to ensure gene transcription initiation fidelity. This security feedback is probably lost during cancer development, where a global intragenic hypomethylation frequently occur, which increases transcription instability and promotes (stochastic) tumor cell heterogeneity.

Biography

Francesco Neri obtained PhD in Biotechnology in Siena (Italy) working on embryonic stem cells epigenetics. Then he worked as Postdoc between Human Genetics Foundation (HuGeF) in Torino (Italy) and the Radboud University Medical Centre, Nijmegen (Netherlands) where specialized his research on the DNA methylation specific epigenetic mark on stem cell, differentiation and colon cancer. During this period, he characterized new mechanisms of gene transcriptional regulation, developed new genome-wide methods and identified the role of the intragenic methylation. Since 2016, he is the Group Leader of the "Epigenetics research group" at the Fritz Lipmann Leibniz Institute on Aging (FLI) in Jena (Germany). His current research is supported by the Sofja Kovalevskaja starting grant of the von Humboldt foundation and it is focused on the aging-dependent epigenetic aberrations occurring in adult stem cells promoting colon cancer.

francesco.neri@leibniz-fli.de

Notes: