frontiers in Oncology

REVIEW
published: 29 June 2020
doi: 10.3389/fonc.2020.01024

SERS-Based Assessment of MRD in Acute Promyelocytic Leukemia?

Cristina Turcas[1,2], Vlad Moisoiu[1,3], Andrei Stefancu[3], Ancuta Jurj[4], Stefania D. Iancu[3], Patric Teodorescu[1,2], Sergiu Pasca[1,4], Anca Bojan[1,2], Adrian Trifa[2], Sabina Iluta[1,2], Alina-Andreea Zimta[5], Bobo Petrushev[5], Mihnea Zdrenghea[1,2], Horia Bumbea[6], Daniel Coriu[6], Dalia Dima[2], Nicolae Leopold[3]* and Ciprian Tomuleasa[1,2,4]*

[1] Department of Hematology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania, [2] Department of Hematology, "Ion Chiricuta" Institute of Oncology, Cluj-Napoca, Romania, [3] Faculty of Physics, Babeş-Bolyai University, Cluj-Napoca, Romania, [4] Research Center for Functional Genomics and Translational Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania, [5] Medfuture Research Center for Advanced Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania, [6] Department of Hematology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

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***Correspondence:**
Cristina Turcas
turcascristinam@gmail.com
Nicolae Leopold
nicolae.leopold@phys.ubbcluj.ro

Specialty section:
This article was submitted to Pharmacology of Anti-Cancer Drugs, a section of the journal Frontiers in Oncology

Received: 02 March 2020
Accepted: 22 May 2020
Published: 29 June 2020

Citation:
Turcas C, Moisoiu V, Stefancu A, Jurj A, Iancu SD, Teodorescu P, Pasca S, Bojan A, Trifa A, Iluta S, Zimta A-A, Petrushev B, Zdrenghea M, Bumbea H, Coriu D, Dima D, Leopold N and Tomuleasa C (2020) SERS-Based Assessment of MRD in Acute Promyelocytic Leukemia? Front. Oncol. 10:1024. doi: 10.3389/fonc.2020.01024

Acute promyelocytic leukemia (APL) is characterized by a unique chromosome translocation t(15;17)(q24;q21), which leads to the PML/RARA gene fusion formation. However, it is acknowledged that this rearrangement alone is not able to induce the whole leukemic phenotype. In addition, epigenetic processes, such as DNA methylation, may play a crucial role in leukemia pathogenesis. DNA methylation, catalyzed by DNA methyltransferases (DNMTs), involves the covalent transfer of a methyl group (-CH3) to the fifth carbon of the cytosine ring in the CpG dinucleotide and results in the formation of 5-methylcytosine (5-mC). The aberrant gene promoter methylation can be an alternative mechanism of tumor suppressor gene inactivation. Understanding cancer epigenetics and its pivotal role in oncogenesis, can offer us not only attractive targets for epigenetic treatment but can also provide powerful tools in monitoring the disease and estimating the prognosis. Several genes of interest, such as RARA, RARB, p15, p16, have been studied in APL and their methylation status was correlated with potential diagnostic and prognostic significance. In the present manuscript we comprehensively examine the current knowledge regarding DNA methylation in APL pathogenesis. We also discuss the perspectives of using the DNA methylation patterns as reliable biomarkers for measurable residual disease (MRD) monitoring and as a predictor of relapse. This work also highlights the possibility of detecting aberrant methylation profiles of circulating tumor DNA (ctDNA) through liquid biopsies, using the conventional methods, such as methylation-specific polymerase chain reaction (MS-PCR), sequencing methods, but also revolutionary methods, such as surface-enhanced Raman spectroscopy (SERS).

Keywords: DNA methylation, acute promyelocytic leukemia, measurable residual disease, disease monitoring, patient follow-up

BACKGROUND ON DNA METHYLATION

Realizing that all cells in an organism are derived from a single cell (the zygote) and that they share an almost identical genetic information has left open a crucial question: what is the molecular substrate accounting for the differences between cell types. At the beginning of the twentieth century, Waddington has famously proposed that lineage commitment happens akin to