HemaSphere

EHA EUROPEAN HEMATOLOGY ASSOCIATION

PB1917 EXPRESSION OF THE LONG NON-CODING RNA MALAT1 IN CHRONIC LYMPHOCYTIC LEUKEMIA

Topic: 5. Chronic lymphocytic leukemia and related disorders - Biology & Translational Research

Teodora Karan-Đurašević*[1], Milena Ugrin[1], Vojin Vukovic[2,3], Darko Antic[2,3], Sanja Stankovic[4,5], Irena Marjanovic[1], Tatjana Kostic[1], Vladimir Otasevic[2], Kristina Tomic[2], Sofija Sarac[2], Biljana Mihaljevic[2,3], Sonja Pavlovic[1], Nataša Tošić[1]

[1]Laboratory For Molecular Biomedicine, Institute Of Molecular Genetics And Genetic Engineering, University Of Belgrade, Belgrade, Serbia; [2]Clinic Of Hematology, University Clinical Center Of Serbia, Belgrade, Serbia; [3]Medical Faculty, University Of Belgrade, Belgrade, Serbia; [4]Center For Medical Biochemistry, University Clinical Center Of Serbia, Belgrade, Serbia; [5]Department Of Biochemistry, Faculty Of Medical Sciences, University Of Kragujevac, Kragujevac, Serbia

Downloaded from http://journals.lww.com/hemasphere by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 10/18/2023

Background:

The long non-coding RNA (lncRNA) MALAT1 (metastasis-associated lung adenocarcinoma transcript 1) dysregulated expression and prognostic significance have been reported in a variety of cancers, including hematological malignancies, but have been poorly investigated in chronic lymphocytic leukemia (CLL). Acting through regulation of gene expression at transcriptional and post-transcriptional level, lncRNA MALAT1 is involved in many cellular processes such as proliferation, apoptosis, migration and drug resistance. However, its role as either an oncogene or a tumor-supressor is still controversial, and clearly tumor type-dependent.

Aims:

To analyze the expression pattern of lncRNA MALAT1 in CLL, and evaluate its prognostic relevance.

Methods:

This study enrolled 114 unselected CLL patients (pts) and 20 healthy controls (hcs). Clinical and laboratory characteristics of pts were determined at diagnosis, while genetic analyses were performed during the period prior to first treatment. The expression of MALAT1 was analyzed in peripheral blood mononuclear cells by RQ-PCR, using TaqMan chemistry and GAPDH as endogenous control; relative quantification was made by comparative ddCt method, using hcs as calibrator.

Results:

CLL cohort consisted of 81 males and 33 females (male/female=2.45), with median age at diagnosis of 59 years (range 33-80). Hcs group consisted of 15 males and 5 females (male/female=3), with median age at diagnosis of 71 years (range 65-85). Distribution of Binet stages (112/114 pts) was as follows: A-46.4%, B-39.3%, C-14.3%. Del13q, normal karyotype, trisomy12, del11q and del17p were detected by FISH in 33%, 35%, 9.3%, 10.3% and 12.4% of pts, respectively (97/114 pts). CD38 status (85/114 pts) was negative in 70.6% and positive in 29.4% of pts. Regarding *IGHV* mutational status (114 pts), 41.2% of pts were mutated, and 58.8% unmutated. Median follow-up was 72 months (range 1-360). LncRNA MALAT1 was overexpressed in CLL pts compared to hcs ($p<0.001$). Median value of MALAT1 expression was used to divide the cohort into $MALAT1^{low}$ and $MALAT1^{high}$ groups, and association with clinical and biological features at diagnosis was assessed. In both pts and hcs MALAT1 expression was not associated with age but, unlike hcs, $MALAT1^{high}$ status was significantly associated with male sex in CLL ($p=0.003$). Regarding laboratory parameters, MALAT1 expression showed no correlation with leukocyte, lymphocyte and platelet counts, and serum β2-microglobulin, but exerted a positive correlation with hemoglobin level ($r=0.315$, $p=0.003$) and a negative correlation with lactate dehydrogenase (LDH) level ($r=-0.303$, $p=0.004$). MALAT1 expression was higher in Binet A and B pts vs. Binet C pts ($p=0.037$). There was also a trend toward higher MALAT1 expression in pts with favorable (del13q) and intermediate (normal karyotype,

Copyright Information: (Online) ISSN: 2572-9241
© 2023 the Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the European Hematology Association. This is an open access Abstract Book distributed under the Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) which allows third parties to download the articles and share them with others as long as they credit the author and the Abstract Book, but they cannot change the content in any way or use them commercially.

Abstract Book Citations: Authors, Title, HemaSphere, 2023;7(S3):pages. The individual abstract DOIs can be found at https://journals.lww.com/hemasphere/pages/default.aspx.

Disclaimer: Articles published in the journal HemaSphere exclusively reflect the opinions of the authors. The authors are responsible for all content in their abstracts including accuracy of the facts, statements, citing resources, etc.

Downloaded from http://journals.lww.com/hemasphere by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 10/18/2023

trisomy12) cytogenetics in comparison to pts with unfavorable (del11q and del17p) cytogenetics (p=0.059). In addition, MALAT1^{high} status was associated with CD38-negative status (p=0.017), but not with IGHV mutational status. Finally, while the association of MALAT1 expression with the time to first treatment was not detected, longer median overall survival (OS) in MALAT1^{high} vs. MALAT1^{low} group was observed (142 vs. 82 months, log rank p=0.032).

Summary/Conclusion:

LncRNA MALAT1 is up-regulated in CLL. However, high MALAT1 expression is associated with several favorable prognostic markers (high hemoglobin, low LDH, early clinical stages, negative CD38 status), as well as longer OS. The exact mechanisms of MALAT1 function in CLL pathogenesis and/or progression remain to be determined.

Copyright Information: (Online) ISSN: 2572-9241
© 2023 the Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the European Hematology Association. This is an open access Abstract Book distributed under the Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) which allows third parties to download the articles and share them with others as long as they credit the author and the Abstract Book, but they cannot change the content in any way or use them commercially.

Abstract Book Citations: Authors, Title, HemaSphere, 2023;7(S3):pages. The individual abstract DOIs can be found at https://journals.lww.com/hemasphere/pages/default.aspx.

Disclaimer: Articles published in the journal HemaSphere exclusively reflect the opinions of the authors. The authors are responsible for all content in their abstracts including accuracy of the facts, statements, citing resources, etc.