



MINIHOUSTY WYELIZN

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P17

Hematologie  
Jan TRKA

Satna - clo a K I O

REGISTRACE  
NA MÍSTĚ

Hematologie 2024  
17.-19. 1. 2024

REGISTRACE VIP  
ČLENOVÉ P...  
A VĚDECKÝ...  
ČESTNÍ ČLENOVÉ O...  
PREZENTACE...  
ČESTNÍ HOSTI...

CERTIFIKÁTY BUDOU  
ZASLÁNY ELEKTRONICKY  
DO 14 DNŮ PO  
SKONČENÍ KONFERENCE.

24. PRAŽSKÉ HEMATOLOGICKÉ DNY  
**Hematologie 2024**  
KAM NÁS POSOUVÁ TO NEJLEPŠÍ Z ČESKÉ  
A SVĚTOVÉ HEMATOLOGIE  
17.-19. 1. 2024

**REGISTRACE**



PSÍ Z ČESKÉ



**Froňková E.**

**Shadman M.**

**Jelinek T.**

**Klener P.**

vystavovatelům  
st a podporu!

Všem partnerům a vystavovatelům  
děkujeme za účast a podporu!

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24. PRAŽSKÉ HEMATOLOGICKE DNY  
**Hematologie 2024**  
KAM JINDA POSOUVA TO NEJLEPŠÍ Z ČESKÉ  
A SVĚTOVÉ HEMATOLOGIE  
17.-19. 1. 2024

**Pořadatel:**  
SPOLEK ČESKÝCH LÉKAŘŮ  
V PRAZE ČLS JEP

**ve spolupráci s:**

- 1. Interní klinikou 1. lékařské fakulty UK a VFN v Praze  
Ústavem hematologie a krevní transfuze  
Klinickou dědičnou hematologií a onkologií FN Motol
- 2. Lékařské fakulty UK v Praze
- Interní hematologickou klinikou FN Královské Vinohrady
- 3. Lékařské fakulty UK v Praze

**pod záštitou:**  
Česká hematologická společnost ČLS JEP  
České společnosti pro transfuzi a hematologii ČLS JEP





CATOLICA  
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LISBOA




24. PRAŽSKÉ HEMATOLOGICKÉ DNY  
**Hematologie 2024**  
JAK MÁM PŘÍSTUP K TUDÉŽE ALEPSŽI Z ČESKA  
A SVĚTOVÉ HEMATOLOGIE  
17.–19. 1. 2024

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**pod záštitou:**  
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České společnosti pro trombózu a hemostázu ČLS JEP



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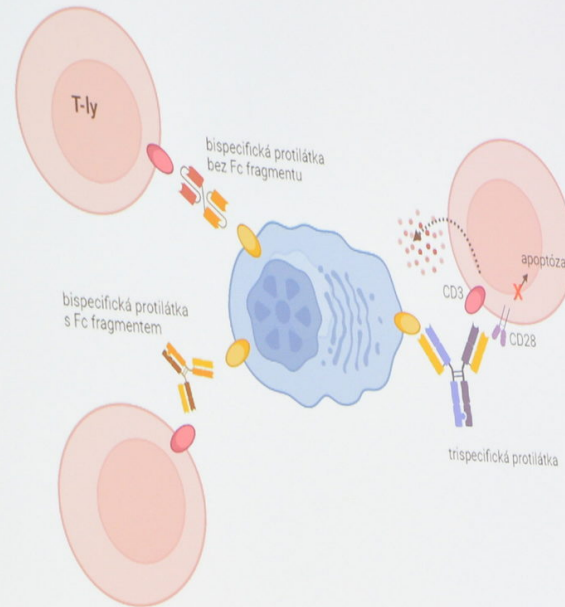
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## Bispecifické protilátky



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17.-19. 1. 2024

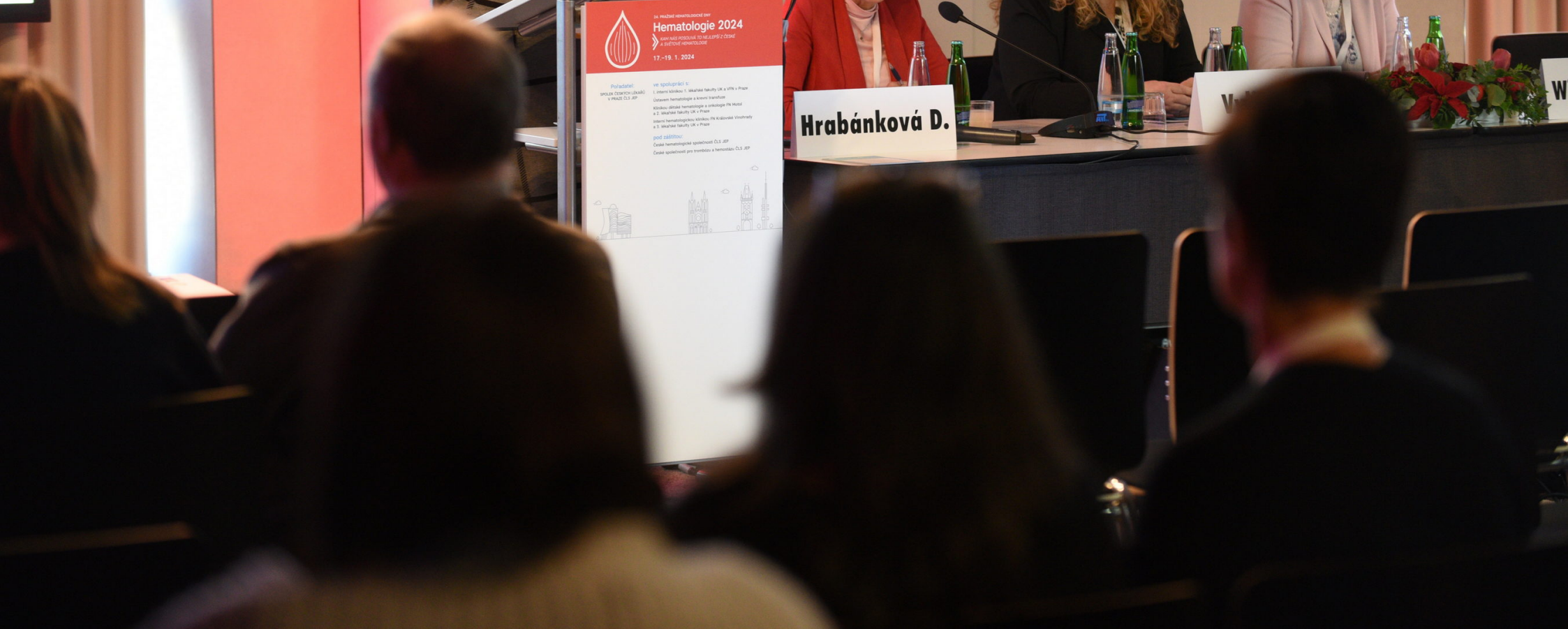
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České společnosti pro transfúzi a hematologii ČLS JEP



**Hrabánková D.**

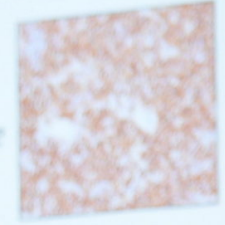
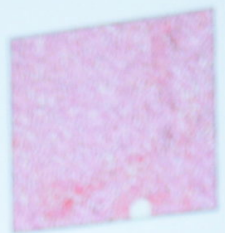
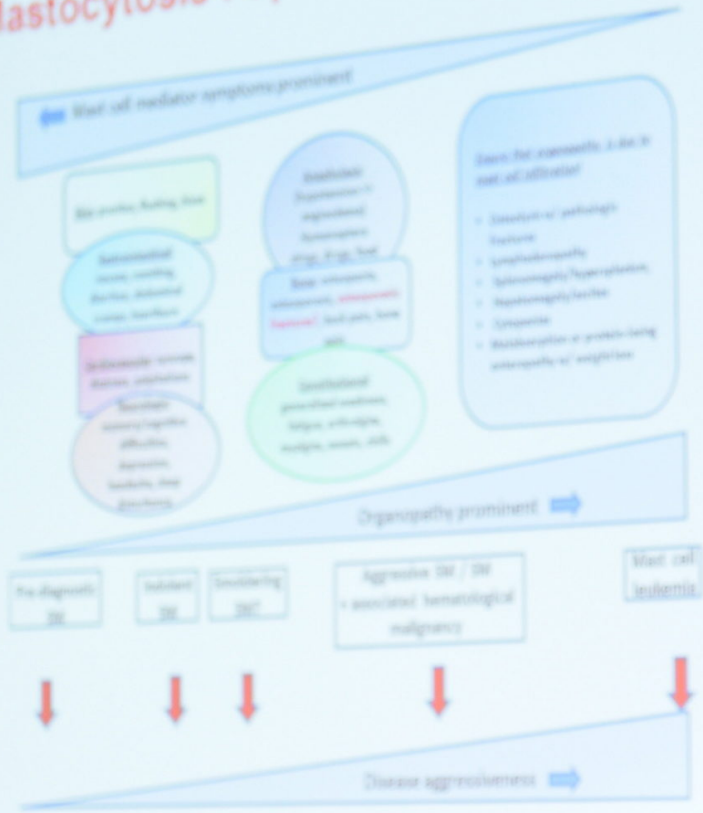






# Mastocytosis : Spectrum of the disease

Most cell infiltration  
Aggregates+++  
Kit++/Tryptase+++  
CD117/CD25+



Tryptase

Tryptase

Adapted from Pandarum et al



24. PRAŽSKÉ HEMATOLOGICKÉ DNY  
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 A SÚVĚNĚ HEMATOLOGIE  
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Rusinová K

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24. PRAŽSKÉ HEMATOLOGICKÉ DNY

# Hematologie 2024

» KAM NÁS POSOUVÁ TO NEJLEPŠÍ Z ČESKÉ  
A SVĚTOVÉ HEMATOLOGIE

17. - 19. 1. 2024

Clarion Congress Hotel Prague



Rusinová K.



# P34

## P34

Aim: We aimed to uncover the mechanisms of accelerated progression in lower-risk MDS patients.

Conclusions: Decreased cell cycle and metabolic activity, downregulated DNA damage response, and dysregulated cell adhesion gene expression were identified to be associated with accelerated progression in lower-risk MDS patients.

# MDS II

### ACCELERATED PROGRESSION IN LOWER-RISK MYELODYSPLASTIC NEOPLASMS: ATTENUATED CELL CYCLE, DNA DAMAGE RESPONSE, AND AUGMENTED ONCOGENIC TRANSCRIPTOME SIGNATURES

**uhkt**  
UNIVERSITY HOSPITAL KARLOVOFAKULTY  
UNIVERSITY OF SOUTH BOHEMIA

**MONIKA KASSELKOVÁ, ZUZANA LENKEROVÁ<sup>1</sup>, PAŮLA KORÁLKOVÁ<sup>1</sup>, IVA TRSOVÁ<sup>1</sup>, HANA VOTAVOVÁ, ZDĚNEK KŘEČEK<sup>1</sup>, ANNA JONASOVÁ<sup>1</sup>, JAROSLAV CERMÁK<sup>1</sup>, VLADIMÍR DIVOKÝ<sup>1</sup>, and MONIKA BELKOVÁ<sup>1</sup>**  
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#### INTRODUCTION

Patients with myelodysplastic neoplasms (MDS) face the risk of transformation to acute myeloid leukemia (AML), although prognostic scoring systems exist for risk stratification and treatment decisions. In MDS patients, disease management remains challenging due to the heterogeneity of clinical courses and long-term outcomes. The natural history of patients with lower-risk MDS (LR-MDS) is very heterogeneous and some LR-MDS patients experience rapid progression despite a generally favorable prognosis.

#### AIM

To uncover the molecular mechanisms underlying accelerated progression in hematopoietic stem/progenitor cells of patients with LR-MDS regardless of driver mutations by transcriptome analysis including differentially expressed protein-coding genes, and long non-coding RNAs (lncRNAs) as well as differential alternative splicing events.

#### METHODS

- Discovery cohort: 41 LR-MDS, 146 progressed within 24 months (pMDS)
- Validation sample set: 7 LR-MDS patients (LR-MDS), pMDS
- RNA-seq of bone marrow (BM) CD34+ cells: doublet selection with MacqChip RNA Depletion Kit, library preparation with NEBNext Ultra II Directional RNA Library Prep Kit for Illumina, and sequencing on HiSeq 2500 or NovaSeq.
- Transcriptome data functional annotation: String 11.0, Gene Set Enrichment Analysis (GSEA), software 3.0, Gene Ontology (GO), and Reactome Pathway.
- Long non-coding RNA expression analysis of the non-coding profile of 13 LR-MDS associated genes; the probability of progression-free disease was calculated in our cohort.
- Differential alternative splicing events (MATS 2.1.2).
- Immunofluorescence (IF) formalin-fixed paraffin-embedded sections from 9 LR-MDS patients were stained with CD34, ZEB1, and ZEB2 antibodies.

#### RESULTS

- The differential expression analysis showed 845 differentially expressed genes (DEGs) in pMDS compared to LR-MDS. Cell cycle and cell cycle checkpoint-associated genes and activation of ATM in response to replication stress were significantly under-represented in pMDS CD34+ BM. Cellular pathways associated with cellular response to stress and DNA damage response (DDR) were downregulated in pMDS compared to LR-MDS. CD34+ cells of pMDS exhibited a transcriptional pattern of quiescent-like cell state with overall decreased metabolism signatures and significantly reduced lineage differentiation compared to LR-MDS CD34+ cells.
- Only processes related to cell-matrix adhesion or cell-cell adhesion were significantly upregulated in pMDS. A key transcription factor controlling changes in cell-cell adhesion, ZEB1, was significantly overexpressed in pMDS BM CD34+ cells. Correlations with its protein target suggest a key role for ZEB1 in LR-MDS transcriptional regulatory network.
- The protein expression of ZEB1 in CD34+ BM cells was detected immunohistochemically, and this protein level was positively moderately correlated with lncRNA GDCAT1 expression which is a lincRNA associated with cancer.
- Among the top 50 upregulated genes in the pMDS, overexpression of previously identified markers of leukemic progression and/or MDS/AML, such as LINC01551, DNMT3A, and others were demonstrated.
- Overexpression of ATRX, a gene not previously associated with LR-MDS progression, showed predictive power for accelerated progression in LR-MDS and its expression had an independent prognostic impact (p=0.003) on progression-free survival in a multivariate analysis of important clinical and genetic factors.
- We selected a prognostic DDR-associated gene signature consisting of 18 genes. This cell-subpopulation and pathway also showed autonomous upregulation in pMDS. This cell-subpopulation was negatively, and ZEB1 might be an important transcriptional regulator in pMDS. We propose new essential biomarkers, such as ZEB1 and DDR gene signature for high DDR gene expression had a significantly higher probability of progression-free disease (p=0.001) compared to low DDR gene expression.

#### CONCLUSIONS

In conclusion, the accelerated progression phenotype of pMDS appears to be a consequence of the downregulation of DNA damage response and cell cycle genes for increased protein synthesis. This cell-subpopulation and pathway also showed autonomous upregulation in pMDS. This cell-subpopulation was negatively, and ZEB1 might be an important transcriptional regulator in pMDS. We propose new essential biomarkers, such as ZEB1 and DDR gene signature for high DDR gene expression had a significantly higher probability of progression-free disease (p=0.001) compared to low DDR gene expression.

#### ACKNOWLEDGMENTS

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**Froňková E.**

**Shadman M.**







Hematology Foundation of Hematological Quality  
Hematology Award 2024  
For the year 2023  
**Prof. Dr. Andrei Hochhaus**  
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**Hematologie 2024**  
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**Podcast:**  
SPLEEN VERMEEREN (SPLENOMEGALIE)  
C. DIBAKI D. S. DEB

**in samenwerking met:**  
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IN POKOLJEVIŠTU  
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HEMATOLOGISTS OF CROATIA  
17-19. 1. 2024

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