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Cover

Abstracts submitted to the 'EACR 2025 Congress: Innovative Cancer Science', from 16–19 June 2025 and accepted by the Congress Organising Committee are published in this Supplement of *Molecular Oncology*, an affiliated journal of the European Association for Cancer Research (EACR).

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EACR 2025 Congress Abstracts

Contents

Proffered Papers

10-minute talks awarded for the highest scored abstracts, embedded in the scientific symposia sessions. These presentations are not accompanied by a poster.

Posters in the Spotlight

Tuesday 17 June, 18:40-20:00 and
Wednesday 18 June, 18:40-20:00

Dedicated sessions taking place in the spotlight area within the Exhibition Hall. Poster presenters with high-scoring abstracts will give short presentations of up to 5 minutes each. Their posters will also be available to view during the Poster Discussion Sessions.

Addendum to the EACR 2025 Abstracts

Due to a technical error, 84 abstracts were omitted from the initial version of this published Abstract Book. We apologise for this omission, which has been corrected with an Addendum from page 895 of this volume. Please navigate directly to the Addendum section to view the omitted abstracts.

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transcriptional dynamics in ALCL and to assess its therapeutic potential.

Material and method

Formalin-fixed paraffin-embedded sections from diagnostic/relapsed primary lymphoma biopsies were used for retrospective cohort analysis. In vitro experiments combined omics approaches (RNA-seq, ChIP-seq, ATAC-seq and CMap) with functional assays.

Result and discussion

To investigate the transcriptional function of HELLS in ALK- ALCL, we integrated ChIP-seq on the TLBR-2 cell line, the principal model in prior studies elucidating HELLS role in lymphomagenesis, with RNA-seq in HELLS knockdown (HELLS KD) and control cells. We identified 467 deregulated and directly bound by HELLS based on ChIP-seq, termed HELLS-direct genes (HDGs). Their clinical significance was confirmed in vivo in a retrospective cohort of 44 ALCL patients (15 ALK^+ and 29 ALK^- ALCL) through the NCounter platform. Merging HDGs with RNAPII-ChIP seq data revealed that about 60% of HDGs showed defects in RNAPII elongation, while 40% exhibited a significant alteration in RNAPII occupancy after HELLS KD. Gene ontology analysis showed that these last HDGs were enriched in T-cell mediated immunity, cytokines signaling and the JAK/STAT pathway, highlighting HELLS' underscored role in immune-related pathways. ATAC-seq analysis showed that HELLS modifies chromatin accessibility mainly at immune-related promoters in T-cell lymphoma cells. This process facilitates RNAP recruitment and transcription factor binding, enhancing transcriptional activity. Immune-related gene promoters were enriched for H3K4me3, further suggesting chromatin structural changes are necessary for their precise gene expression. To assess the therapeutic potential of HELLS, we performed an HDGs-based drug repurposing analysis by interrogating the CMap. We identified PI3K, JAK/STAT, and DNA-PK as top-scored synergistic pathways with HELLS depletion In vitro experiments confirmed that Ruxolitinib (JAKi) and AZD7648 (DNA-PKi), caused significant synthetic lethality combined with HELLS depletion.

Conclusion

These findings demonstrate the direct role of HELLS in transcriptional regulation and pave the way for the development of targeted and clinically translatable strategies for HELLS inhibition.

EACR25-0800
Unraveling Inflammation-Related microRNAs in Pleural Mesothelioma: Gene Regulation and Pathway Analysis

G. Tonnini[1], C. Mazziotta[1], J. Rotondo[2], M. Tramarin[1], G. Badiale[1], M. Oimo[1], C. Cervellera[1], M. Tognon[1], F. Martini[1]

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Introduction

Pleural mesothelioma (PM) is a rare and highly aggressive malignancy originating from the pleural lining. Approximately 80% of cases result from the inhalation of asbestos fibers. This exposure triggers a chronic inflammatory response in the pleura, leading to tissue damage, uncontrolled cell growth and genetic mutations that promote cancer. There are three main PM histotypes, epithelioid, biphasic, and sarcomatoid. Recent studies highlight the importance of non-coding RNAs in PM, including microRNAs (miRNAs), as potential diagnostic and prognostic cancer biomarkers.

Material and method

Herein, we investigated the differential expression of inflammation-related miRNAs by RT^2 Profiler PCR Array Human Inflammatory Response (n = 84 miRNAs) in primary mesothelioma cell lines of different histotypes, epithelioid (n = 2), biphasic (n = 2), and sarcomatoid (n = 2), and normal human mesothelial cell lines (n = 2). miRNA expression analysis was analyzed using the 2-ΔΔCt method. Log2 fold change <-2/>2 was considered statistically significant. Algorithm, i.e. miRSYSTEM was used for miRNA target genes prediction using the default setting. Gene ontology (GO)/Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses were employed to categorize genes and identify relevant pathway.

Result and discussion

Our results demonstrate distinct miRNA expression profiles in PM compared to control group. A total of 10/84 (12%) miRNAs were differentially expressed when comparing PM to normal cells: of these 6/10 (60%) were upregulated and 4/10 (40%) were downregulated. To determine the potential biological relevance of the differentially expressed miRNAs to PM, we predicted the target spectrum of individual deregulated miRNAs and assessed which biological pathways were enriched with their putative targets. A total of 2,201 targets were predicted for the 4 downregulated miRNAs. GO for biological process showed that regulation of transcription of cell cycle G1/S phase transition were the most enriched processes in PM cell lines. GO for molecular function exhibited that activin receptor activity, protein serine/threonine kinase activity and DNA binding were the most enriched. Moreover, GO indicated that serine/threonine protein kinase complex, activin receptor activity, nucleus and heterochromatin were the most enriched cellular component.

Conclusion

Our investigation highlights that inflammation-related miRNAs are differentially regulated in PM, underscoring their potential as diagnostic biomarkers and therapeutic targets. Future studies will focus on validating these miRNA signatures in a larger panel of cell lines and patient sera, and on elucidating their functional roles in PM pathogenesis.

EACR25-0822
Promoter methylation regulates CDHR5 and UPB1 expression in clear cell Renal Cell Carcinoma with sarcomatoid differentiation

F. Fernandes-Pontes[1,2,3], V. Constâncio[4,2,5], J. Lobo[6,2,7], M. Alzamora[6,2], R. Silva-Santos[6,2], R. Henrique[6,2,7], V. Miranda-Gonçalves[4,2], C. Jerónimo[4,2,7]