

1. BIOLOGY AND PRECLINICAL

MODULATION OF MIR-29B EXPRESSION AND APOPTOSIS IN MULTIPLE MYELOMA CELL LINES FOLLOWING TREATMENT WITH HALF-SANDWICH OS(II) COMPLEXES**D. Švehlová¹, L. Slavičková¹, I. Frydrych², P. Štarha⁴, K. Smešný Trtková^{1|2|3}**

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Background. MicroRNAs are short non-coding RNAs of 20-22 nucleotides that regulate gene expression through epigenetic mechanisms and play an important role in signaling pathways controlling the cell cycle, differentiation, cell proliferation, and apoptotic cell death. The miR-29 family consists of two clusters - miR-29a/miR-29b-1 and miR-29c/miR-29b-2 located on chromosome 7q32.3 and 1q32.2. The miR-29 family is involved in numerous pathophysiological processes, including multiple myeloma pathogenesis.

Objective. Previous studies have shown that miR-29 family members act as tumor suppressors in different cancers, including multiple myeloma, where miR-29b upregulation is linked to decreased proliferation, cell cycle arrest, and apoptosis. Therefore, the aim of the study is to investigate the effects of half-sandwich osmium compounds on the expression of miR-29b members (miR-29b-1-5p, miR-29b-2-5p, miR-29b-3p) and on apoptosis induction in multiple myeloma cell lines.

Materials and Methods. RNA was isolated from two myeloma cell lines - KMS12-BM and U266 treated with [Os(η^6 -pcym)Cl(L1)]PF₆ and [Os(η^6 -pcym)Cl(L2)]PF₆ complexes, where L1 is N,N'-bis[naphthalen-2-ylmethylidene]ethane-1,2-diamine and L2 N,N'-bis[phenanthren-9-ylmethylidene]ethane-1,2-diamine. The expression of miR-29b-1-5p, miR-29b-2-5p and miR-29b-3p was quantified by RT-PCR us-

ing probes specific for the mature miRNA sequence. Apoptosis in treated myeloma cells was assessed by flow cytometry (FACS).

Results. Treatment of U266 multiple myeloma cells with three different concentrations of the complex [Os(η^6 -pcym)Cl(L1)]PF₆ resulted in increased expression of miR-29b family members. Notably, miR-29b-2-5p expression was significantly upregulated, reaching statistical significance (1.2 μ M: $p < 0.0001$, 2.4 μ M: $p < 0.0001$, 3.6 μ M: $p = 0.00018$). Concurrently, treatment with the [Os(η^6 -pcym)Cl(L1)]PF₆ complex induced in a concentration-dependent increase in apoptotic cell populations in U266 cells. Statistically significant increases were observed at 2.4 μ M ($p < 0.01$) and 3.6 μ M ($p < 0.001$) concentrations compared to control.

Conclusion. The increased expression of miR-29b is a consequence of the application of the [Os(η^6 -pcym)Cl(L1)]PF₆ complex, and may contribute to its pro-apoptotic effects in multiple myeloma cells. *This study was funded in part by IGA_LF_2025_001; RVO (FNOL, 00098892); the Czech Health Research Council (AZV) of the Ministry of Health of the Czech Republic (NW25-03-00462) and the financial support of the European Union under the LERCO project CZ10.03.01/00/22_003/0000003 via the Operational Programme Just Transition. Dedication: EXCELES, ID Project No. LX22NPO5102; Funded by the European Union - Next Generation EU.*