

## **THE ROLE OF ALDEHYDE DEHYDROGENASE IN COLORECTAL CANCER CHEMORESISTANCE AND METASTASIS**

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Enzymes belonging to the aldehyde dehydrogenase (ALDH) family are involved in the detoxification processes, which puts them in an important position for the proper function of the organism. On the other hand, ALDHs are involved in tumour initiation and progression. In several types of tumours, high ALDH expression is associated with increased chemoresistance and poor prognosis. The aim of the study was to evaluate the impact of ALDH1A1 and ALDH1A3 knockout in chemoresistant colorectal cancer (CRC)-derived cells and the role of c-Met and CXCR4 signalling pathways in CRC chemoresistance and metastasis.

Expression of ALDH isoforms 1A1 1A3 was inhibited by CRISPR/Cas-9 method. Expression of c-Met and CXCL12-CXCR4 was evaluated by flow cytometry. ALDH activity was quantified by ALDEFLUOR™. Signalling pathways were pharmacologically inhibited by AMD3100 and SU11274. The impact on gene expression was evaluated by qPCR and CellTiter-Glo® Luminescent Cell Viability Assay was used to assess the response to chemotherapy.

Inhibition of CXCL12-CXCR4 and c-Met pathways led to significant decrease of ALDH1A1 expression and reduction of overall ALDH activity. ALDH1A3 knockout in chemoresistant cells led to increased sensitivity to 5-fluorouracil and decreased migratory potential in vitro.

Funding: The study was supported by Ministry of Health of the Slovak Republic under the contract 2019/60-BMCSAV-4, by the VEGA grant No. 2/0050/19 and by funding from the European Union's Horizon 2020 Research and Innovation Strategies to Programme under grant agreement No. 857381.