Title of the project: Elucidation of the role of cadherins and EMT in the development of chemotherapy resistance in metastatic colorectal cancer

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Principal Investigator: E. Rudolf


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Summary of 2019 results

Title of the presentation: Role of E and N-cadherin in colon cancer cell behavior in vitro and in vivo

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Our project was focused on elucidation of the role of cadherins and epithelial-to-mesenchymal transition (EMT) in the development of chemotherapy resistance in metastatic colon cancer. The outcomes of specific aims of the project are as follows:

1) Established primary colon cancer (CRC) cell lines were compared with corresponding immortalized cell lines (SW480 and SW620) and the expression of selected markers associated with cancer progression were determined on microRNA, mRNA and protein levels. Moreover, oxaliplatin and irinotecan, chemotherapeutics commonly used for treatment of advanced colon cancer, were used for treatment of both types of cell lines and their effect on proliferation, viability and migration was determined.

2) The comparison of EMT markers and resistance markers expression on miRNA and mRNA levels was investigated and significant differences between primary CRC, healthy colon tissue and lymph node metastases were correlated with pathological and clinical data. In addition, significant differences in the expression of select microRNAs in primary tumor and healthy tissue were found too.

3) The results from experiments with E-cadherin (CDH1) knockdown and N-cadherin overexpressed CRC cells were evaluated and compared with established cell lines with naturally low, resp. high level of cadherins. The cells with different expressions were implanted into the nude mice and molecular analyses of the tumor tissue were performed.

4) LC-MS analysis of irinotecan and oxaliplatin and their metabolites were detected and accumulation inside the cells were compared.

Obtained data contributed to understanding of the behavior of the CRC cells with various expression of the cadherins and showed the diverse effect of this expression on established and immortalized cell lines proliferation as well as the expression of the markers related with cancer progression.

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