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

Grant Agency: Czech Republic  
Project Number: 17-10331S

Principal Investigator: E. Rudolf


Starting date: 01.01.2017  
Duration (years): 3

Total funds allocated for project - Kč (thousands): 8.222

Summary of 2017 results

Title of the presentation: Oxaliplatin and irinotecan induce heterogenous changes in the EMT markers of metastasizing colorectal carcinoma cells

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Colorectal cancer is one of the most common malignancies in developed countries. Treatment of this type of cancer has been significantly improved, but tumor resistance is still frequent cause of chemotherapy failure. Our study should provide insight into tumor survival mechanisms and suggest potential novel targets to improve CRC treatment strategies.

1) In total (8 months in 2017), 22 samples of colorectal cancer and/or metastasis to lymph node were chosen for cell derivation and 15 cell lines were successfully established. The most effective establishment was observed in poorly differentiated tumors (grade 3) of advanced local stage (T3 stage of tumors). The most successful isolation of cancer cells from lymph node was noted in specimens with high stage of nodal involvement.

2) Firstly, established primary colon cancer cells and/or responsible lymph node metastatic cells were subjected to basic immunohistochemical analysis - cytokeratin AE1/AE3 and Giemsa staining. The presence of typical markers of EMT process was also evaluated and confirmed. In addition, mutation analysis of genes involved in the development of advanced colon cancer was performed by Massively Parallel Sequencing (NGS).

3) Next, established cell lines were compared with corresponding immortalized cell lines (SW480 and SW620) and selected markers associated with cancer progression were determined on microRNA, mRNA and protein levels. Simultaneously, the expression of multidrug resistant proteins (MDR1, MRP1, MRP2) participating in the chemotherapeutic resistance in colon cancer cell lines, as well as in metastatic cells derived from lymph node was evaluated. Oxaliplatin, irinotecan and 5-fluorouracil, chemotherapeutics commonly used for treatment of advanced colon cancer, were used for treatment of established cancer cell lines and their effect on proliferation, viability and migration was determined by endpoint assays and real-time analysis. The expression of cancer progression markers was also examined and compared in untreated and/or treated cells.

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