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

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Summary of 2018 results

Title of the presentation: Role of E-cadherin in metastatic colorectal cancer treatment
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Resistance of tumour cells to treatment with antineoplastic drugs remains a major problem in management of both primary as well as metastatic tumors including colorectal cancer. EMT occurs at the tumor-normal tissue interface and through a series of changes is responsible for an increased migration and later invasion and metastasis. The linkage between EMT and chemoresistance in this type of malignancy remains unresolved. Our study should provide insight into tumor survival mechanisms and suggest potential novel targets to improve CRC treatment strategies.

1) Established cell lines from colon cancer tissue were tested and expression of E-cadherin and N-cadherin was compared. The cells with significant differences were chosen for further testing i.e. chemosensitivity or LC-MS analysis of commonly used chemotherapeutics.

2) A model of E-cadherin (CDH1) knockdown immortalized colon cancer cells (CaCo2, HT29, SW480 and SW620 cell lines) was prepared using transfection by siRNA CDH1. These cell lines were subjected for analysis of expression profiles of EMT markers (microRNA, mRNA and proteins) and processes related with progression and drug resistance. Equally, LC-MS analysis was carried out in the above mentioned E-cadherin knockdown immortalized cell lines.

3) Determination of invasive potential of obtained colon cancer cells was carried out using real time analysis X-CELLigence system (CIM plate 16) as well as endpoint detection – transwell plate. The semipermeable membrane of both systems was coated with different chemically defined layers, for example with collagen type IV, fibronectin, ECM and/or with endothelial cells EA.hy926.

4) N-cadherin (CDH2) plasmid transfection was carried out and optimal conditions (transfection reagent, concentration etc.) for preparation of N-cadherin (CDH2) overexpressed immortalized colon cancer cells (CaCo2, HT29, SW480 and SW620 cell lines) were determined. These models will be used for further testing next year (2019).

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