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Knockout of ABCC10 in human colorectal Caco-2 cancer cells affects cell viability.

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Colorectal cancer (CRC) is the third most common cancer form detected annually. The majority of patients experience dose-related toxicities and develop resistance to the drug over time. Oncogenomic association analysis of TCGA colorectal datasets revealed that high ABCC10 mRNA expression was significantly associated with lower survival probability in the disease-free interval. The ABCC10 is a membrane efflux pump which extrudes anticancer drugs outside of cells.

The research hypothesis is that inactivating the *ABCC10* gene will increase the sensitivity of colorectal cancer cells to chemotherapy. CRISPR-Cas9-mediated gene editing technology was used to disrupt the *ABCC10* gene in colorectal cancer cell line Caco-2. The *ABCC10* knockout clone and the wild-type Caco-2 cells were then tested for sensitivity against docetaxel using MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assays, followed by colony formation assays for cell growth rate and viability.

PCR and gene sequencing confirmed a 102 bp deletion in the *ABCC10* open reading frame. The MTT assay found that the IC50 value of docetaxel was approximately 7 times higher in the wild-type cells compared to the knockout clones (IC50 = 1.84 µM for wild-type Caco-2 cells compared to 0.27 µM in *ABCC10* knockout clones). The colony formation assay also revealed that the knockout clones had a significantly lower growth rate and viability compared to the wild-type cells ($P < 0.0001$). These results suggested that a CRISPR-Cas9 system could potentially be used to increase sensitivity to chemotherapeutics. Furthermore, silencing *ABCC10* in colorectal cancer cells is associated with a decrease in cell proliferation, suggesting its multifaceted roles in cancer.

This poster presentation will outline some of the main findings of my research and provide a basis for targeting *ABCC10* to overcome chemoresistance in CRC.

Keywords
ABCC10, CRISPR Cas9, gene Knockout, Colorectal cancer