

## **siRNA-mediated silencing of MDR1 reverses the resistance to oxaliplatin in SW480/OxR colon cancer cells**

### **Abstract**

One of the most challenging aspects of colon cancer therapy is rapid acquisition of multidrug resistant phenotype. The multidrug resistance gene 1 (MDR1) product, p-glycoprotein (P-gp), pump out a variety of anticancer agents from the cell, giving rise to a general drug resistance against chemotherapeutic agents. The aim of this study was to investigate the effect of a specific MDR1 small interference RNA (siRNA) on sensitivity of oxaliplatin-resistant SW480 human colon cancer cell line (SW480/OxR) to the chemotherapeutic drug oxaliplatin. SW480 cells were made resistant by continuous incubation with stepwise serially increased concentrations of oxaliplatin over a 6-months period. Resistance cell were subsequently transfected with specific MDR1 siRNA. Relative MDR1 mRNA expression was measured by Quantitative real-time PCR. Western blot analysis was performed to determine the protein levels of P-gp. The cytotoxic effects of oxaliplatin and MDR1 siRNA, alone and in combination were assessed using MTT and the number of apoptotic cells was determined with the TUNEL assay. MDR1 siRNA effectively reduced MDR1 expression in both mRNA and protein levels. MDR1 down-regulation synergistically increased the cytotoxic effects of oxaliplatin and spontaneous apoptosis SW480/OxR. Our data demonstrates that RNA interference could down regulate MDR1 gene expression and reduce the P-gp level, and partially reverse the drug resistance in SW480/OxR cells in vitro. Therefore, the results could suggest that MDR1 silencing may be a potent adjuvant in human colon chemotherapy