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NONO and RALY are required for YB-1 oxaliplatin induced resistance in colon adenocarcinoma cell lines

Serges P. Tsofack
Université Laval, Canada

YB-1 is a multifunctional protein that affects transcription, splicing, and translation. Overexpression of YB-1 in breast cancers causes cisplatin resistance. In this study, we determined that YB-1 confers oxaliplatin resistance in colorectal adenocarcinomas. We also identify by mass spectrometry analyses important YB-1 interactors required for such oxaliplatin resistance in two colorectal cancer cell lines. A tagged YB-1 construct was used to identify proteins interacting directly to YB-1 in such cells. We then focused on proteins that are potentially involved in colorectal cancer progression based on the Oncomine public microarray database. Genes encoding for these YB-1 interactors were also examined in the public NCBI comparative genomic hybridization database to determine whether these genes are localized to regions of chromosomes rearranged in colorectal cancer tissues. From these analyses, we obtained a list of proteins interacting with YB-1 and potentially involved in oxaliplatin resistance. Oxaliplatin dose response curves of SW480 and HT29 colorectal cancer cell lines transfected with several siRNAs corresponding to each of these YB-1 interactors were obtained to identify proteins significantly affecting oxaliplatin sensitivity upon gene silencing. Only the depletion of either NONO or RALY sensitized both colorectal cancer cell lines to oxaliplatin. Furthermore, depletion of NONO or RALY sensitized otherwise oxaliplatin resistant overexpressing YB-1 SW480 or HT29 cells. These results suggest that NONO and RALY are significant potential target to counteract oxaliplatin resistance in colorectal cancers including tumors overexpressing the YB-1 protein.

Biography

Mr Serges P. Tsofack is a Ph.D. student at age of 27 at Cancer research center of Université Laval, Qc, Canada, working on deciphering the molecular mechanism(s) of chemoresistance in colon cancer, used Oxaliplatin drug. He carries out his Master's work at J. Craig Venter Institute, MD, USA. During the 2008-2009 on Oseltamivir (Tamiflu) drug resistance of H1N1 influenza virus and defended it at University of Dschang, Cameroon.