C-MYC-DRIVEN AND PRMT5-DEPENDENT REGULATION OF MULTIPLE MYELOMA CELL PROLIFERATION THROUGH SMCHD1 GENE

Abstract Body

The protein arginine methyltransferase 5 catalyzes the symmetrical bimethylation of arginine residues, which is important in life. C-Myc is proved involved in the development of tumors, while the mechanism of c-Myc-mediated gene expression is still unknown. Here we investigate the functional of PRMT5 and c-Myc in regulating MM cell. The protein and mRNA expression levels of PRMT5 in myeloma cells and normal cells were detected by Western Blot and qPCR. Lentivirally transduced shRNAs targeting PRMT5 was constructed using lentivirus mediated RNAi technology, and was packaged to infect MM cells to select positive colonies. The effect of PRMT5 was detected by cck-8 assay. Annexin V/7-AAD double staining flow cytometry was used to detect cell survival and apoptosis rate. The expression of apoptotic suppressor gene c-Myc in sh-PRMT5 cell lines was detected by Western Blot and qPCR. Finally, double-knockdown of PRMT5 and c-myc was performed and gene expression differentiation were identified by RNA-seq. PRMT5 expression in MM cell lines (RPMI8226 and U266) was relatively high compared with peripheral blood mononuclear cells, which was correlated with PFS and OS in MM. After sh-PRMT5 infection to MM cell lines, puromycin selection was performed and efficient gene knockdown was evaluated by Western Blot and qPCR. After targeted silencing of PRMT5 expression, the proliferation of MM cells was decreased and apoptosis was significantly increased (P < 0.05). C-Myc's expression were downregulated after it. It showed PRMT5 promoted the proliferation of MM cells and inhibited the apoptosis of it by regulating the expression of c-Myc. Subsequently, RNA-seq confirmed SMCHD1 as the common candidate target gene of c-myc and PRMT5. It speculated that PRMT5 and c-Myc may regulate SMCHD1 gene to promote the proliferation of MM cells. Our study not only proposed the mechanism PRMT5 and c-myc in regulating MM related gene expression, but also provided a new strategy and theoretical basis for clinical treatment of MM.