miR-1271 Regulates Cisplatin Resistance of Human Gastric Cancer Cell Lines by Targeting IGF1R, IRS1, mTOR, and BCL2.

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**Abstract**
Numerous studies showed that drug resistance of gastric cancer cells could be modulated by the abnormal expression of microRNAs (miRNAs) which target multiple cell signaling pathways. The possible function of miR-1271 in the formation of cisplatin resistance in gastric cancer cells has been investigated in this study. miR-1271 was significantly down-regulated in gastric cancer tissues and various gastric cancer cell lines. Moreover, it was down-regulated in the cisplatin-resistant gastric cancer cell line SGC7901/cisplatin (DDP) and the down-regulation of miR-1271 in SGC7901/DDP cells was accompanied by the up-regulation of insulin-like growth factor 1 receptor (IGF1R)/insulin receptor substrate 1 (IRS1) pathway-related proteins, i.e., IGF1R, IRS1, serine/threonine-protein kinase mTOR (mTOR), and the apoptosis regulator Bcl-2 (BCL2), compared with the parental SGC7901 cells. Over-expression of miR-1271 sensitized SGC7901/DDP cells to cisplatin. Changes in the luciferase activity of reporter constructs harboring the 3'-untranslated region of the above proteins in SGC7901/DDP cells suggested that IGF1R, IRS1, mTOR, and BCL2 were target genes of miR-1271. Enforced miR-1271 expression repressed the protein levels of its targets, inhibited proliferation of SGC7901/DDP cells, and sensitized SGC7901/DDP cells to DDP-induced apoptosis. Overall, on the basis of the results of our study, we proposed that miR-1271 could regulate cisplatin resistance in human gastric cancer cells, at least partially, via targeting the IGF1R/IRS1 pathway.