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High Blood Sugar Levels Significantly Increase the Oxaliplatin Resistance of Colorectal Cancer Patients through Down-regulation of MicroRNA-877 by Targeting G9a

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The high prevalence of type 2 diabetes mellitus in colorectal cancer (CRC) patients is a crucial public health issue worldwide. The deregulation of microRNAs (miRs) has been shown to be associated with the progression of CRC; however, the effects of high blood sugar levels on miR deregulation and, in turn, CRC remain unexplored. In this study, 153 patients with stage III CRC after FOLFOX adjuvant chemotherapy were classified into two groups according to their blood sugar levels (≧126 or <126 mg/dL). Clinicopathologic features, clinical outcomes, and serum miR-877 levels of the two groups were then analyzed, while cell proliferation, migration, and cellular miR-877 expression were investigated via D-(+)-glucose administration. Additionally, the target genes of miR-877 were identified. Through chi-square analysis, Oxaliplatin resistance of the CRC patients were found to be associated with the high blood glucose levels (P= 0.013). Serum miR-877 levels were significantly lower in the high blood glucose patients than in the normal blood glucose patients (P = 0.004). With D-(+)-glucose administration, the proliferation and migration of CRC cells *in vitro* increased remarkably (P < 0.05). Cellular miR-877 expression was suppressed by D-(+)-glucose administration. The expression levels of two target genes, *Smad3* and *G9a*, were affected significantly by miR-877, while glucose administration inhibited miR-877 expression and enhanced tumor cell proliferation and oxaliplatin resistance. Hyperglycemia can impact the clinical outcomes of CRC patients, probably by inhibiting miR-877 expression and the downstream genes, *Smad3* and *G9a*.