EPSTEIN-BARR VIRUS MIR-BART1-3P REGULATES THE MIR-17-92 CLUSTER BY TARGETING E2F3

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EBV is associated with several tumors and generates BamHI A rightward transcript microRNAs. To test the effects of EBV miRNA on the cell cycle and cell growth, we transfected miR-BART1-3p into gastric carcinoma cells. We found that miR-BART1-3p induced G0/G1 arrest and suppressed cell growth in gastric carcinoma cells. As our microarray analyses showed that E2F3, a cell cycle regulator, was inhibited by EBV infection, we hypothesized that miR-BART1-3p regulates E2F3. Luciferase assays revealed that miR-BART1-3p directly targeted the 3'-UTR of E2F3 mRNA. Both E2F3 mRNA and protein levels were reduced following miR-BART1-3p transfection. As E2F3 has been shown to regulate the expression of highly conserved miR-17-92 clusters in vertebrates, we examined whether this expression is affected by miR-BART1-3p, which can downregulate E2F3. The expression of E2F3, miR17HG, and miR-17-92 cluster miRNAs was significantly reduced in EBV-associated gastric carcinoma patients compared with EBV-negative gastric carcinoma patients. Further, miR-BART1-3p as well as the siRNA specific to E2F3 inhibited the expression of the miR-17-92 cluster, while inhibition of miR-BART1-3p enhanced the expression of the miR-17-92 cluster in cultured GC cells. Our results suggest a possible role of miR-BART1-3p in cell cycle regulation and in regulation of the miR-17-92 cluster through E2F3 suppression.