Abstract:

The MUC1 oncoprotein is overexpressed in most human breast cancers by mechanisms that are incompletely understood. The microRNA, miR-125b, is downregulated in breast cancer cells. The present studies demonstrate that the MUC1 3'UTR contains a site for binding of the miR-125b seed region. The results show that the MUC1 3'UTR suppresses luciferase expression and that this effect is abrogated by mutation or deletion of the miR-125b binding site. Expression of an anti-sense miR-125b in BT-549 breast cancer cells was associated with induction of MUC1 protein, but not MUC1 mRNA, levels. The anti-sense miR-125b also increased BT-549 cell growth by a MUC1-dependent mechanism. In addition, overexpression of exogenous miR-125b downregulated MUC1 protein, and not MUC1 transcripts, in ZR-75-1 breast cancer cells. Silencing of MUC1 in ZR-75-1 cells with a siRNA has been shown to promote DNA damage-induced apoptosis. In concert with these observations, miR-125b-induced decreases in MUC1 levels increased the apoptotic response of ZR-75-1 cells to cisplatin treatment. These findings indicate that miR-125b suppresses translation of the MUC1 oncoprotein and that miR-125b thereby functions as a tumor suppressor in breast cancer cells.