MicroRNA-155 inhibits Bone Morphogenetic Protein (BMP) signaling and BMP mediated Epstein Barr virus reactivation.

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Abstract
MicroRNA-155 is expressed at elevated levels in human cancers including cancers of the lung, breast, colon, and a subset of lymphoid malignancies. In B cells, miR-155 is induced by the oncogenic latency gene expression program of the human tumor virus, Epstein Barr Virus. BMP signaling is involved in an array of cellular processes including differentiation, growth inhibition, and senescence through context dependent interactions with multiple signaling pathways. Alteration of this pathway contributes to a number of disease states including cancer. Here we show that miR-155 targets the 3' UTR of multiple components of the BMP signaling cascade including SMAD1, SMAD5, HIVEP2, CEBPB, RUNX2, and MYO10. Targeting of these mediators results in the inhibition of BMP2, BMP6, and BMP7 induced ID3 expression as well as BMP mediated EBV reactivation in the EBV positive B cell line, Mutu I. Further, miR-155 inhibits SMAD1 and SMAD5 expression in the lung epithelial cell line, A549, it inhibits BMP mediated induction of the cyclin dependent kinase inhibitor, p21, and it reverses BMP-mediated cell growth inhibition. These results suggest a role for miR-155 in controlling BMP mediated cellular processes and provide evidence for the inhibition of anti-tumor effects of BMP signaling.