Abstract:

Signal transducer and activator of transcription 1 (STAT1) is activated in the inflammatory response to interferons. The MUC1 oncoprotein is overexpressed in human breast cancers. Analysis of genes differentially expressed in MUC1-transformed cells has identified a network linking MUC1 and STAT1 that is associated with cellular growth and inflammation. The results further show that the MUC1-C subunit associates with STAT1 in cells and the MUC1-C cytoplasmic domain binds directly to the STAT1 DNA-binding domain. The interaction between MUC1-C and STAT1 is inducible by IFNgamma in non-malignant epithelial cells and constitutive in breast cancer cells. Moreover, the MUC1-STAT1 interaction contributes to the activation of STAT1 target genes, including MUC1 itself. Analysis of two independent databases showed that MUC1 and STAT1 are coexpressed in about 15% of primary human breast tumors. Coexpression of MUC1 and the STAT1 pathway was found to be significantly associated with decreased recurrence-free and overall survival. These findings indicate that (i) MUC1 and STAT1 function in an auto-inductive loop, and (ii) activation of both MUC1 and the STAT1 pathway in breast tumors confers a poor prognosis for patients.