

# Androgen receptor regulates expression of the MUC1-C oncoprotein in human prostate cancer cells.

## Abstract:

The MUC1 heterodimeric oncoprotein is aberrantly overexpressed in human prostate cancers with more aggressive pathologic and clinical features. However, the signals that regulate MUC1 expression in prostate cancer cells are not well understood. **METHODS:** MUC1 expression was studied in androgen-dependent and -independent prostate cancer cell lines by quantitative RT-PCR, immunoblotting and assessment of MUC1 promoter activation. Chromatin immunoprecipitation (ChIP) studies were performed to assess androgen receptor (AR) occupancy on the MUC1 promoter. Post-transcriptional regulation of MUC1 expression was assessed by miR-125b-mediated effects on activity of the MUC1 3' untranslated region (3'UTR). **RESULTS:** The present studies demonstrate that AR occupies a consensus AR element on the MUC1 promoter in androgen-dependent LNCaP, but not in androgen-independent DU145 and PC3, prostate cancer cells. The results further show that AR downregulates MUC1 gene transcription. Stable introduction of exogenous AR in PC3 (PC3/AR) cells and then silencing of AR confirmed AR-mediated repression of the MUC1 promoter. AR signaling has also been shown to drive miR-125b expression. The present studies further demonstrate that miR-125b suppresses MUC1 translation in LNCaP cells and that an anti-sense miR-125b upregulates expression of MUC1 protein. In addition, stable expression of miR-125b in DU145 cells resulted in decreases in MUC1 levels. **CONCLUSIONS:** These findings demonstrate that AR signaling regulates MUC1 expression by transcriptional and posttranscriptional mechanisms in prostate cancer cells.