CBX7 and HMGA1b proteins act in opposite way on the regulation of the SPP1 gene expression.

Sepe R[1], Formisano U[1], Federico A[1], Forzati F[1], Bastos AU[1,2], D'Angelo D[1], Cacciola NA[1], Fusco A[1,3], Pallante P[1].

Author information

Abstract

Several recent studies have reported the Polycomb Repressive Complex 1 member CBX7 as a tumor-suppressor gene whose expression progressively decreases in different human carcinomas in relation with tumor grade, malignant stage and poor prognosis. We have previously demonstrated that CBX7 is able to inhibit the expression of the SPP1 gene, encoding the chemokine osteopontin that is over-expressed in cancer and has a critical role in cancer progression. Here, we have analyzed the mechanism by which CBX7 regulates the SPP1 gene expression. We show that the SPP1 transcriptional regulation mechanism involves the CBX7-interacting protein HMGA1b, that acts as a positive regulator of the SPP1 gene. In fact, we demonstrate that, in contrast with the transcriptional activity of CBX7, HMGA1b is able to increase the SPP1 expression by inducing the activity of its promoter. Moreover, we show that CBX7 interferes with HMGA1b on the SPP1 promoter and counteracts the positive transcriptional activity of HMGA1b on the SPP1 expression. Furthermore, since we found that also the NF-κB complex resulted involved in the modulation of the SPP1 expression in thyroid cells, we suppose that CBX7/HMGA1b/NF-κB could take part in the same transcriptional mechanism that finally leads to the regulation of the SPP1 gene expression. Taken together, our data show the important role played by CBX7 in the negative regulation of the SPP1 gene expression, thus contributing to prevent the acquisition of a malignant phenotype.