BCL6

B cell lymphoma 6 protein is a protein that in humans is encoded by the BCL6 gene.

Like BCL2, BCL3, BCL5, BCL7A, BCL9, and BCL10, it has clinical significance in lymphoma.

The protein encoded by this gene is an evolutionarily conserved zinc finger transcription factor and contains an N-terminal POZ/BTB domain. This protein acts as a sequence-specific repressor of transcription, and has been shown to modulate the STAT-dependent Interleukin 4 (IL-4) responses of B cells. This protein can interact with several corepressor complexes to inhibit transcription. This gene is found to be frequently translocated and hypermutated in diffuse large B cell lymphoma (DLBCL), and contributes to the pathogenesis of DLBCL. An exon 7 skipping splice variant encodes a shorter form of the protein which lacks the first two zinc fingers of the DNA binding domain.

Physiologically, BCL6 is a master transcription factor which leads the differentiation of naive helper T cells in Follicular Helper T cells (TFH cells).

Its action is negatively regulated by the gene PRDM1 encoding the transcription factor Blimp-1.

The presence of BCL6 can be demonstrated in tissue sections using immunohistochemistry. It is exclusively present in the B-cells of both healthy and neoplastic germinal centres. It therefore demonstrates both reactive hyperplasia in lymph nodes and a range of lymphomas derived from follicular B-cells, such as Burkitt's lymphoma, follicular lymphoma, and the nodular lymphocyte predominant subtype of Hodgkin's disease. It is often used together with antibodies to Bcl-2 antigen to distinguish neoplastic follicles from those found in benign hyperplasia, for which Bcl-2 is negative.

BCL6 corepressor like 1 (BCORL1) plays an oncogenic role in hepatocellular carcinoma (HCC) via promoting epithelial-mesenchymal transition (EMT) and tumor metastasis. However, the regulation of BCORL1 mediated by microRNAs (MicroRNAs) remains poorly known.The analysis of our clinical samples indicated that BCORL1 expression was markedly higher in HCC tissues than that in tumor-adjacent normal tissues. The Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO) datasets revealed that high BCORL1 expression associated with high tumor grade, advanced tumor stage and poor survival of HCC patients. miR-875-5p expression was down-regulated and negatively correlated with BCORL1 mRNA expression in HCC tissues. Furthermore, miR-876-5p inversely regulated BCORL1 abundance in HCC cells by directly targeting the 3'-untranslated region (3'-UTR) of BCORL1. Ectopic expression of miR-876-5p suppressed cell migration and invasion in both HCCLM3 and MHCC97H cells. In accordance, miR-876-5p knockdown promoted the metastatic behaviors of Hep3B cells. Mechanistically, miR-876-5p suppressed the EMT progression of HCC cells. HCC tissues with high miR-876-5p level showed a higher E-cadherin staining compared to cases with low miR-876-5p level. Moreover, the repression of cell metastasis mediated by miR-876-5p was rescued by BCORL1 restoration in HCCLM3 cells. Notably, low miR-876-5p expression associated with venous infiltration, high tumor grade and advanced tumor stage. HCC patients with low miR-876-5p expression had a significant poorer overall survival and disease-free survival. To conclude, miR-876-5p inhibits EMT progression, migration and invasion of HCC cells by targeting BCORL1. Therefore, miR-876-5p/BCORL1 axis may represent as a novel therapeutic target for HCC treatment [1)].

1)

Xu Q, Zhu Q, Zhou Z, Wang Y, Liu X, Yin G, Tong X, Tu K. MicroRNA-876-5p inhibits epithelial-

mesenchymal transition and metastasis of hepatocellular carcinoma by targeting BCL6 corepressor like 1. Biomed Pharmacother. 2018 Apr 18;103:645-652. doi: 10.1016/j.biopha.2018.04.037. [Epub ahead of print] PubMed PMID: 29679906.