SHOX2

Short stature homeobox 2, also known as homeobox protein Og12X or paired-related homeobox protein SHOT, is a protein that in humans is encoded by the SHOX2 gene.

SHOX2 is a member of the homeobox family of genes that encode proteins containing a 60-amino acid residue motif that represents a DNA-binding domain.

Several human genetic disorders are caused by aberrations in human homeobox genes. This locus represents a pseudoautosomal homeobox gene that is thought to be responsible for idiopathic short stature, and it is implicated in the short stature phenotype of Turner syndrome patients. This gene is considered to be a candidate gene for Cornelia de Lange Syndrome.

SHOX2 localises on chromosome 3, so it is an autosomal and not a pseudoautosomal homeobox (SHOX, which localises on the PAR1 region of chromosome X and Y, has a pseudoautosomal hereditability).

SHOX2 expression and gene body methylation varied among low-grade glioma (LGG) patients and highly significantly predicted poor overall survival. While they were tightly correlated, SHOX2 expression appeared more potent as a prognostic marker and was used for most further studies. The SHOX2 prognostic roles were maintained after analyses by histology subtypes or tumor grade.

Zhang et al., found that the combination of SHOX2 expression and IDH genotype status identified a subset of LGG patients with IDH wild type (IDHwt) and low SHOX2 expression with considerably favorable survival.

They further investigated the combination of SHOX2 with other known clinically relevant markers of low-grade glioma (LGG) (TERT expression, 1p19q chromosome co-deletion, MGMT methylation, ATRX mutation and NES expression). When combined with SHOX2 expression, they identified subsets of LGG patients with significantly favorable survival outcomes, especially in the subgroup with worse prognosis for each individual marker. Finally, multivariate analysis demonstrated that SHOX2 was a potent independent survival marker.

They have identified that SHOX2 expression or methylation are potent independent prognostic indicators for predicting LGG patient survival, and have potential to identify an important subset of LGG patients with IDHwt status with significantly better overall survival. The combination of IDH or other relevant markers with SHOX2 identified LGG subsets with significantly different survival outcomes, and further understanding of these subsets may benefit therapeutic target identification and therapy selections for glioma patients [1].

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Zhang YA, Zhou Y, Luo X, Song K, Ma X, Sathe A, Girard L, Xiao G, Gazdar AF. SHOX2 is a Potent Independent Biomarker to Predict Survival of WHO Grade II-III Diffuse Gliomas. EBioMedicine. 2016 Nov;13:80-89. doi: 10.1016/j.ebiom.2016.10.040. PubMed PMID: 27840009.