Abstract

Cancer Res. **2014** Nov 1;74(21):5999-6009. doi: 10.1158/0008-5472.CAN-13-2513. Epub **2014** Aug

MYCN-dependent expression of sulfatase-2 regulates neuroblastoma cell survival.

Solari V[1], Borriello L[2], Turcatel G[3], Shimada H[4], Sposto R[5], Fernandez GE[3], Asgharzadeh S[6], Yates EA[7], Turnbull JE[8], DeClerck YA[9].

Author information

Abstract

Heparan sulfate proteoglycans (HSPG) play a critical role in the interaction of tumor cells and their microenvironment. HSPG activity is dictated by sulfation patterns controlled by sulfotransferases, which add sulfate groups, and sulfatases (Sulf), which remove 6-O-sulfates. Here, we report altered expression of these enzymes in human neuroblastoma cells with higher levels of Sulf-2 expression, a specific feature of MYCN-amplified cells (MYCN-A cells) that represent a particularly aggressive subclass. Sulf-2 overexpression in neuroblastoma cells lacking MYCN amplification (MYCN-NA cells) increased their in vitro survival. Mechanistic investigations revealed evidence of a link between Sulf-2 expression and MYCN pathogenicity in vitro and in vivo. Analysis of Sulf-2 protein expression in 65 human neuroblastoma tumors demonstrated a higher level of Sulf-2 expression in MYCN-A tumors than in MYCN-NA tumors. In two different patient cohorts, we confirmed the association in expression patterns of Sulf-2 and MYCN and determined that Sulf-2 overexpression predicted poor outcomes in a nonindependent manner with MYCN. Our findings define Sulf-2 as a novel positive regulator of neuroblastoma pathogenicity that contributes to MYCN oncogenicity. Cancer Res; 74(21); 5999-6009. ©**2014** AACR.

PMID: 25164011 [PubMed - indexed for MEDLINE] PMCID: PMC4216758 [Available on 2015-05-01]