MyoD Is a Tumor Suppressor Gene in Medulloblastoma.

Dey J, Dubuc AM, Pedro KD, Thirstrup D, Mecham B, Northcott PA, Wu X, Shih D, Tapscott SJ, Leblanc M, Taylor MD, Olson JM.

Authors’ Affiliations: Molecular and Cellular Biology Program, University of Washington; Clinical Research Division, Human Biology Division, and Public Health Sciences Division, Fred Hutchinson Cancer Research Center; Presage Biosciences; Sage Bionetworks; Seattle Children's Hospital, Seattle, Washington; Arthur and Sonia Labatt Brain Tumor Research Center and Division of Neurosurgery, The Hospital for Sick Children, Toronto, Ontario, Canada.

Abstract

While medulloblastoma, a pediatric tumor of the cerebellum, is characterized by aberrations in developmental pathways, the majority of genetic determinants remain unknown. An unbiased Sleeping Beauty transposon screen revealed MyoD as a putative medulloblastoma tumor suppressor. This was unexpected, as MyoD is a muscle differentiation factor and not previously known to be expressed in cerebellum or medulloblastoma. In response to deletion of one allele of MyoD, two other Sonic hedgehog-driven mouse medulloblastoma models showed accelerated tumor formation and death, confirming MyoD as a tumor suppressor in these models. In normal cerebellum, MyoD was expressed in the proliferating granule neuron progenitors that are thought to be precursors to medulloblastoma. Similar to some other tumor suppressors that are induced in cancer, MyoD was expressed in proliferating medulloblastoma cells in three mouse models and in human medulloblastoma cases. This suggests that although expression of MyoD in a proliferating tumor is insufficient to prevent tumor progression, its expression in the cerebellum hinders medulloblastoma genesis. Cancer Res; 73(22); 6828-37. ©2013 AACR.

PMID: 24092238 [PubMed - in process]