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# Novel gene networks regulating self-renewal and differentiation in medulloblastoma

SEMINAR & VISITING SPEAKER SERIES

DATE
Friday, May 31, 2019
9:00 AM

LOCATION
PX236/238 PsycHealth Blding


SPEAKER
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OBJECTIVES

1. Understand the genetic, molecular and cellular heterogeneity associated with the pediatric brain tumor medulloblastoma

2. Understand the multifaceted role of OTX2 in medulloblastoma pathogenesis

3. Describe the functional outcome of increased PAX gene expression on medulloblastoma tumorigenic properties in vitro and in vivo


ABSTRACT

OTX2 is a potent oncogenic driver of tumor growth and cell cycle progression in Group 3 medulloblastoma. However, the specific mechanisms by which OTX2 represses neural differentiation in these highly aggressive tumors are not well characterized. We have utilized ChIP-sequencing combined with extensive medulloblastoma patient transcriptome and proteomics data to identify and subsequently validate a novel OTX2 regulatory network that controls Group 3 medulloblastoma cell fate decisions. OTX2 directly restricts the expression of neuronal differentiation genes encoding transcription factors including the novel target genes PAX3 and PAX6. Expression of PAX3 and PAX6 is significantly lower in Group 3 MB patients and is correlated with reduced survival. Similar to OTX2 silencing, PAX3 and PAX6 overexpression inhibit self-renewal and enhance neuronal differentiation in vitro while PAX3, on its own, increases survival in vivo. Finally, we identify mTORC1 and EPHB2 forward signaling as downstream effectors of OTX2-PAX3, thus highlighting axon guidance and protein synthesis pathways as novel therapeutic targets and key players in Group 3 medulloblastoma pathogenesis. gies to be develop and hopefully prevent drug resistance in GBM.



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