Review Neuropathol Appl Neurobiol. 2023 Apr 6;e12903. doi: 10.1111/nan.12903.

Online ahead of print.

Timing is everything: A connection between medulloblastoma prognosis and fetal cerebellar development

Daniel Williamson [1], Edward C Schwalbe [1 2], Simon Bailey [1], Steven C Clifford [1]

PMID: 37021628 DOI: 10.1111/nan.12903

Abstract

The childhood brain tumour medulloblastoma is typically classified into multiple discrete molecular subgroups with characteristic DNA methylation and expression patterns. Several of these subgroups are used as, or proposed to be, an effective basis for treatment stratification. Here, we highlight the close connection between the findings described in a recent series of studies which, together, strongly imply a continuous association between survival outcome, the transcriptional profile of a Group3/Group4 (i.e., non-WNT/non-SHH) medulloblastoma and the specific point during early fetal cerebellar development at which initial pathogenic disruption took place. This has important implications for future efforts to model the disease by incorporating driving molecular features into their specific developmental context. This further suggests that instead of relying upon discrete DNA methylation subgroups, using expression biomarkers as the basis of a continuous risk predictor may produce a more effective risk stratification of patients with Group3/Group4 medulloblastoma.