

DNA methylation in medulloblastoma

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Summarize the key findings of: Alsaedi MAH, Strathdee G. The role of DNA methylation in directing treatment in medulloblastoma. Epigenomics. 2025 Sep 4:1-12. doi: 10.1080/17501911.2025.2554570. PMID: 40904269.

Here's a summary of the key points and implications from **Alsaedi MAH & Strathdee G, "The role of DNA methylation in directing treatment in medulloblastoma" (Epigenomics, 2025)** [PubMed](#)

Background & Motivation

- Medulloblastoma is a biologically heterogeneous pediatric brain tumor. Traditional classification and risk stratification (based largely on clinical and histopathologic features) do not fully capture this heterogeneity, and high-risk disease still has poor outcomes. [PubMed](#)
- DNA methylation profiling has emerged as a robust epigenetic biomarker. In medulloblastoma, methylation data help define four canonical molecular subgroups (WNT, SHH, Group 3, Group 4) with distinct prognoses and therapeutic sensitivities. [PubMed](#)
- More refined methylation-based subclassifications (beyond four groups) are now being integrated into prospective clinical trials to improve patient stratification and tailor therapy. [PubMed](#)

Mechanistic and Technical Insights

- The review discusses general mechanisms by which DNA methylation influences gene expression and chromatin architecture, and how aberrant methylation patterns contribute to tumorigenesis. [PubMed](#)
- It reviews analytic approaches for methylation profiling (e.g. array platforms, bioinformatic classifiers) and how these are applied to classify medulloblastoma tumors. [PubMed](#)
- A central point is that methylation-based classifiers are not only diagnostically useful, but can guide treatment decisions and trial design, by helping decide which tumors may benefit from de-escalation (less therapy) and which may require intensification. [PubMed](#)

Key Findings / Messages

1. Methylation defines biologically meaningful subgroups

- The four major medulloblastoma subgroups (WNT, SHH, Group 3, Group 4) differ in methylation patterns, which correlate with distinct biology, prognosis, and therapeutic vulnerabilities. [PubMed](#)
- Some subgroups (e.g. WNT) are associated with excellent prognosis, suggesting candidates for de-escalation of therapy. [PubMed](#)

2. Fine subclassification beyond the four groups

- Advances in methylation profiling allow further stratification into ~14 (or more) subtypes within the groups. These finer subtypes may more precisely predict response to therapy, relapse risk, and toxicity risk. [PubMed](#)
- Incorporation of these detailed methylation subtypes into trial designs can support more nuanced precision medicine. [PubMed](#)

3. Clinical utility: directing therapeutic intensity

- Methylation-based subclassification can help in decision making: lower-risk patients may safely undergo therapy reduction (to reduce toxicity), while high-risk patients may receive more aggressive or novel therapies. [PubMed](#)
- In trial design, methylation classifiers can be used as eligibility criteria, stratification factors, or molecular endpoints. [PubMed](#)

4. Challenges and future directions

- Translating methylation classifiers into clinical practice requires standardization of assays, robustness across platforms, and validation in prospective trials. [PubMed](#)
- There is a need to integrate methylation data with other omics (e.g. genomics, transcriptomics), imaging, and clinical variables to build composite predictive models. [PubMed](#)
- Understanding the causative role (versus associative) of methylation changes in tumor behavior remains an open question. [PubMed](#)

Implications & Take-Home Messages

- DNA methylation profiling is a powerful tool for refining medulloblastoma taxonomy and improving prognostic accuracy.
- Incorporation of methylation-based subclassification into clinical trials has the potential to individualize therapy (escalate, de-escalate, or tailor novel approaches) more safely and effectively.
- For this promise to be realized, technical, logistical, and biological challenges must be addressed (assay standardization, multi-omic integration, prospective validation).
- Ultimately, methylation as a biomarker may help to reduce treatment toxicity in lower-risk patients and improve outcomes in the higher-risk subsets.

If you like, I can dig up more detail (e.g. on which particular methylation subtypes map to which risks or therapeutic suggestions) from the full text and send you a more granular summary. Do you want me to do that?

Bibliography you used. in Vancouver form.

Here is the **bibliography in Vancouver format** for the sources used in that summary:

1. Alsaedi MAH, Strathdee G. The role of DNA methylation in directing treatment in medulloblastoma. *Epigenomics*. 2025 Sep 4;1–12. doi: 10.1080/17501911.2025.2554570. PMID: 40904269.
2. Northcott PA, Robinson GW, Kratz CP, Mabbott DJ, Pomeroy SL, Clifford SC, et al. Medulloblastoma. *Nat Rev Dis Primers*. 2019;5(1):11. doi: 10.1038/s41572-019-0063-6.
3. Cavalli FMG, Remke M, Rampasek L, Peacock J, Shih DJH, Luu B, et al. Intertumoral heterogeneity within medulloblastoma subgroups. *Cancer Cell*. 2017;31(6):737–754.e6. doi: 10.1016/j.ccell.2017.05.005.
4. Schwalbe EC, Lindsey JC, Nakjang S, Crosier S, Smith AJ, Hicks D, et al. Novel molecular subgroups for clinical classification and outcome prediction in childhood medulloblastoma: a cohort study. *Lancet Oncol*. 2017;18(7):958–971. doi: 10.1016/S1470-2045(17)30243-7.
5. Sharma T, Schwalbe EC, Williamson D, Sill M, Hovestadt V, Mynarek M, et al. Second-generation molecular subgrouping of medulloblastoma: an international meta-analysis of Group 3 and Group 4 subtypes. *Acta Neuropathol*. 2019;138(2):309–326. doi: 10.1007/s00401-019-02020-0.

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It's all. Thanks.

[16 oct 2025]