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Comment

Comment on Karaulic et al. Exploring Novel Applications: Repositioning Clinically Approved Therapies for Medulloblastoma Treatment. *Cancers* 2025, *17*, 3659

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We read with great interest the recent study by Karaulic et al. entitled "Exploring Novel Applications: Repositioning Clinically Approved Therapies for Medulloblastoma Treatment" [1]. This study reports a comprehensive identification of candidate targets for medulloblastoma (MB) treatment, based on RNA-sequencing data from multiple datasets. The authors then went on to propose potential candidate drug treatments by aligning existing targeted therapies used in other cancer types with associations between gene expression and patient survival in MB. Among the many target genes identified by these analyses are *NTRK1* and *NTRK2*, which encode tropomyosin receptor kinase (Trk) neurotrophin receptors TrkA and TrkB, respectively. Karaulic et al. propose *NTRK1* and *NTRK2* as candidate genes, specifically in the sonic hedgehog (SHH)-activated molecular subgroup of MB, and suggest that the Trk inhibitor larotrectinib could be investigated as a treatment for metastatic or non-metastatic SHH MB.

These findings and conclusions are consistent with previous findings by our group. In a study published in *Cancers*, we showed that high gene expression of *NTRK1* or *NTRK2* was associated with shorter overall survival (OS) in patients with SHH MB, but not in other MB subgroups [2]. In a xenograft mouse model, we found that treatment with the selective TrkB inhibitor ANA-12 reduced MB tumor growth [3], an effect that was associated with increased apoptosis, reduced extracellular-regulated kinase (ERK) activity, enhanced expression of signal transducer and activator of transcription 3 (STAT3), modulation of p21 expression, morphological cellular changes consistent with differentiation, increased levels of the neural differentiation marker β-III tubulin (TUBB3), and reduced expression of the stemness marker Nestin [3].

Taken together, these findings point toward a broader role for Trk receptors in MB biology, one that extends beyond *NTRK* gene fusions. Inhibiting wild-type TrkA and TrkB may therefore represent a meaningful therapeutic avenue. The results reported by Karaulic et al. further reinforce the rationale for investigating these receptors as therapeutic targets in MB.

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Abbreviations

The following abbreviations are used in this manuscript:

ERK	Extracellular-regulated kinase
MB	Medulloblastoma
NRP1	Neuropilin-1
OS	Overall survival
SHH	Sonic hedgehog
STAT3	Signal transducer and activator of transcription 3
Trk	Tropomyosin receptor kinase
TUBB3	β-III tubulin

References

1. Karaulic, A.; Fournier, C.; Pagès, G. Exploring novel applications: Repositioning clinically approved therapies for medulloblastoma treatment. *Cancers* **2025**, *17*, 3659. [CrossRef] [PubMed]
2. Thomaz, A.; Jaeger, M.; Brunetto, A.L.; Brunetto, A.T.; Gregianin, L.; de Farias, C.B.; Ramaswamy, V.; Nör, C.; Taylor, M.D.; Roesler, R. Neurotrophin signaling in medulloblastoma. *Cancers* **2025**, *12*, 2542. [CrossRef] [PubMed]
3. Thomaz, A.; Pinheiro, K.V.; Souza, B.K.; Gregianin, L.; Brunetto, A.L.; Brunetto, A.T.; de Farias, C.B.; Jaeger, M.D.C.; Ramaswamy, V.; Nör, C.; et al. Antitumor activities and cellular changes induced by TrkB inhibition in medulloblastoma. *Front. Pharmacol.* **2019**, *10*, 698. [CrossRef] [PubMed]

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