Jak2-mediated Phosphorylation of Atoh1 is Critical for Medulloblastoma Growth

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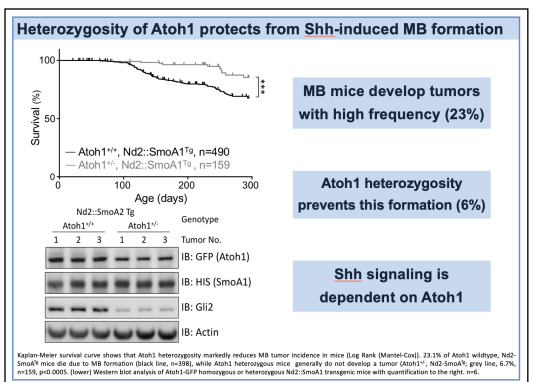
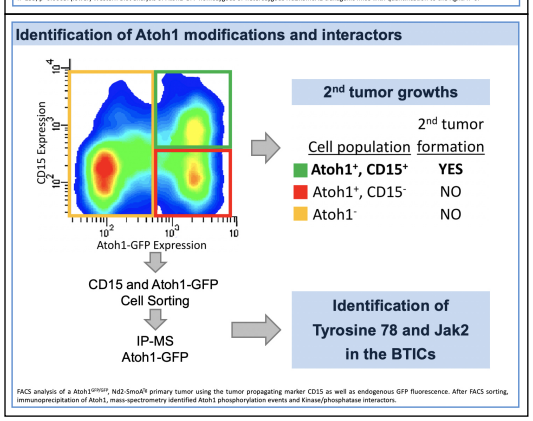
Introduction

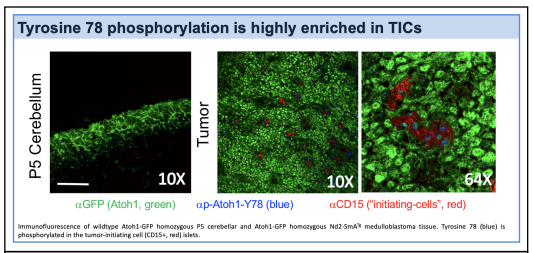
Treatment for medulloblastoma, the most common malignant brain tumor in children, remains limited to surgical resection, radiation, and traditional chemotherapy; with long-term survival as low as 50-60% for Sonic Hedgehog (Shh)-type medulloblastoma. We have shown that the transcription factor Atonal homologue 1 (Atoh1) is required for Shh-type medulloblastoma development in mice. To determine whether reducing either Atoh1 levels or activity in the tumor after its development, we studied Atoh1 dosage and modifications in Shh-type medulloblastoma.

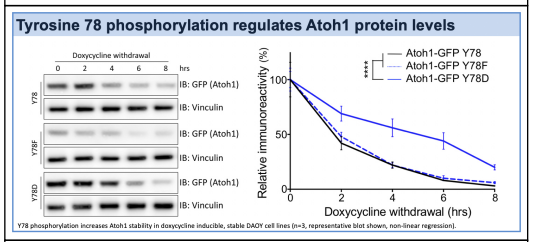
Atoh1 is an oncogene

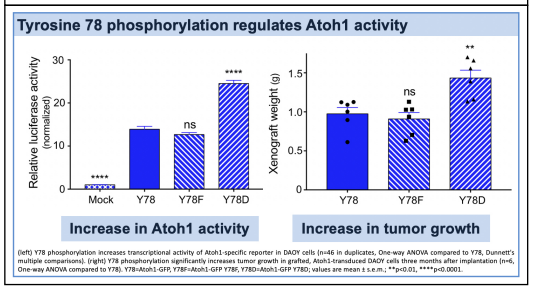




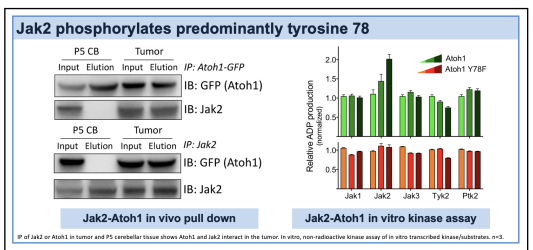
Tyrosine 78 phosphorylation

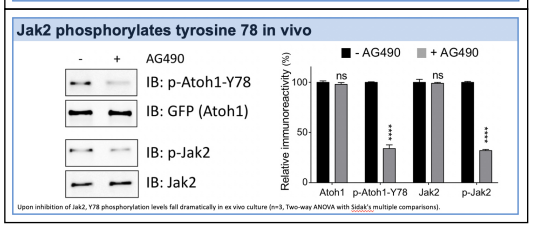


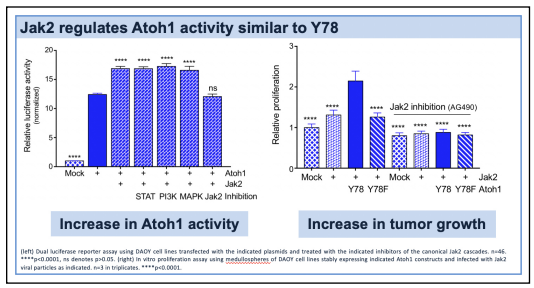




Jak2 phosphorylates Atoh1

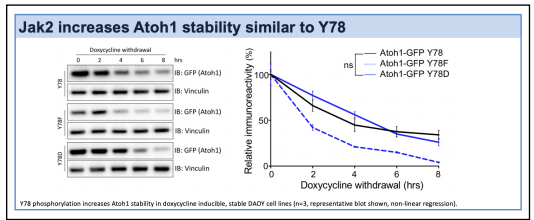


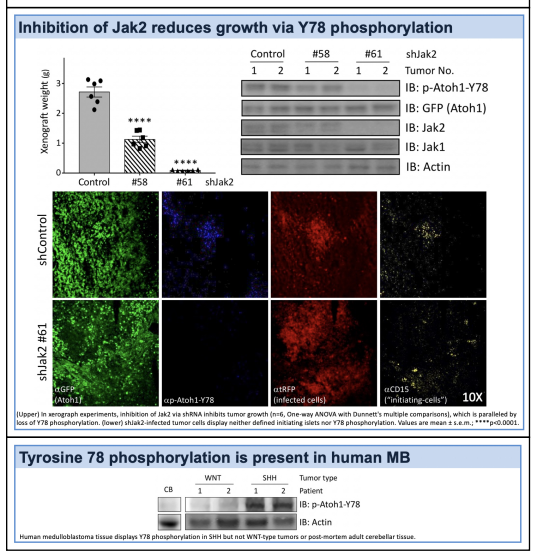




Jak2 - Atoh1 signaling cascade

Tyrosine 78 is a target of Jak2





Learning Objectives

1) Atoh1 is critical for medulloblastoma growths.

2) Jak Signaling is a novel pathway in medulloblastoma.

3) Targeting multiple signaling pathways will benefit patients with medulloblastoma.

References

Klisch TJ, Vainshtein A, Patel A, Zoghbi HY. (2017) Medulloblastoma growth is dependent on Jak2-mediated phosphorylation of Atoh1. eLife 6

Conclusions

We conclude that inhibiting Jak2-mediated tyrosine 78 phosphorylation could provide a viable therapy for medulloblastoma.