

# The Aryl Hydrocarbon Receptor (AhR) as a Novel Therapeutic Target in Neuroblastoma

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## Introduction

- Neuroblastoma is the most common extracranial tumor in children<sup>1</sup>.
- ~50% of high-risk patients die from relapses due to retinoic acid therapy resistance<sup>2,3</sup>.
- MYCN* amplification correlates with poor response to retinoid therapies, but MycN is “undruggable.”<sup>4</sup>
- The aryl hydrocarbon receptor (AhR) is a transcription factor that modulates Myc in other cancers<sup>5</sup>, but its role in neuroblastoma is poorly understood.

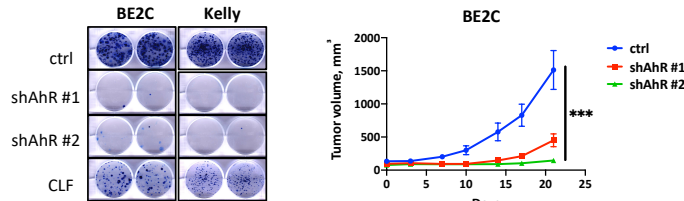
## Hypothesis

AhR is a novel tumor promoter that regulates MycN and alters retinoic acid treatment efficacy in neuroblastoma.

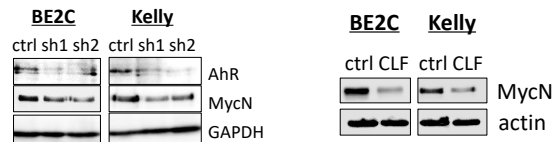
## Methods

- Genetically under-express AhR with shRNA or treat human neuroblastoma cells with the novel AhR antagonist, clofazimine (CLF)
- Assess:
  - Tumorigenicity by colony formation and *in vivo* tumor growth
  - AhR-MycN regulation by Western blot
  - Retinoic acid efficacy by microscopy

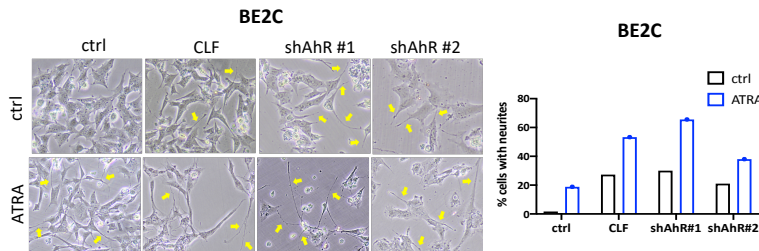
## AhR is a novel tumor promoter in neuroblastoma



## AhR inhibition lowers MycN levels in neuroblastoma

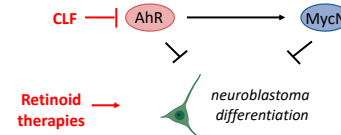


## AhR inhibition induces neuroblastoma differentiation and augments retinoic acid therapy efficacy



## Conclusions

- AhR is a previously unrecognized and novel tumor promoter in neuroblastoma.
- AhR inhibition with CLF decreases neuroblastoma growth and MycN levels and augments retinoic acid therapy-induced differentiation.



## Significance

- AhR is a novel therapeutic target in neuroblastoma.
- CLF, an FDA-approved novel AhR antagonist, is non-toxic, orally bioavailable & inexpensive<sup>6</sup>, representing a potential promising new neuroblastoma therapy.

## Acknowledgements

This work was supported by Roswell Park Start-Up Funds and Roswell Park Alliance Foundation Grant (A.B.S.)

## References

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