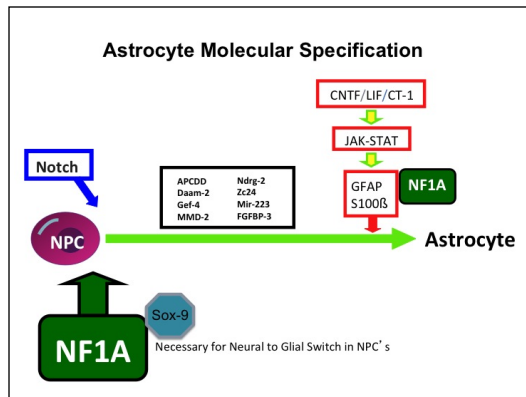


# Introduction

The regulatory gene network involving Nuclear Factor 1A (NF1A) has recently been established as a necessary component in the cell fate determination of glial cells in the developing CNS. The preservation of this regulatory network has not previously been applied to glial tumor types, specifically to GBM.



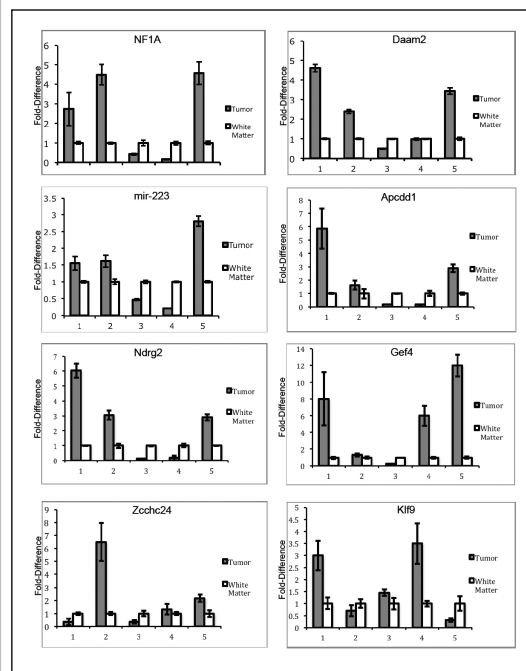
**Figure 1:** The NF1A glial regulatory network controls the molecular specification of neural progenitor cells into glia.

## Methods

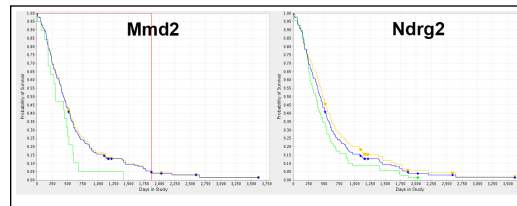
Using the NF1A downstream gene network established in our lab, we performed RT-PCR and quantitative PCR analysis on GBM samples paired with same-patient normal white matter samples and analyzed expression patterns in GBM versus normal white matter within patient samples.

## Results

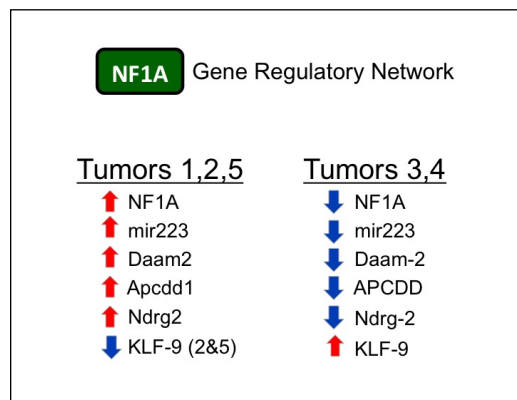
NF1A was expressed in either a high- or low- level pattern in GBM samples analyzed, compared with normal WM samples. Downstream expression of the established NF1A regulatory network genes Daam-2, APCDD, Ndrdg-2, Klf-9, Gef-4, and mir223 was also preserved in a pattern corresponding to the expression level of NF1A, indicating preservation of this glial regulatory gene network.



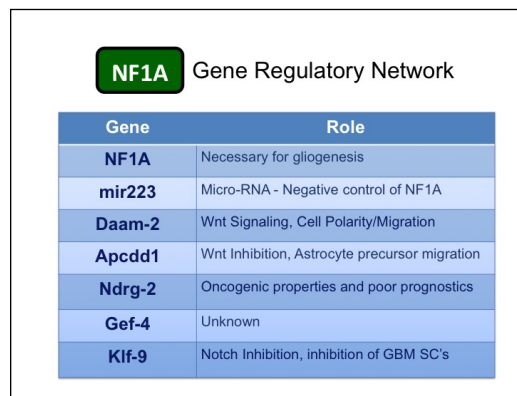
**Figure 2:** Molecular expression patterns for NF1A and downstream genes in GBM samples with white matter controls. High in samples 1, 2, and 5, or Low in samples 3 & 4.



**Figure 3:** Patient survival is greater with tumors having Low-expression of genes in the NF1A regulatory network.



**Figure 4:** Summary of NF1A expression patterns in GBMs.



**Figure 5:** Known functions of NF1A network genes.

## Conclusions

The glial developmental gene regulatory network involving NF1A is conserved in GBM in a High- or Low-expression pattern, and represents a novel category for GBM classification.

## References

1. Deneen B, Ho R, Lukaszewicz A, Hochstim CJ, Gronostajski RM, Anderson DJ. (2006) The transcription factor NFIA controls the onset of gliogenesis in the developing spinal cord. *Neuron* 52:953-68.
2. Peng Kang, Hyun Kyoung Lee, Stacey M. Glasgow, Meggie Finley, Tataka Donti, Zachary B. Gaber, Brett H. Graham, Aaron E. Foster, Bennett G. Novitch, Richard M. Gronostajski, and Benjamin Deneen (2012) Sox9 and NFIA Coordinate a Transcriptional Regulatory Cascade during the Initiation of Gliogenesis. *Neuron* In Press.

## Learning Objectives

By the conclusion of this session, participants should be able to:

1. Understand the glial cell-fate regulatory gene network involving NF1A.
2. Identify key downstream genes involved in the NF1A gene network.
3. Apply the preservation of developmental gene networks in GBM for potential categorization and treatment stratification in GBM.