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Fibroblast Growth Factor (FGF)-2 regulates astrocyte differentiation in a region specific manner in the hindbrain

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Fibroblast growth factor (FGF)-2 is known to have important, pleiotropic effects on neuronal and glial cells during various physiological and pathological events. This thesis focuses on the role of endogenous FGF-2 in the differentiation of astrocytes. To address this question, the expression of Glial Fibrillary Acidic Protein (GFAP) was studied in the hindbrain of the FGF-2 null mouse. GFAP was drastically decreased in a region specific manner in the hindbrain of the adult and developing FGF-2 null mouse while the expression of alternate markers for astrocytes was not affected. Interestingly, the deficit in GFAP was evident in the astrocytes of pontine and medullary grey matter but not in the white matter. The astrocytes of the grey and white matter were seen to express FGF-2 and FGF receptors, in a distinct pattern. The methylation of Histone H3 at Lysine 4 residue (H3K4me2) associated with the STAT (signal transducer and activator of transcription) binding site of the GFAP promoter was significantly decreased in the grey matter of the FGF-2 null mouse, indicating the role of FGF-2 in the epigenetic regulation of astrocyte differentiation. The anatomical areas displaying GFAP deficits included nuclei which regulate functions disturbed in the FGF-2 null mouse, such as sleep duration and baroreceptor reflex, thus

suggesting impaired astrocyte-neuron interaction in the FGF-2 null mouse. In summary, these findings underscore the importance of FGF-2 in astroglial differentiation in the hindbrain and the heterogeneity of astrocytes in their requirement for FGF-2 as a differentiation inducing signal.