

Wnt Signaling Plays A key Role in Human Neural Stem Cell Differentiation into Oligodendrocyte Progenitors

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Embryonic stem cell-derived neural cells and adult neural stem cells are promising sources of tissue for testing cellular and gene therapies for CNS disorders. Recently, significant progress has been made towards the goal, yet key questions about global perspectives for the neural differentiation pathway remain to be answered including molecular determinants of neural fate and distinctive stages of differentiation. To this end, we have established and characterized olig2-overexpressed subclone of human neural stem cell, HB1.F3 : F3.Olig2. F3.Olig2 provides a model for characterizing the downstream effects of olig2 transcription factor. We performed a phenotypic characterization and microarray analysis of HB1.F3, an immortalized human cell line, and F3.Olig2, an olig2-overexpressed subclone of HB1.F3. SILAC(Stable Isotope Labeled Amino acid in Culture) method and Nano-LC FT-ICR were employed for quantitative analysis of the protein profile change during differentiation process. Systemic molecular biological validation were performed for the genes and proteins of several signaling pathways including Wnt/b-catenin pathway which has been known to promote self-renewal in a variety of tissue stem cells including neural stem cells with western blotting, real time PCR, and immunohistochemical staining. Together, these approaches have allowed us to characterize Wnt signaling and Dkk1 plays a key role in changes initiated by olig2 upon the differentiation of oligodendrocytes from neural stem cells.

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