

Chronic Morphine Treatment on MOR-1 Gene Expression in the SH-SY5Y CellsIvy Kwapong¹, R. Johnson², Z.-P. Zhu² and R. Badisa² and C.B. Goodman²

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Background: The mu receptor is one of three major types of opioid receptors (μ , δ , κ), which are coupled to the G protein. The mu opioid receptor (MOR) accounts for many of the effects that are seen with morphine and other structurally related opioids. Chronic morphine exposure has been shown to induce tolerance with both *in vivo* and *in vitro* models, which is possibly regulated at the protein and/or mRNA levels for the MOR. The study was performed to determine the chronic effects of morphine treatment for 24 h on the gene expression of MOR-1 in undifferentiated and differentiated SH-SY5Y cells. Moreover, we examined the regulation of the MOR-1 transcript by chronic morphine involved an epigenetic influence via histone methylation.

Method: The human neuroblastoma cell line, SH-SY5Y cells were treated with retinoic acid (10 μ M) to induce differentiation for 72 h. MOR-1 expression was measured using real-time RT-PCR after morphine sulfate (10 μ M) was chronically administered to the undifferentiated and differentiated SH-SY5Y cells for 24 h.

Results: The results showed a 23% significant increase in MOR-1 gene expression after differentiation. Although chronic morphine treatment did not alter the MOR-1 expression in the undifferentiated SH-SY5Y cells, it produced a significant down-regulation in the MOR-1 transcript by 30% in the differentiated SHS-SY5Y cells when compared to the controls. Naloxone, an opioid antagonist was used to block the down-regulation in gene expression seen by morphine treatment.

Conclusion: These results suggest that the development of morphine tolerance involves the regulation at the gene expression level as seen by a decrease in MOR-1 mRNA level.