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Poster Presentation

Selective HCRTR2 Antagonism Increases Embryonic Mouse Cortex Neural Stem Progenitor Cells Proliferation

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Abstract

In multiple sclerosis Oligodendrocytes are obliterated by the immune system. neural stem/ progenitor cells (NS/P Cs) have the capacity to differentiate into mature myelinating oligodendrocytes. In embryonic mouse cortex oligodendrocyte progenitor cells (OPCs) are more abundant than the ganglionic eminence. Doing gene set enrichment analysis using DAVID and Panther websites it was shown that Gpr37l1 is highly expressed in oligodendrocyte progenitor cells (OPCs) in comparison to oligodendrocytes. The selective orexin 2 recptor (HCRTR2) antagonist jnj-10397049 has been shown to inhibit this orphan GPCR. In this study we sought to scrutinize NS/P Cs survival after the inhibitor on gpr37l1 and HCRTR2 by jnj-10397049. primary cortex NS/PCs were derived from embryonic mouse 13.5 as described before. cytotoxicity effect of varying doses of JNJ10397049 was screened using MTT assay. The expression of gpr37l1, hcrtr2, PDGFRalpha and Cnpase expression was analyzed using real time PCR. MTT analysis demonstrated that JNJ10397049 at 15 and 10 micromolar dramatically increases proliferation of neural stem cells by 2.62 and 2.43 respectively. Gpr37l1 and orexin2 receptor are more expressed in embryonic mouse cortex NS/PCs than embryonic mouse ganglionic eminence by 3.45 and 4.57, respectively. PDGFRalpha and Cnapse genes are also highly expressed on cortex NS/PCs by 112.36 and 76.56, respectively in comparison to ganglionic eminence NS/PCs. Here it was shown that Orexin 2 receptor and GPR37L1 can be valid drug targets in demyelination diseases by inducing proliferation of NS/PCs. Further study is under process to confirm and expand these results.

Keywords: Neural Stem Cells, Neural Progenitor Cells, Orexin Receptor, Gpr37l1, Oligodendrocyte Progenitor Cells

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