1, 25-dihydroxyvitamin D3 enhances neural stem cell proliferation and oligodendrocyte differentiation

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Background: 1, 25-dihydroxyvitamin D3 (VD3) has recently been found to have an anti-inflammatory effect and to suppress experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis; however, whether it can directly function on neural cells is not clear. The present study investigates the effect of different concentrations of VD3 on EAE progression, and on neural stem cell (NSC) proliferation and their differentiation to oligodendrocytes, the myelinating cells.

Methods: Vitamin D receptor (VDR) expression was first determined in NSCs by RT-PCR. Then different concentrations of VD3 (1.0×10⁻¹⁰ - 1.0×10⁻⁴ M) were added to NSC cultures for their proliferation and neural cell differentiation. For treatment of EAE, female C57BL/6 mice were immunized with MOG35-55 peptide in CFA, and VD3 was injected i.p. at the optimal dose (0.1 µg) every other day for 15 days, starting from disease peak (day 16 post immunization; p.i.). Spinal cords were harvested for central nervous system (CNS) histopathology, and splenocytes were analyzed for cytokine production by ELISA and flow cytometry.

Results: VDR was constitutively expressed on NSCs, and the expression was upregulated by VD3 with the optimal concentration of 1.0×10⁻⁴ M. VD3 enhanced proliferation of NSCs and their differentiation into oligodendrocytes. In vivo, VD3 treatment significantly suppressed clinical scores of EAE mice and CNS inflammatory infiltration and demyelination in comparison with vehicle-treated mice. VD3-treated mice exhibited reduced pro-inflammatory cytokines IFN, GM-CSF, and IL-17, and increased production of anti-inflammatory cytokines IL-4 and IL-10. Greater numbers of oligodendrocytes, neurons and fewer astrocytes were also observed in the CNS of VD3-treated EAE mice.

Conclusion: It was demonstrated that VD3 suppressed EAE not only by its immune-inhibitory effect, but also by its effect on NSC proliferation and oligodendrocyte differentiation, thus promoting endogenous remyelination.

Biography
Hasti Atashi Shirazi has completed her Master degree in Shahid Beheshti University of Medical Sciences, Tehran, IRAN and become the grantee of “Multiple Sclerosis International Federation (MSIF)” for six months to generate of oligodendrocyte precursor cells and evaluate their remyelination potential in an EAE model under the supervision of Professor Guang-Xian Zhangin Thomas Jefferson University of Medical College, Neurology Department, and currently, she is working as a researcher in there.

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