ecules such as BDNF in the hippocampus in Pls knock-down and Pls-diet feeding mice.

Results: Morris water maze test showed an impairment of spatial memory in Pls knock-down mice. We also found a significant reduction of BDNF and its target genes, synapsin-1 and synaptotagmin-1, in the hippocampus. On the other hand injection of LPS down-regulated Pls synthesizing enzymes. Interestingly, lipid rafts fractionation study of the hippocampus tissue showed that BDNF receptor, TrkB, and Pls were accumulated in the similar lipid rafts fractions. Furthermore, the mice receiving Pls-containing diet for 6 weeks showed increases in Pls content and doublecortin-positive neuronal precursor cells in the hippocampus. Memory function enhanced in these animals, which was blocked by knock-down of BDNF gene.

Conclusion: The present study confirms that the endogenous Pls in the hippocampus are very important to maintain our memory through regulating the expression of BDNF and its related genes and suggest preventive and therapeutic strategies for treating AD.

Classically Activated Macrophages Trigger Multipotent Adult Progenitor Cells (MAPC®) to Modulate Crucial Immune Features of Multiple Sclerosis

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Objective: This study explores the effects of factors secreted from Multipotent Adult Progenitor Cells (MAPC®) upon encountering the proinflammatory environment that M1 macrophages (MΦ) generate, on antigen presentation capacity of MΦ as well as on antigen-specific proliferation of T cells.

Material and Methods: Rat MAPC, provided by ReGenesys BVBA, were treated with supernatant (LSN) of lipopolysaccharide (LPS) activated primary macrophages (MΦ) or NR8383 cells (rat macrophage cell line). After 12 hrs, the LSN was removed and fresh medium was added for another 24 hrs (50 or 100 µl) resulting in double-conditioned medium (DCM50 and DCM100). Alternatively, MAPC were treated with a mixture of cytokines (TNFα, IL-6, IL-1β) generating licensed conditioned media (LCM50 or LCM100). These conditioned media were applied to NR8383 cells along with LPS to explore its effect on their polarization. In additional experiments, DCMs were added to MΦ along with myelin basic protein (MBP). After 24 hrs, MBP was removed and CFSE labeled MBP-reactive T cells were added. T cell proliferation was determined via CFSE dilution. MBP induced proliferation of T cells in presence of DCMs was determined using [^{3}H] thymidine incorporation.

Results: NR8383 cells exhibit increased expression of Arginase-1, IL-10, YM-1 and CCL18 (M2 markers) when seeded in DCMs supplemented with LPS. In contrast, the expression of iNOS and CD86 (M1 markers) was reduced. The proliferation of T cells was reduced when they were exposed to MΦ previously exposed to MBP along with DCMs and LCMs. The observed effect was more prominent when MΦ were treated with DCMs than LCMs. Secreted factors from challenged MAPCs also diminished ex-vivo T cell proliferation against MBP.

Conclusion: M1 MΦ stimulate MAPC to secrete factors that lead to reduced M1 responses, by down regulating M1 markers and lowering the antigen presentation capacity towards antigen –specific T cells. Additionally, we show that MAPC challenged by LSN or recombinant cytokines show suppressive effects towards T cell proliferation. These features are important for a stem cell based strategy targeting the modulation of myeloid cell mediated neuroinflammation, indicating a possible in vivolicensing of MAPC in diseases where M1 MΦ prevail, such as Multiple Sclerosis.

HDL Modulates the Human Monocyte Phenotype and Its Subclass Levels Are Altered in MS Patients

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Objective: Macrophages are major effector cells in multiple sclerosis (MS). In MS, lipoprotein levels in the blood are altered and an association between plasma lipoprotein levels and neurologic events is reported. Interestingly, lipoproteins influence the inflammatory phenotype of monocytes in the blood. In atherosclerosis, recombinant high density lipoprotein (HDL) is known to beneficially influence the disease status by inducing cholesterol efflux in macrophages which is accompanied by an anti-inflammatory phenotype in these cells. In this study we aim to determine the interaction between changes in lipoproteins in the blood, their influence on the phenotype and function of monocytes and subsequently on disease progression.

Material and Methods: Human monocyte gene expression was measured using qPCR. Fasting plasma samples were collected from healthy controls, relapsing remitting (RRMS) patients and progressive patients matched by age, gender and BMI. Detailed lipoprotein profiles were determined in plasma samples with NMR spectroscopy. Serum cholesterol efflux capacity was measured in vitrousing 3H cholesterol-labeled baby hamster kidney (BHK) cells expressing human ABCA1 or ABCG1.

Results: HDL suppresses both basal and LPS induced expression of the pro-inflammatory markers TNFα, CD40, IFNγ, IL6 and IL1β in a dose-dependent manner in human monocytes. Furthermore, we report that RRMS but not progressive MS patients have an atherogenic, insulin resistant lipoprotein profile. RRMS patients have hypertryglyceridemia, a higher lipoprotein insulin resistance index, increased amounts of small HDL and LDL particles and a tendency towards lower HDL-c levels. Moreover, in RRMS patients, levels of small HDL particles correlate negatively with serum cholesterol efflux capacity through ABCA1 and ABCG1.