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SHIFT 6 - MS & DEMYELINATING DISEASES

Circulating exosomes analysis reveals microRNA biomarkers of relapsing-remitting multiple sclerosis

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Background: Exosomes are a membrane vesicles released from the endocytic compartment of live cells that play an important role in cell-to-cell communication via transmitting RNA between cells.

Objective: To analyze the role of exosomes in the relapsing remitting multiple sclerosis (RRMS).

Patients and Methods/Material and Methods: We have isolated exosomes from serum of the 19 RRMS patients (9 in relapse, 10 in remission) and 10 healthy controls (HS), generated exosomal RNA libraries and performed next generation sequencing with 5 million reads and 50,000 transcripts per sample. We accomplished a detailed analysis of microRNA (miRNA) differentially expressed in RRMS. The discovery set data were validated using digital quantitative PCR with an independent cohort of 63 RRMS patients and 32 HC. Peripheral blood mononuclear cells (PBMCs) have been isolated from blood of the RRMS patients and from controls and cultured for 72hrs under various TLR stimulations or unstimulated.

Results: We have found that serum exosomes are a reach source of the short RNA in MS patients both during relapse and remission. The sequences represented 14 RNA categories: CDBox, HAcaBox, RefSeq_antisense, lincRNA, lincRNA_antisense, miRNA, other_ncRNA, other_ncRNA_antisense, rRNA, piRNA, rfam, scaRNA, tRNA and tRNA_like. We have identified four exosomal miRNA that were differentially expressed during relapse in comparison to remission. Interestingly, these miRNA have been also differentially secreted within the exosomes by PBMCs from RRMS patients and from controls.

Conclusion: Our data highlight a differences in serum exosomes miRNA in RRMS patients related to the clinical status of the patients that could lead to a discovery of a new biomarkers of RRMS.

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Comprehensive cytokine profile in optic neuritis with antibodies to myelin oligodendrocyte glycoprotein

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Background: Antibodies (Abs) to myelin oligodendrocyte glycoprotein (MOG) are often relevant to demyelinating optic neuritis (ON) and encephalomyelitis. We previously reported the clinical features of idiopathic ON with MOG Abs in 2015.

Objective: The aim of this study is to investigate the association between MOG Abs and its comprehensive serum cytokine profile in the patients with idiopathic ON.

Patients and Methods/Material and Methods: We continuously enrolled thirty-six patients with idiopathic ON from April 2011 to September 2015 and used a cell-based assay (CBA) to detect serum MOG-IgG, and enzyme-linked immunosorbent assay (ELISA, MILLIPLEX®) to evaluate the levels of thirty-eight types of serum cytokines and chemokines.

Results: The CBAs and ELISAs showed eight patients were positive and twenty-eight patients were negative. Two of the eight patients with MOG-Abs had encephalitis and epilepsy and one had myelitis as a complication. Finally, we compared the level of all cytokines tested for all ON patients with MOG-Abs to those without them. Statistical analysis proved that the serum concentration of IL-1ra ($p = 0.020$), IL-5 ($p = 0.042$), and TGF-α ($p = 0.041$) in the patients with MOG-Abs were at a high level compared to those in negative patients.

Conclusion: This result is meaningful to understand the pathogenesis of MOG-Ab related disorders.

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SHIFT 6 - MS & DEMYELINATING DISEASES

Prognostic significance of free light chains for long-term and short term disability progression in multiple sclerosis

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Background: Intrathecal activation of B-cell is a major pathological finding in multiple sclerosis (MS) that is characterized by increased intrathecal synthesis and oligoclonal banding of immunoglobulins in cerebrospinal fluid (CSF). Free light chains (FLC) are fragments of immunoglobulins that are produced in parallel with OCB.

Objective: To define prognostic significance of FLC

Patients and Methods/Material and Methods: 381 patients with MS participated in this study. We reviewed two patient groups: long term prognosis (LTP) ($n = 284$) and short term prognosis (STP) ($n = 97$). STP and LTP were also divided on subgroups with high FLC concentration and low FLC concentration. FLC were measured using ELISA. In LTP Multiple Sclerosis Severity Score (MSSS) and Expanded Disability Status Scale (EDSS) were measured at the date of the last follow-up. EDSS at the moment of the first relapse and after 2 years was measured in STP.

Results: In LTP positive correlations were detected between EDSS and kappa-FLC in CSF ($r = 0{,}181$; $p = 0{,}002$), MSSS and kappa-FLC in CSF ($r = 0{,}121$; $p = 0{,}044$). Survival analysis revealed an increased risk for long-term progression of disability ($EDSS = 6.0$) for high kappa-FLC in CSF ($HR = 2.055$, $p = 0.026$). In STP positive correlation was detected between EDSS after 2 years and kappa-FLC in CSF ($r = 0{,}377$; $p = 0{,}00019$). EDSS in all subgroups of STP significantly decreased after 2 years, except for subgroup with high kappa-FLC in CSF where EDSS level at the moment of the first relapse and EDSS after 2 years didn't change significantly after 2 years ($p = 0{,}1844$).

Conclusion: Kappa-FLC in CSF possess prognostic value for long-term and short-term disability progression.

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