Characteristics of anti-lipid IgG antibodies in patients with relapsing-remitting multiple sclerosis: physico-chemical properties and biological activity

Objectives: Multiple sclerosis (MS) is a chronic disease of the central nervous system (CNS), with a complex background. Multifocal damage to CNS results in variety of symptoms and accumulating disability. Despite recent progress in the early diagnosis and availability of several disease modifying therapies, the course of MS and response to treatment are still very difficult to predict and follow-up. There is ongoing search for reliable biomarkers – molecules which could be measured in the body fluids and identify the risk of disease, its severity and/or predict its outcomes. Antibodies against bioactive sphingolipids (the major components of the myelin sheath protecting and improving conduction in the neurons of the brain and spinal cord), seem promising candidates for this role. Belonging to bioactive sphingolipids ceramide (Cer), supposed to be relevant players in injury to myelin sheath (acute neuroinflammation) while cermide-1-phosphate (C1P) seems to be related with chronic damage to neurons (neurodegeneration) in the CNS – the main processes underlying disease progression.
The aim of the project: The project assumes analysis of antibodies against bioactive sphingolipids (Cer and C1P) in human specimens of serum and cerebrospinal fluid derived from patients with relapsing-remitting multiple sclerosis (RRMS). The presence and properties (physico-chemical and biological) of these antibodies will be compared between patients with RRMS, healthy subjects (HS) and patients with other neurological diseases (OND). The results will be also analyzed with regard to clinical status.
Material and methods: The study will comprise 40 subjects diagnosed with RRMS and the two age- and sex-matched reference groups: 10 healthy subjects and 30 patients indicated OND. Immunological parameters – presence and level of antibodies anti-C1P – will be determined in serum and cerebrospinal fluid (CSF) in the RRMS group and reference groups. Physico-chemical analysis will include kinetic analysis using surface plasmon resonance (SPR) technique. Biological characteristic will include functional analysis in regard their influence to cell death (apoptosis) of other cells and its markers (Bax, Bcl-2, caspase 3) as well as their influence to synthesis of the pro-inflammatory mediators called eicosanoids, their markers (prostaglandin E2) and related enzymes (cytosolic phospholipase A2, cyclooxygenase 2) using *in vitro* model. In addition, relationships will be analyzed between biochemical and immunological parameters in the MS group and clinical outcomes of disease by using appropriate statistical tools.
Expected results: As a result, we expect to identify particular lipid molecules specific for MS and associated with acute inflammatory injury to myelin sheath and/or with chronic damage to neurons. These molecules would undergo further investigation, to check if their measurement allows to distinguish active from progressive phase of MS and reflects the changes in the disease severity. Within a few years, a panel of such lipid biomarkers is supposed to be defined.
Potential clinical applications of lipid biomarkers may include improved early diagnosis of MS (distinguishing MS from other neurological diseases, especially in atypical cases) and careful follow-up of the disease course (to appropriately evaluate the disease severity and adjust the treatment). They might be also helpful in predicting response to treatment and choosing optimal drugs for individual patients, improving management of the disease.