ABSTRACT

MHC complex is the most polymorphic, most complex and one of the most important parts of a genome which takes a part in the immunity response of an organism. In a human body, it is tagged as HLA (human leukocyte antigen) and consists of 224 genes. HLA genes are associated as a risk factor in numerous autoimmunity diseases. One of systemic autoimmunity diseases is idiopathic inflammatory myopathy. It is a disease with a clinical manifestation of a chronical muscle inflammation with a destruction of own cells and leading to a damage of the whole organs. IIM involves several diagnoses - polymyopathy (PM), dermatomyopathy (DM) myopathy associated with tumor diseases (CDM) myopathy with inflammatory inclusion corps (IBM) and others.

MHC complex consists of three parts, two of which - MHC class I and II - are already examined rather well and have been associated with numerous (mainly autoimmunity) diseases. Last part of MHC is located between class I and II is an area of around 150 genes called „non Class I/II“ (Remákova, Novota, 1999).

The main subject for my thesis are three genes of the HLA complex in which has been proven a function in regulation mechanism of some autoimmunity diseases. These genes play a part in the immunity response, because they are able to stimulate the adaptive and native immunity. These are genes heat shock protein (HSP70 specifically) lying in a "non Class I / II". These include two that are stress-inducible HSPA1A (HSP70–1) HSPA1B (HSP70–2) and a tissue-specific gene and a constitutively expressed HSPA1L (HSP70–Hom) (Wu Y. et all., 2003). The genes we observed association of polymorphisms in the gene localized HSPA1A (-110 / C ~ +190 and rs1008438 G / C ~ rs 1043618), the gene of HSPA1B (+1267 A / G ~ rs 1061581 and +2074 G / C ~ rs539689) in the HSPA1L (+2437 T / C ~ rs 2227956) and in one pentanucleotide HSP70 gene mutation – HSPA1B (rs9281590) in the Czech cohort of patients with inflammatory myopathies.

Altogether we have analyzed five SNP polymorphisms and a one pentanucleotid tandem duplication. To exclude possible interference of these risk factors, we have adjusted the results to known risks focused on the HLA area (locus HLA-DRB1 and HLA-DQB1). The aim of this study was to discover a relation between all types of polymorphism, gather data using HLA typing on DRB1 and DQB1 in each of three HSP70 genes and to compare the results with healthy cohorts.
Statistically, we confirmed the association of three polymorphisms and mutations in one Pentanucleotide all we examined HSP70 genes. The results also show the close link between gene allele ins HSPA1B with HLA-DRB1*03:01.

Subsequently, we obtained the most frequent HLA typing of HLA locus alleles – HLA-DQB1 and HLA-DRB1, which have enriched the knowledge of the disease idiopathic inflammatory myopathy. Haplotype analysis of the HLA-DQB1-DRB1, we further expanded the allelic genes HSP70, we have gained the most common haplotypes, which have not yet been published.

Keywords: major histocompatibility complex (MHC), heat shock proteins (HSP), idiopathic inflammatory myopathy, autoimmunity.