ABSTRACT

MHC complex is the most polymorphic, most complex and one of the most important parts of human genome which participates in the immune response. MHC in humans is known as HLA complex (human leukocyte antigen), and consists of about 224 genes (Beck et al., 1999; Robinson et al., 2000). HLA genes are well known risk factors associated with number of autoimmune diseases (Beck et al., 1999). Idiopathic inflammatory myopathy belongs to the systemic autoimmune diseases. It is a disease with clinical manifestation of chronic muscle inflammation with a destruction of muscle cells, leading to a damage of the whole muscles. Idiopathic inflammatory myopathy (IIM) includes several diagnoses - polymyositis (PM), dermatomysitis (DM), cancer associated myositis (CDM), inclusion bodies myositis (IBM), and others.

Human MHC complex consists of three parts. First two of them - the MHC class I and MHC class II genes, are already well studied and published results show their associated with numbers of (mostly immune system mediated) diseases. The third part of MHC is located between class I and II antigens and covers an area of about 150 genes. It is also called „non Class I/II“ antigens (Beck et al., 1999; Carole et al., 1988; Lie, Thorsby, 2005).

My work was focused on three MHC-located genes, which are known to be involved in the etiopathogenesis of several autoimmune disorders. These genes are important in the regulation of immune response, because they are able to trigger the adaptive and native immunity. These are the three heat shock protein coding genes (HSP70), located within the "non Class I / II" area of MHC. Two of these genes are stress-inducible: HSPA1A (HSP70–1), HSPA1B (HSP70–2). The third one is a tissue-specific and constitutively expressed HSPA1L (HSP70–Hom) gene (Wu Y. et al., 2003).

We have studied association of polymorphisms located in the HSPA1A (-110A/C ~ rs1008438 and +190G/C rs1043618), in the HSPA1B (+1267A/G rs 1061581 and +2074G/C rs539689 and pentanucleotide tandem duplication rs9281590), in the HSPA1L (+2437T/C rs2227956), in a cohort of Czech patients suffering from inflammatory myopathy. In total, we have analyzed five SNP polymorphisms and one pentanucleotide tandem duplication. Results found, were adjusted to known genetic risk factors for autoimmunity development - the genes of HLA complex (loci HLA-DRB1 and HLA-DQB1).
The aim of this study was to find a relation between the pathogenesis of IIM and all types of analyzed polymorphisms of MHC genes (HLA-DRB1, HLA-DQB1, three HSP70 genes).

Our results confirm the association of HLA-DRB1 (DRB1*16:01, DRB1*03:01), and HLA-DQB1 (DQB1*02:01) risk alleles with IIM. Moreover, we have found new genetic associations between polymorphisms in the HSP70 genes and IIM. Results of the study will potentially help to better diagnose of the myositis in the future.

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