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MS risk allele rs1883832T is associated with decreased mRNA expression of *CD40*

Marta Wagner · Maciej Sobczyński · Malgorzata Bilińska · Anna Pokryszko-Dragan · Malgorzata Cyrul · Piotr Kuśnierczyk · Monika Jasek

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Abstract CD40-CD40L interactions mediate T-dependent B cell response and efficient T cell priming. Therefore, genes encoding these molecules are attractive candidates for studies on autoimmune diseases, such as multiple sclerosis (MS), in which activated T and B cells are involved. Thus, we analyzed *CD40* and *CD40L* mRNA expression in whole blood samples from MS patients and controls. Additionally, we examined the effect of three SNPs of *CD40* (rs1883832C>T, rs11569343C>G, and rs752118C>T) and two SNPs of *CD40L* (rs3092923T>C and rs3092952A>G) on their mRNA expression. Our results showed that the rs1883832C>T SNP affects *CD40* gene expression. Our analysis revealed that individuals possessing CT and TT genotypes (predisposing to MS) had decreased level of *CD40* mRNA in comparison to those with CC. Moreover, we demonstrated the potential role of impaired CD40-CD40L interaction in developing of multiple sclerosis.

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M. Wagner (✉) · P. Kuśnierczyk · M. Jasek (✉)
Laboratory of Immunogenetics and Tissue Immunology, Department of Clinical Immunology, Ludwik Hirszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, ul. Weigla 12, 53-114 Wrocław, Poland
e-mail: marta_wagner@o2.pl
e-mail: jasek@iitd.pan.wroc.pl

M. Wagner
e-mail: marta.wagner@iitd.pan.wroc.pl

M. Sobczyński
Department of Genomics, Faculty of Biotechnology, University of Wrocław, ul. Fryderyka Joliot-Curie 14a, 50-383 Wrocław, Poland

M. Bilińska · A. Pokryszko-Dragan · M. Cyrul
Department and Clinic of Neurology, Wrocław Medical University, ul. Borowska 213, 50-566 Wrocław, Poland

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Introduction

CD40 (TNFRSF5) is a member of the tumor necrosis factor receptor superfamily which is expressed as a costimulatory molecule on the surface of variety of immune cell types like B cells, macrophages, dendritic cells, and microglia. Its ligand, CD40L (CD154), is expressed mainly on the surface of CD4+ T cells (Australia and New Zealand Multiple Sclerosis Genetics Consortium 2009; Peters et al. 2009). CD40-CD40L interactions mediate T-dependent B cell response and efficient T cell priming (Peters et al. 2009) and play an important role in the initiation and progression of cellular and humoral adaptive immunity (Elgueta et al. 2009; Peters et al. 2009). Therefore, CD40 together with its ligand, CD40L, are attractive candidates for studies on autoimmune diseases such as multiple sclerosis (MS) in which activated T and B cells are involved (Peters et al. 2009).

MS is an inflammatory demyelinating disease of the central nervous system that gradually leads to physical and cognitive disability (Goris et al. 2012; Sawcer et al. 2014). It affects about 2.5 million people worldwide. Moreover, it is suggested that the incidence of MS is increasing. The disease starts mainly between 20 and 40 years of age, and it is at least twice as common in women as in men (Sawcer et al. 2014). The precise etiology of MS is still not well established; however, it is believed that understanding of the genetics of MS requires analysis of both gene-environment and gene-gene interactions.

In our previous study (Wagner et al. 2014), we investigated three single nucleotide polymorphisms (SNPs) of *CD40*