RELATIVE EXPRESSION STRENGTH OF HLA-DRB1 IN HETEROZYGOTES IS ASSOCIATED WITH RHEUMATIC DISEASES

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Background HLA-DRB1 is characterized by highly complex genetic variants associated with susceptibility to and autoantibodies of rheumatic autoimmune diseases including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), highlighting the primary associations of multiple amino acid changes on the epitope-binding groove of HLA-DR molecules. However, in contrast to the missense variants in HLA-DRB1, an effect of expression changes in HLA-DRB1 has been poorly understood.

Methods Both three-field HLA-DRB1 alleles (# of alleles>10) and RNA-Seq data in 48 Koreans and 357 Europeans were simultaneously analyzed to determine the most likely HLA-DRB1 genotypes in each individual and to measure allele-specific expression levels. The relative expression strength of each HLA-DRB1 allele compared to all the other alleles was calculated and tested for contribution to phenotypes associated with amino-acid changes in HLA-DRB1.

Results Strong cis-eQTL signals of HLA-DRB1 were detected around HLA-DRB1, causing highly imbalanced allelic expressions in HLA-DRB1 heterozygotes. The reported associations of HLA-DRB1 with the level of anti-cyclic citrullinated peptide (anti-CCP) autoantibodies in RA or the susceptibility to SLE were re-assessed in Korean RA (n>1,000) and SLE-control (n>5,000) genetic data, taking the relative allelic expression strength into account, and were additionally explained by the skewed allelic expressions of HLA-DRB1 in heterozygotes.

Conclusions This study identified the allele-specific expression of HLA-DRB1 that contributed to disease risk and autoantibody production in rheumatic autoimmune diseases.

Funding Source(s): This study was supported by Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Science, ICT & Future Planning (2017R1E1A1A01076388) and Korea Healthcare Technology R and D Project funded by the Ministry for Health and Welfare (HI15C3182) in Republic of Korea.

PD-L1 EXPRESSING MYELOID-DERIVED SUPPRESSOR CELLS (MDSCs) HAVE POTENT IMMUNOREGULATORY ACTIVITY AND CONTROL LUPUS-LIKE AUTOIMMUNITY

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Background Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of myeloid cells that modulate pathogenic response in the autoimmune microenvironment. However, the precise roles of MDSCs in systemic lupus erythematosus (SLE), the prototype autoimmune disease, are not completely understood. Indeed, their immunosuppressive functions in lupus model remain controversial with heterogeneity among MDSCs and differential effects among subpopulations receiving much attention. Programmed death-ligand 1 (PD-L1) is an inhibitory ligand that binds to PD-1 to suppress T cell activation. Multiple studies have explored the potential role of PD-L1 as a mediator of MDSC effects in various cancers. However, the role PD-L1 expression in MDSCs on autoimmune disease is still largely unknown.

Methods In the present study, we investigate the role of PD-L1 expressing MDSC in the MRL/Mpj-Faslpr (MRL-lpr) mouse model. Results Here we show that the PD-L1 expressing MDSCs express higher amount of immunosuppressive mediators including arginase-1, iNOS and IL-10 than PD-L1 negative MDSCs and exhibit more potent immunoregulatory activity in vitro. We have also identified that in vivo treatment with PD-L1 expressing +MDSC reduced serum autoantibody titres, proteinuria level and mitigated the development of kidney damage. Infusion of PD-L1 expressing MDSCs significantly reduce the double negative T cell population and Tfh cell population in spleens of MRL-lpr mice. Moreover, treatment of PD-L1 expressing MDSCs resulted in an expansion of the regulatory B cell population.

Conclusions Our results indicate PD-L1 expression is critical in MDSCs to maintain MDSC immune regulatory function. Taken together, our results suggest that PD-L1-expressing MDSCs may be a potential cell therapeutics for the treatment of autoimmune diseases like SLE.

Funding Source(s): None

COEXISTENCE OF AXIAL SpondyloarthritIs, sYstemIC lupUs erythematosus, sJögrens sYndrome and secondary antiphospholipid sYndrome: Case rEport tArhan F, kEsEr g, cElIk ö, kLnÇ rM*, aKAR s

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Background Axial spondyloarthritis (AxSpA) is a chronic inflammatory disease of the axial skeleton which manifests as inflammatory back pain and progressive stiffness of the spine. Patients with axial disease and other features of SpA but no unequivocal sacroiliitis in conventional X-ray now termed as non-radiographic axial spondyloarthritids (nr-AxSpA). Those patients can be diagnosed on the basis of the presence of active inflammation in magnetic resonance imaging (MRI) or human leukocyte antigen B27 (HLA-B27).Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown etiology that may affect the skin, joints, kidneys, lungs, nervous system, serous membranes, and/or other organs of the body. Sjögrens syndrome (SS) is the second most common autoimmune rheumatic condition characterized by lymphocytic infiltrate of the exocrine glands, resulting in dysfunction and destruction of them. Antiphospholipid syndrome (APS) is the association of thrombosis and/or pregnancy morbidity with antiphospholipid antibodies (aPL) (lupus anticoagulant [LA], anticardiolipin antibodies [aCL], and/or anti-2-glycoprotein-I antibodies [a2 GPI]).

Methods Case Presentation

We report a 55-year-old female patient having the association of nr-AxSpA, SLE, secondary APS, and SjS. Diagnosis of