

Title	Autoantibodies to IgG/HLA class II complexes are associated with rheumatoid arthritis susceptibility
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Citation	大阪大学, 2014, 博士論文
Version Type	
URL	https://hdl.handle.net/11094/34277
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論 文 内 容 の 要 旨
Synopsis of Thesis

氏 名 Name	金 暉
論文題名 Title	Autoantibodies to IgG/HLA class II complexes are associated with rheumatoid arthritis susceptibility (IgG/HLAクラスII複合体に対する自己抗体は関節リウマチの発症リスクと相関する)
論文内容の要旨	
<p>[目 的(Purpose)]</p> <p>Rheumatoid factor (RF) is an IgM autoantibody that binds to denatured IgG or Fc fragments of IgG, and is detected in about 80% of RA patients, but also in 5-10% of healthy individuals as well as in other autoimmune diseases. However, the natural antigens that are recognized by RF are unknown, partly because such denatured IgG does not exist in physiological situations. Specific HLA class II alleles are strongly associated with susceptibility to many autoimmune diseases. A recent report of a large-scale genetic study indicates that several amino acid residues within the HLA-DR peptide-binding groove determine susceptibility to rheumatoid arthritis (RA). However, it has remained enigmatic for decades how specific HLA class II molecules control the immune response in autoimmune diseases.</p>	
<p>[方法ならびに成績(Methods/Results)]</p> <p>1. IgG heavy chain alone is expressed on the cell surface in association with MHC class II molecules.</p> <p>The secreted forms of IgG heavy chain (IgGH) cloned from human PBMC that have different V regions were co-transfected with HLA-DRα, DRB1*04:04 (HLA-DR4), and GFP. Cell surface IgG on GFP-expressing cells was detected with anti-human IgG Fc-specific Ab.</p> <p>2. Autoantibodies from RA patients bind to IgG heavy chain complexed with MHC class II molecules.</p> <p>The IgGH, GFP were co-transfected with or without HLA-DR4. Cell surface expression of HLA-DR or IgG, and binding of autoantibodies in the RF standard serum and RF61 monoclonal Ab by GFP-positive cells were detected.</p> <p>3. A strong correlation between autoantibody binding to IgG complexed with each HLA-DR allele and the odds ratio for that allele's association with RA.</p> <p>The IgGH was co-transfected with Ig light chain, Ii, and HLA-DRα in combination with each HLA-DRB1 allele, and the mean fluorescence intensities (MFI) of binding of autoantibodies in the RF standard serum to IgG complexed with HLA-DR were plotted against the odds ratios for RA susceptibility for each HLA-DRB1 allele.</p> <p>4. <i>In situ</i> association of IgGH with HLA-DR in synovial membrane from RA patients.</p> <p><i>In situ</i> association of IgGH with HLA-DR in tissue sections from synovial membranes of RA patients and osteoarthritis patients were analyzed by proximity ligation assay.</p>	
<p>[総 括(Conclusion)]</p> <p>Our findings suggest that IgGH complexed with certain HLA class II alleles is a target for autoantibodies in RA, which might explain why these HLA class II alleles confer susceptibility to RA.</p>	

