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審査の結果の要旨

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Current study was conducted to current study was conducted with the two major purposes: first, to establish a plate-based peptide binding assay system where peptide binding to HLA II protein can be tested using cell-lysates of HLA-DR or -DQ -expressing cells. Second, to screen the synthetic peptide ligands derived from autogenic peptide ZnT8 in order to identify the regions that are able to be presented by the T1D risk or protective HLA-DR and -DQ T1D alleles in Japanese and might act as pathogenic self-epitopes. As a result, major findings were determined as followed.

1. A plated based peptide binding assay was successfully established to improve the efficiency and to overcome the limitation of previously reported plated based peptide binding assays. That is, the use of HLA II protein containing lysate instead of purified proteins has exempt the process of protein purification and limit the use of large quantity monoclonal antibody. Moreover, current assay system allows an efficient way to examine a large variety of alleles at once.

2. Three potential binding epitope were determined in ZnT8, which has not only proven the success of the establishment of peptide binding assay but also provide an inventory for mapping the epitopes for ZnT8 peptides, one of the newest established auto-antigens in T1D in which provide new insights underlying the mechanism of T1D especially in the Japanese and the Asian populations.

With the results of current study should promote the screening of large numbers of candidate peptide library for diverse HLA allele products and with such screening should promote identifying the disease-relevant self-epitopes involved in the pathogenesis of T1D. Thus, a phD degree should be given.