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Euro Diabetes 2019: HLA- DR3, DQ2 transgenic mice for identification of immunodominant peptides of pancreatic autoantigens- Rossino R- Università degli Studi di Cagliari

Rossino R

Università degli Studi di Cagliari, Itlay

Background: Diabetes mellitus type 1/type 1 diabetes) is a type of diabetes mellitus that results from the immune system extermination of the insulin-delivering beta cells in the pancreas. The resulting absence of hypoglycaemic agent stimulates expanded aldohexose in the blood. The recognized manifestations are expanded thirst, expanded yearning, regular pee and weight reduction. Type 1 diabetes is recognized from antibody testing. The C-peptide test, that measures endogenous insulin generation, can also be utilized.

Organization of insulin is fundamental for survival. Insulin treatment should be continued with commonly does not disable ordinary routine exercises. Individuals usually take care of their diabetes; for a few it is a challenge. Untreated diabetes can bring about much confusion. Intense confusions include diabetic ketoacidosis and non-ketotic hyperosmolar trance kind of state. End of the day complexities known as high glucose include coronary unwellness, kidney disappointment, foot ulcers, stroke and visual challenges (eye related diseases). Confusions could arise from low aldohexose caused by treatment of extortionate hypoglycemic agent.

Aims: Sardinians have one of the highest insulin dependent autoimmune diabetes mellitus (T1DM) incidence in the world (38/100.000 in the age range 0-14 years) associated with a low grade of genetic heterogeneity and a high frequency of the HLA-DR3-DQ2 haplotype. This HLA haplotype confers a high risk for T1D, celiac disease, and multiple sclerosis. The aims of the study are: a) the identification of immunodominat T cell epitopes of preproinsulin and GAD65 pancreatic autoantigens immunizing HLA- DR3-DQ2 transgenic mice with these autoantigens and deriving T cell specific hybridomas and b) the design of variant peptides of these epitopes able to bind HLA class II molecules without triggering a T cell activation.

Methods. HLA- DR3-DQ2, human CD4, IA class II KO triple transgenic mice in the NOD background will be immunized with human PPI and GAD65 autoantigens to generate antigen specific T cells. These cells will be fused with the BW5147 cell line to produce T cell hybridomas and specific T cell responses will be identified stimulating the hybridomas with overlapping peptides of PPI and GAD65 and measuring IL-2 production. PPI and GAD65 will be produced in vitro, purified and quantified in order to immunize each mouse with 100 µg of antigen. The pepscan of overlapping PPI and GAD65 13 Mer peptides will be purchased from the Alphalyse Company.

Results: With the aim of improving T cell response and the generation of antigen specific T cell hybridoma, the HLA- DR3-DQ2 transgenic mice, initially obtained in the C57BL/6, have been backcrossed in the class II KO human CD4 NOD mice. These animals are more suitable for immunization since they maintain the autoimmunity background of NOD mice (an animal model of spontaneous human T1DM) in absence of murine class II molecules. At the present time these animals have obtained and are maintained in our animal facility. Moreover, the expression vector to produce both PPI and GAD65 have been generated.

Conclusions: By the present study the portion more immunogenic of PPI and GAD65 pancreatic autoantigens presented by HLA, DR3 and HLA DQ2 molecules will be identified. This information will be used to construct variant peptides able to bind diabetogenic HLA class II molecules without triggering a T cell activation providing a possible peptide vaccine for T1DM.

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