

Characterization of HLA DR2 and DQ8 transgenic mouse with a New Engineered Mouse Class II deletion, Which Lacks All Endogenous Class II genes

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Human autoimmune diseases are a class of complex immune system disorders characterized by loss of tolerance to self-antigens. HLA Class II molecules play a central role in the initiation, propagation and prolongation of the disease process. HLA Class II transgenic mice with mouse endogenous Class II gene Ab knockout were used successfully in several mouse models for human autoimmune diseases, such as IDDM, SLE and EAE in our Lab. However, these mice carry the functional mouse Eb gene from the Ab0/0 construct and could express Eb/Dra(Ea) molecules and shape the T cell repertoire in these mice. Recently, We have obtained a new MHCIIID/D mice from Mathis' lab that are devoid of all endogenous conventional mouse MHC class II genes. When these mice are mated with our transgenic mice, only human class II genes are expressed since they lack all endogenous Class II genes. Normally, mouse class II genes are not expressed on T cells while human class II genes are. The expression pattern of the HLA class II molecules of these new transgenic mice mirrors the human pattern closely. Both DR and DQ molecules are expressed on T cells of these mice like in humans, and are the only class II molecules shaping the T cell repertoire and regulating the immune response in these mice. Therefore, this new class of HLA transgenic mice is the first to be completely "humanized" in their MHC class II genes and will be an invaluable mouse model for human MHC class II associated autoimmune diseases.