

## **Myelin Oligodendrocyte Glycoprotein-Induced Immune responses in HLA Class II transgenic Mice: Characterization of T and B Cell**

### **Epitopes**

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To analyze the role of human HLA class II molecules in immune response during experimental autoimmune encephalomyelitis (EAE), a mouse model of multiple sclerosis (MS), we immunized transgenic (Tg) mice expressing HLA-DR2 (DRB1\*1502), DR3 (DRB1\*0302), DR4 (DRB1\*0401), DQ6 (DQB1\*0601; DQB1\*0604) and DQ8 (DQB1\*0302) genes with recombinant rat myelin oligodendrocyte glycoprotein (rMOG, aa1-125). MOG is an auto antigen present on outer surface of myelin sheath in CNS, and act as a target antigen for T and B cells. T cell proliferation and IFN- $\gamma$  ELISPOT assay showed strong response with rMOG in all the Tg mice, which were CD4 T cell mediated and HLA class II restricted. HLA DR2 mice developed severe EAE associated with large inflammatory foci and extensive demyelination. Mild disease was seen in HLA DR3 and DR4 mice while no disease was observed in HLA DQ mice. Cytokine analysis showed that both pro-inflammatory cytokines (IFN- $\gamma$ , IL-12 and IL-6) and anti-inflammatory cytokine (IL-10) were elevated in all Tg mice. Furthermore, in this study we have characterized the T and B cell epitopes of human MOG restricted by HLA class II molecules. T cell epitope mapping using a panel of overlapping, synthetic peptides of human MOG revealed that T cell auto-reactivity to MOG was directed mainly against peptides 1-20, 31-50, 61-80 and 91-110. Moreover, a strong B cell response to rMOG was also observed in all the Tg mice and major B cell epitopes recognized were located with in amino acids 1-30, 51-80 and 101-120 of MOG. These Tg mice would be valuable in elucidating the role of HLA class II genes and auto-antigens in MS.