

POSTER SESSION 2 ABSTRACTS
12th Annual HMO Research Network Conference

May 1-3, 2006 Boston, MA

Chronic Disease
PS2-22

Genetic Studies of Familial Multiple Sclerosis from Rural Wisconsin

Khemissa Bejaoui¹, Melissa A. Gebhardt¹, Chengfeng Zhao¹, Loren A. Rolak²

¹Marshfield Clinic Research Foundation; ²Marshfield Clinic

Background: Multiple sclerosis (MS) is a chronic disease of the central nervous system that leads to severe neurological disabilities. The cause of MS is not known. People of Scandinavian descent are more vulnerable to the disease than others. Latitude is also a risk factor for MS; the further north one lives the higher the likelihood of occurrence. The prevalence rate of MS in Wisconsin is twice the National rate, suggesting that Wisconsin is at high risk for MS. However, the reasons for this high prevalence are not known. Genetic epidemiological studies indicate that both genetic and environmental factors are necessary for the disease to manifest in a person at risk. To date, the human leucocytes antigen HLA-DRB1*15 alleles represent the only well established risk factor. However, the DRB1*15 alleles only account for a small fraction of the overall effect. This suggests that in HLA-DRB1*15 positive patients, additional genetic variants may act synergistically with the DRB1*15 alleles in determining the susceptibility to MS. It is therefore essential to stratify MS patients according to their HLA-DRB1*15 haplotype to identify additional MS susceptibility genes.

Objectives: (1) Ascertain and characterize MS families from rural Wisconsin; and (2) Stratify these families according to the presence or absence of the HLA- DRB1*15 alleles. This will allow us to reduce the genetic heterogeneity characteristic of MS.

Methods: DNA samples are genotyped for the HLA-DRB1 gene, using the polymerase chain reaction and sequence-specific primers (PCR-SSP). Genetic linkage analysis is then performed under two different models, dominant and recessive, to calculate pair-wise lod scores.

Results: We have successfully recruited and characterized a set of 30 families that were born and raised in rural Wisconsin. Each family includes more than one case of MS. All probands have been diagnosed and are being followed by one of the authors (LAR). Extensive clinical, radiological, laboratory, and paraclinical data exist on all probands as well as other affected family members.

Conclusions: Preliminary results indicate that our established data base of MS families from rural Wisconsin is suitable for the identification of MS susceptibility genes outside the HLA locus.