Reviewer’s report

**Title:** An examination of the Apo-1/Fas promoter Mva I polymorphism in Japanese patients with multiple sclerosis

**Authors:**

Masaaki Niino (niino@med.hokudai.ac.jp)
Seiji Kikuchi (skikuti@med.hokudai.ac.jp)
Toshiyuki Fukazawa (fukazawa@my.email.ne.jp)
Ryuji Miyagishi (miyagisi@med.hokudai.ac.jp)
Ichiro Yabe (yabe@med.hokudai.ac.jp)
Kunio Tashiro (tashiro@med.hokudai.ac.jp)

**Version:** 1  **Date:** 19 Jul 2002

**Reviewer:** Prof Maria Giovanna Marrosu

**Level of interest:** A paper whose findings are important to those with closely related research interests

**Advice on publication:** Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

The Authors examined the association between Mva I polymorphism of the Apo-1/Fas promoter gene in Japanese multiple sclerosis (MS) patients. Rational basis of the study was a positive LOD score near the chromosome 10q23/10q24, where the gene has been mapped, reported in UK and Canadian screens, a previous report of association of polymorphism with MS in another population and the role of candidate gene assigned to Apo-1/Fas.

The study was performed on 114 MS patients, compared to 121 healthy population-matched controls. No evidence for a role of Mva I polymorphism in MS susceptibility was found. Moreover, no difference in the Mva I allele and genotype frequencies was found in DRB1*1501 (DR2) positive or negative patients. Stratification of patients according to age at onset showed a tendency to later onset in patients with A/A genotype.

The main concern in this paper is the low number of subjects studied. Association studies in complex diseases may have a relatively high power if sample size is really consistent. Calculations as frequency of polymorphism in a determined population, number of alleles of polymorphism analyzed.. and others define the optimal size of sample. Considering that "western type" MS in Japanese is less common that in European countries and that comparation between ethnically different populations may be of aid in comprehension of MS pathogenesis, the study may be considered of interest despite the fact that sample size of patients is small. Nevertheless, number of controls must be consistently higher (almost twofold). This point is crucial.

Moreover, data regarding “tendency” of A/A carriers to have a later onset cannot be stressed in absence of a statistical significance.

**Competing interests:**

None declared.