Reviewer’s report

Title: Exacerbated inflammatory cellular immune response characteristics of HAM/TSP is observed in a large proportion of HTLV-I asymptomatic carriers

Version: 2 Date: 21 November 2003

Reviewer: Ryuji Kubota

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General
The authors describe that HAM/TSP patients show increased spontaneous lymphocytes proliferation and IFN-g production when compared to asymptomatic HTLV-I carriers, however, 40% of the carriers have spontaneous lymphoproliferation and IFN-g production similar to HAM/TSP patients.

Discretionary Revisions (which the author can choose to ignore)
1. The authors argue that 40 percent of the carriers have the immunological responses similar to HAM/TSP patients. How were they able to calculate 40%, since the IFN-g production is significantly higher in HAM/TSP patients as compared to the carriers as shown in Fig1A? It would be more helpful if they describe in more detail their calculations. I could not assess whether the title is appropriate, because it includes “a large proportion”.

2. The authors performed cytoplasmic cytokine staining after 20 hr culture. The time kinetics of cytokine production is difference in each cytokine, with or without stimuli (i.e. PHA); therefore I think a preliminary experiment is needed to decide the appropriate culture time. If they did a preliminary experiment to set the time, it should be written in the article.

3. Are there any differences in neurological symptoms between the carriers with low IFN-g production and those with high production? It is of interest to know whether the HAM/TSP and carrier state are completely different neurological states, or some carriers with high immune responses, as in HAM/TSP, show any neurological symptoms (e.g. hyperreflexia, sphincter dysfunction).

4. The authors claim that the CD8 is a major source for the TNF-a production based on the results from Figure 3C. Is there any significant difference between CD4+/TNF-a and CD8+/TNF-a in HAM/TSP patients?

5. The authors discussed that IFN-g producing cells switch mainly from CD4 cells to CD8 cells during the development to HAM/TSP from the carrier state. However, in figure 3C, it seems that the frequencies of IFN-g producing cells are higher in the CD8 cell population than in the CD4 cell population both in patients with HAM/TSP and the carriers. How did they arrive at that conclusion?

Minor Compulsory Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

What next?: Accept after discretionary revisions
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests: None