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: 1 December 2003

Reviewer: Joseph Urban

Reviewer's report:

General

Discretionary Revisions (which the author can choose to ignore)

The authors have been able to identify segregating immunological factors from a group of patients with Human T cell Leukemia Virus type-1 (HTLV-1)-associated myelopathy/tropical spastic paraparesis (HAM/TSP) from the common pool of asymptomatic carriers of HTLV-1. The key observations are an increase in the spontaneously level of lymphocyte proliferation in vitro of HAM/TSP patients, higher frequencies of cells synthesizing IFN-g and TNF-a that are mainly represented in the set of CD8+ T cells, and an increase frequency of CD28-/CD8+ T cells. The study suggests that these markers may be useful for identifying patients that may move from asymptomatic HTLV-1 carriers to those that express the symptoms of HAM/TSP. The limitation of the study is in the details of patient selection for the various assays that were run and the reproducibility of the observations. This study provides an important advance in the identification possible markers for HAM/TSP.

Specific criticisms:

The original study population included 17 patients described with HAM/TSP and 36 as HTLV-1 asymptomatic carriers. Various subsets of this population pool are selected for different data presentations, but it is not clear how and why certain patients were excluded. The spontaneous proliferation data was described for 10 HAM/TSP and 11 asymptomatic HTLV-1 patients; the IFN-g synthesis data for 14 HAM/TSP and 36 asymptomatic HTLV-1; the intracytoplasmic staining for cytokines and cell surface phenotype analysis were done on 4 HAM/TSP patients and 8 HTLV-1 asymptomatic carriers. This last observation is particularly novel and should have been replicated or conducted with a greater sample size to substantiate the data.

The data presented in Figure 2 uses a population of 40% of the HTLV-1 patients in the study that express a high IFN-g level of production comparable to HAM/STP patients for longitudinal analysis of IFN-g production over an eight month period. Firstly, the criteria for the selection of high IFN-g producers should be better defined since it is a key component of the analysis (details should be expanded from the description in reference #22) and, secondly, the choice of an eight-month interval for evaluation should be justified.

Where technical limitations the explanation for examining IL-5 expression in figure 1 and IL-4 in data generated for figure 3 or was this only to use signature type 2 cytokines to contrast the level of type 1 cytokine expression?

What are the current therapeutic options that would be suggested from the definition of markers of HAM/TSP within the population of asymptomatic HTLV-1 carriers that are alluded to in the last line of
the manuscript?

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

The acronyms for HTLV-1 and HAM/TSP should be spelled out in the title or at least in the abstract. In the current context, the description of these disease conditions do not appear until the Background section and are not included as a full description even in the Key words section; this information should be provided.

There are a few syntax errors in the manuscript. [that] should be included after “to” on line 4 of page 3; [has] should substitute for “have” on line 17 of page 4; and [alpha] should be substituted for “alfa” on line 10 of page 7

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

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:

None