Reviewer's report

Title: CNS Activity Of Pokeweed Anti-Viral Protein (PAP) In Mice Infected With Lymphocytic Choriomeningitis Virus (LCMV)

Version: 1 Date: 6 October 2004

Reviewer: Daniel Bausch

Reviewer's report:

General: Although this manuscript offers some useful information, some revision and more elaborate discussion of a few key points are necessary before publication can be recommended.

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

The results of the study are fairly clear, but the “Discussion” section fails to address various pertinent issues. The following should be addressed:

1) A very vigorous dosing regimen was employed in the study, including two pre- and four post-challenge doses. Do the authors think that they would get the same favorable results if the PAP was given only post-challenge?

2) The authors are encouraged by the possibility that PAP appears to have activity in the CNS. However, the blood-brain barrier was breached by the intracerebral administration of the challenge dose, potentially artificially facilitating PAP’s penetration into the CNS. Is there data on PAP’s normal penetration into the CNS?

3) The authors are encouraged by the results of their study and the possibility that PAP may be useful for HIV infections involving the CNS. However, LCMV infections primarily infect the leptomeninges and ependyma, whereas HIV may entail true neuronal involvement.

4) The study does not demonstrate definitive anti-LCMV activity of PAP. The pathogenesis of LCMV infections in some mouse models is immune mediated. Is it possible that PAP is acting via immunomodulatory effects rather than direct anti-viral activity?

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 manuscript should be revised for various errors in format and grammar, including:

1) The “Results” section of the abstract contains no data, only stated conclusions. Please correct.

2) The “Methods” section does not mention how many animals were used. In addition, as the effects of LCMV on mice can be age-dependent, the age of the animals should be included.

3) There is significant repetition throughout the body of the manuscript. For example, there is no need to again state the dosing schedule, in the first paragraph of the “Results” section when it appears, appropriately, just above in the “Methods” section. Various other similar repetitions can be
found.

4) Once the abbreviation “LCMV” for “lymphocytic choriomeningitis virus” is defined, the authors should simply use “LCMV,” without writing out the long version of the virus name each use.

5) Please correct the typo on the bottom of page 2 which I presume should be “anti-HIV” rather than “anti-HVI”.

6) On pages 5 and 6 the word “invaluable” is incorrectly used to mean “not able to be evaluated.” Please correct.

7) On the top of page 3 it is stated that pokeweed has had “clinical use.” This is usually taken to imply use in humans, but the cited reference pertains to mice. I recommend that the authors amend the sentence to read “…clinical use of PAP in mice. [2]”.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory 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