Reviewer's report

Title: Cerebrospinal fluid CXCL13 in Lyme neuroborreliosis and asymptomatic HIV infection

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Reviewer: Kenneth Tyler

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The observation that CSF CXCL13 levels are elevated in CSF of its with Lyme neuroborreliosis has been prorated repeatedly by other groups and is not novel. The most important, and novel, components of this manuscript relate to data on the effects of doxycycline Rx on CSF CXCL13 in Lyme NB, and the data on CSF levels in HIV-1 infection.

(1) To be honest the data regarding the cross-sectional study of CSF CXCL13 in untreated Lyme NB is neither novel nor particularly informative. It simply confirms what has repeatedly been found by others. The critical and interesting data is that dealing with the 25 pt longitudinal study pre- and post-Rx and this should be the focus.

(2) The second novel piece is the data concerning HIV-1 infected pts. As noted by the authors there was a significant difference in CSF mononuclear cell counts between LNB and HIV infected individuals and controls. Given this difference it would be critical to better understand the correlation in these three groups between CSF CXCL13 levels and CSF cell count (both total and more particularly in terms of the B-cell subset and associated potential markers (IgG, IgG synthesis). Several studies (e.g. Kowarik et al. J Neuroinflamm) have shown that CXCL13 facilitates B cell recruitment into CSF.

(3) The authors understate what it is now unequivocally clear- there is nothing specific about CXCL13 in CSF and either Lyme or spirochetal infection- there are now several papers showing elevations in both inflammatory non-infectious conditions (NMO, MS) and a variety of infections that are non-spirochetal (as diverse as trypanosomiasis and tick-borne encephalitis virus)- they really need to make this point very clear- it is NOT something novel they have discovered. What they have found with HIV is simply "yet another example".

(4) Suggest addition of a 'best fit' regression line to Figure 3 with appropriate statistics? Please show similar data for CXCL13 and cell count in the cross-sectional study subgroups with appropriate statistics. Please use more informative (e.g. box whisker plot) graphics for showing CSF CXCL13 in Figure 1 (you can keep individual data points but superimpose a more instructive analysis)

(5) Given the enormous inter-study cutoff variability as relates to sensitivity and specificity in essentially each study reported to date, do the authors actually think there is anything special about their analysis? It clearly can't and won't be
accepted outside their testing lab, as every group gets a totally different set of values- (this is covered in last paragraph of discussion, but the more global point of the massive inter-institutional variability essentially makes this test pretty worthless diagnostically unless an institution wants to develop their own standardization and ranges...) They never really address whether addition of this to say mononuclear cell count adds additional potential diagnostic sensitivity or specificity? If all this does is correlate with say total mononuclear cell count, or B cells, or IgG- what does it really add?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

No competing interests