Reviewer's report

Title: Epstein-Barr virus infection and clinical outcome in breast cancer patients correlate with immune cell TNF-alpha/IFN-gamma response

Version: 3 Date: 21 June 2014

Reviewer: Tse-Ching Chen

Reviewer's report:

Authors prospectively study the effect of EBV infection on the survival of patients with breast cancers. The study revealed that EBV detection in tumor/PBMCs was not correlated with tumor characteristics. However, patients with anti-ZEBRA antibodies at high titers had worse overall survival. Patients, recovered from the cancer, had a measurable latent form of EBV DNA load and with a high frequency of IFN-# and TNF-# producing peripheral blood mononuclear cells (PBMCs). The survival advantage in BC patients might be through activation of non-specific anti-tumoral immune responses.

The study on the role of EBV on breast cancer is interesting. Major comments are as follows.

1. Latent form of EBV infection had abundant EBER. EBER in situ hybridization is recommended to demonstrate EBV infection on the tumor cells rather than in non-tumoral cells.

2. Authors found a high frequency of IFN-# and TNF-# producing PBMCs in BC patients with EBV infection and recovered from the disease, and jumped into a conclusion “The survival advantage in BC patients might be through activation of non-specific anti-tumoral immune responses” A gap was still present between the finding and the conclusion. It was necessary to realize tumor specific and EBV specific immune response in the EBV-infected BC patients. Therefore, PBMCs should be stimulated at least by dominant tumor antigens and EBV antigens in addition to non-specific stimulation with iono/PMA.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.