

Letter to the Editor

Reply: Is Epstein–Barr virus associated with aggressive forms of breast cancer?

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Sir,

We thank Khan *et al* (2011) for their valuable and insightful comments on our study (Mazouni *et al*, 2011) expounded in their Letter to the Editor (Khan *et al*, 2011).

In our initial publication, we demonstrated the presence of the Epstein–Barr virus (EBV) in malignant breast tumours, which is consistent with findings in previous international publications (Fina *et al*, 2001). In the paper, they are referring to, we observed the same positivity rate as previously noted using a more precise PCR technology. Khan *et al* (2011) suggest that the positivity findings in BC specimens may have been biased by EBV-infected lymphocytes. As mentioned in our paper, our aim was to ascertain the presence of EBV in epithelial cells by isolating these cells using laser microdissection capture (LMC) (Mazouni *et al*, 2011). A large amount of tissue (100 mg) was used to extract DNA from our specimens and this might explain why EBV was detected at a higher frequency than in other studies. In their study, Khan *et al* (2010) did not perform LMC to ensure the validity of epithelial cell positivity.

Besides, another valuable criticism leveled by Khan *et al* (2010) concerns the controversial association between EBV and BC. Other retroviruses have been reported to induce BC. In a previous report, Berebbi *et al* (1990) induced the development of BC in an experimental model by modulating the presence of the polyoma virus during the development of the mammary gland. Moreover, the relationship between EBV and BC has been suggested in an epidemiological study (Yasui *et al*, 2001).

The aggressive profile of EBV-positive BC that we observed has previously been reported in other series (Bonnet *et al*, 1999; Murray *et al*, 2003). Moreover, the differentiation markers evaluated in the breast specimens are associated with the epithelial component.

Finally, we agree that EBV is a ubiquitous infection that makes the physiopathology of BC development difficult to explain. There is still a long road ahead in the field of virus-related cancer before we will be able to formally assess their role and propose prevention.

REFERENCES

- Berebbi M, Martin PM, Berthois Y, Bernard AM, Blangy D (1990) Estradiol dependence of the specific mammary tissue targeting of polyoma virus oncogenicity in nude mice. *Oncogene* 5(4): 505–509
- Bonnet M, Guinebretiere JM, Kremmer E, Grunewald V, Benhamou E, Contesso G, Joab I (1999) Detection of Epstein-Barr virus in invasive breast cancers. *J Natl Cancer Inst* 91: 1376–1381
- Fina F, Romain S, Ouafik L, Palmari J, Ben Ayed F, Benharkat S, Bonnier P, Spyrtos F, Foekens JA, Rose C, Buisson M, Gérard H, Reymond MO, Seigneurin JM, Martin PM (2001) Frequency and genome load of Epstein-Barr virus in 509 breast cancers from different geographical areas. *Br J Cancer* 84(6): 783–790
- Khan G, Philip PS, Al Ashari M (2011) Is Epstein-Barr virus associated with aggressive forms of breast cancer? *Br J Cancer* 104: 1362–1363
- Mazouni C, Fina F, Romain S, Ouafik L, Bonnier P, Brandone JM, Martin PM (2011) Epstein-Barr virus as a marker of biological aggressiveness in breast cancer. *Br J Cancer* 104(2): 332–337
- Murray PG, Lissauer D, Junying J, Davies G, Moore S, Bell A, Timms J, Rowlands D, McConkey C, Reynolds GM, Ghataura S, England D, Carroll R, Young LS (2003) Reactivity with a monoclonal antibody to Epstein-Barr virus (EBV) nuclear antigen 1 defines a subset of aggressive breast cancers in the absence of the EBV genome. *Cancer Res* 63: 2338–2343
- Yasui Y, Potter JD, Stanford JL, Rossing MA, Winget MD, Bronner M, Daling J (2001) Breast cancer risk and 'delayed' primary Epstein-Barr virus infection. *Cancer Epidemiol Biomarkers Prev* 10: 9–16