Letter

Lack of evidence for an association of Epstein–Barr virus infection with breast carcinoma – authors' response

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Introduction

In her letter, recently published in *Breast Cancer Research*, María Victoria Preciado points out that some published evidence suggests a possible association of breast cancer with Epstein–Barr virus (EBV) [1]. EBV DNA has been detected by PCR in up to 50% of cases (for a review see [2]), and expression of the EBV-encoded nuclear antigen EBNA1 has been demonstrated in approximately 40% of cases by immunohistochemistry using the mAb designated 2B4 [3]. In combination, these findings seem to implicate EBV in the pathogenesis of breast carcinoma. Interestingly, however, most investigators agree that the EBV-encoded RNAs (EBERs), a hallmark of latent EBV infection, are not detectable in breast carcinoma tumour cells [2].

In two independent studies, we have analysed breast carcinomas for evidence of EBV infection [4,5]. In whole tissue sections, EBV DNA was detectable by quantitative PCR in up to 21% of cases at low copy number [5]. However, this does not allow conclusions regarding the cellular source of the viral DNA. We therefore attempted to detect viral DNA directly in the neoplastic cells using a sensitive DNA *in situ* hybridisation assay [4] or using quantitative PCR of microdissected tumour cells [5]. These studies yielded negative results [4,5]. In support of these results, *in situ* hybridisation for the detection of the EBERs was also negative in all cases while occasional EBV-positive non-neoplastic lymphocytes were detected by this approach [4]. The latter finding explains the detection of EBV DNA in whole tumour sections by PCR.

There remains the issue of reactivity of breast carcinoma cells with the EBNA1-specific mAb 2B4. We have previously reported that this mAb yields nuclear labelling not only of EBV-infected cells, but also of some EBV-negative cells, notably epithelial cells [6]. We therefore recommended the use of another EBNA1-specific mAb, 1H4, when studying epithelial tumours [6]. In one of our recent studies, 31% of breast cancers, including cases that had tested negative for EBV genomes by PCR of microdissected tumour cells, showed nuclear labelling of tumour cells with the 2B4 mAb [5]. However, no labelling of tumour cells was observed with both mAbs in the other study [4]. The discrepancy between these results may relate to technical differences (e.g. fixation of tissues or antigen retrieval).

We thus conclude that EBV is not present in tumour cells of breast carcinomas. The reactivity of tumour cell nuclei with the EBNA1-specific mAb 2B4 is likely to be the result of cross-reactivity with an unrelated epitope. There is currently no evidence that breast carcinoma is an EBV-associated malignancy.

Competing interests

None declared.

References

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EBER = EBV-encoded RNAs; EBV = Epstein–Barr virus; mAb = monoclonal antibody; PCR = polymerase chain reaction.