Letter

Lack of evidence for an association of Epstein–Barr virus infection with breast carcinoma – another point of view

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Herrmann and Niedobitek have recently ruled out the involvement of Epstein–Barr virus (EBV) in the pathogenesis of breast carcinomas [1]. They looked for EBNA-1 (EBV nuclear antigen 1) and EBER (EBV-encoded small RNA) in 59 breast carcinoma biopsies. They stated that because the available antibodies to detect EBNA-1 usually produce only weak staining, a lack of EBNA-1 expression could not be taken as proof that the virus was absent and, besides, that this antibody could also cross-react with other proteins. Interestingly, they failed to find either specific or nonspecific staining among the 59 cases studied, and concluded that EBV was absent [1].

However, we observed nuclear granular EBNA-1 staining in tumor epithelial cells in paraffin-embedded sections from 14/33 American women with breast carcinoma [2] and 24/69 Argentine ones (data not published), while normal cells (including lymphocytes) were negative for EBNA-1 in all the analyzed cases. Thus, in our own experience and that reported by other authors, the anti-EBNA-1 2B-4 monoclonal antibody reacted specifically in EBV$^+$ tumor epithelial cells [3].

Herrmann and Niedobitek also detected EBV DNA by PCR in paraffin-embedded breast carcinoma biopsies, but they assumed that it was probably related to the presence of EBV-infected lymphocytes in tumor stroma [1]. However, authors of previous studies have reported 21% [4], 51% [3], and 32% [5] of EBV+ breast cancers with various grades of infiltrating lymphocytes identified by *Bam*HIW PCR. We confirmed our positive EBNA-1 results by PCR in 24/69 patients from whom DNA of good quality was also available, detecting amplification fragments of 122 bp from the *Bam*HIW region and 108 bp from the EBER region. No amplification product for EBV was detected, by either *Bam*HIW PCR or EBER PCR, in 30 biopsies of benign breast tumors with no atypia, 8 normal breast tissues, and 45 EBNA-1– breast carcinomas with low, moderate, or high degrees of lymphoplasmocytic infiltration (data not published). Since bystander lymphocytes of the stroma were EBNA-1–, it could be assumed that the cellular source of the PCR EBV signal was the epithelial tumor cells. This hypothesis is supported by the findings of Fina and colleagues, who showed EBV genome localization in specific tumor epithelial cell population of breast carcinoma by laser capture microdissection combined with real-time quantitative *Bam*HIC PCR [5].

In view of the above data, the evidence regarding a possible association of EBV with breast carcinoma is controversial and there are many facts to support arguments both against and in favor of this hypothesis.

Competing interests

None declared.

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bp = base pairs; EBER = EBV-encoded small RNA; EBNA-1 = EBV nuclear antigen 1; EBV = Epstein–Barr virus; PCR = polymerase chain reaction.