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LETTER TO THE EDITOR

Immunohistochemistry for BAG3 in cervical precancerous lesions

Sir,

We thank Kudela and colleagues for their interest in our study.[1,2] The low reproducibility in the diagnosis of cervical squamous intraepithelial lesions (SILs) is a well-known issue, and there are currently no highly reliable markers to support it. On this account, the strict correlation we found between Bcl-2-associated athanogene 3 (BAG3) expression and the grade of dysplasia in SIL specimens appears very promising.[2] Such an accurate marker may significantly improve the management of patients, which is determined by the presence and the grade of intraepithelial dysplasia.[2] As Kudela et al pointed out, although immunohistochemistry is affected by subjectivity, the assessment of the localization of BAG3 expression (ie, cytoplasmic vs nuclear expression) might be more reproducible than the evaluation of intensity of staining.[1,3,4] Moreover, immunohistochemistry shows several advantages that make it easy to be used in the common practice: it is fast, inexpensive and widespread.[2] Of course, the sample size of our study (n = 40) is adequate for a preliminary study, but larger series are necessary to confirm and validate the diagnostic role of BAG3 in SILs.

As remarked by Kudela et al, BAG3 might also have a prognostic role, based on the intensity and localization of its expression. Indeed, we can hypothesize that low-grade SILs (L-SILs) with strong nuclear BAG3 expression may actually be true precancerous lesions which tend to progress to high-grade SILs (H-SILs) and carcinoma. On the other hand, H-SILs with weak cytoplasmic expression might tend to regress, as suggested by Kudela et al. Alternatively, they might also be lesions with slower progression to cancer. Such a prognostic value of BAG3 would be even more clinically useful than its diagnostic value, as it would directly affect the management of patients. However, given the lack of follow-up data in our series, these considerations are merely speculative and we hope to investigate this point further in future studies.

It would be interesting to assess SIL specimens through a multi-omics approach, as proposed by Kudela et al. Although the costs and expertise required for multi-omics techniques would preclude the routine use of such an approach, it might have a strong value for a better definition of the pathogenetic, diagnostic and prognostic role of BAG3 in cervical SILs. In the last few years, medicine is moving ever more towards a precise and tailored approach.[5] In this field, multi-omics techniques appear crucial.

Based on the interesting preliminary results for BAG3 immunohistochemistry in cervical SILs, we are studying this marker in further and larger series to confirm its diagnostic and prognostic value.

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