Reviewer's report

Title: An association of a simultaneous nuclear and cytoplasmic localization of Fra-1 with breast malignancy

Version: 1 Date: 18 October 2006

Reviewer: Dany Chalbos

Reviewer's report:

General
Whereas several in vitro studies have reported a role of Fra-1 in cell transformation and suggested its implication in breast cancer progression there is presently very few data on the evaluation of the interest of Fra-1 expression as a diagnostic or prognostic marker in human cancers. Investigation of Fra-1 expression in breast carcinomas and benign breast diseases is therefore important. The authors report that Fra-1 presence of cytoplasmic Fra-1 is associated with breast malignancy. However I am not convinced that the evidence justifies this conclusion.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
When figure 1 is compared to figures 2 and 3 the major observed difference between benign and malignant tissues is the percentage of stained nuclei. Immunostaining excepted in figure 2B appears mostly nuclear. It is not obvious that cytoplasmic staining is weak in figure 2B and strong in figure 2C and that cytoplasmic staining is higher in fig 3B (cancer) than in figure 1D (fibroadenoma).

In text, the authors state that a strong nuclear staining is evident in all breast cancers (100% or more than 75% positive cells). This is contradictory with table 2 in which 11/41 cancer biopsies are reported to have a low nuclear staining score (less than 75 % positive cells).
Other contradiction: in text, “a cytoplasmic staining is easily observed in 78 % of breast cancers” whereas in the same table 90 % of cancers were reported to have a low or high cytoplasmic Fra-1 expression.
Finally, in table 2, 37/41 breast cancer have a positive Fra-1 staining whereas in table 3 only 32/41 cancer have a positive cytoplasmic Fra-1 expression.

In figure 1A, is the control done in the absence of primary antibody or with non specific immunoglobulin?. It will be important to perform other controls to test the specificity of Fra-1 antibodies (extinction by Fra-1 protein or peptide, analysis in western blot)?

Has an anatopathological analysis of slides been done?

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
The leucine-zipper region is not implicated in DNA binding.
The manuscript should be easily edited for conciseness without lost of information

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Discretionary Revisions (which the author can choose to ignore)

What next?: Reject because too small an advance to publish

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No

Declaration of competing interests:
The reviewer works on Fra-1.