Reviewer's report

Title: Early diagnostic value of Bcl-3 localization in colorectal cancer

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Reviewer: alain Chariot

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In the paper entitled «Early diagnostic value of BCL-3 localization in colorectal cancer», the authors report the finding that the oncogenic protein BCL-3 is overexpressed in human cases of colon cancer and show a cytoplasmic localization that correlates with the proliferative marker Ki-67. Such cytoplasmic localization is also seen in some established colon cancer cell lines. This study reports a quite unexpected finding, given the previously described nuclear localization of BCL-3 in solid and haematological malignancies. The illustrated data are convincing and provide evidence for an unique localization of BCL-3 in transformed intestinal epithelial cells. The authors actually provided some key insights on mechanisms by which the nuclear important of BCL-3 is regulated and they may want to consider the following point to improve the mechanistic part of their study.

1. Some breast cancer cell lines (MCF7, …) show elevated levels of BCL-3. The authors could use them as a control for nuclear localization of BCL-3. The goal would then be to see whether this cytoplasmic localization of BCL-3 is specific to transformed intestinal epithelial cells.

2. The authors previously showed that TPA triggers the nuclear localization of BCL-3 in keratinocytes. What is happening if they treat CACO-2 and HCT116 cells with TPA? Do they trigger the nuclear important of BCL-3? The goal would be to see whether the signaling pathway known to trigger BCL-3 nuclear import is specifically disrupted in colon cancer cells.

3. All tested colon cancer-derived cell lines show constitutive Wnt signaling due to #beta-catenin or Apc mutations. The RKO cell line does not show constitutive Wnt signaling. Therefore, it would be interesting to see whether BCL-3 expression is enhanced and if so, whether BCL-3 is also found in the cytoplasm of those cells. Similarly, does TPA trigger the nuclear import of BCL-3 (assuming that it is detectable)?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: 
No competing interests