Reviewer's report

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

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Reviewer: Ruaidhri J. Carmody

Reviewer's report:

The report by Saamarthy et al. describes their initial observation that in freshly isolated colon cancer tumour tissue the NF-κB regulatory protein Bcl-3 accumulates in the cytoplasm. This is contrast to the nuclear localisation of Bcl-3 in the cells of normal colonic tissue. The authors extend their analysis of Bcl-3 localisation to 270 colonic cancer tissue samples and 70 normal tissue samples. Their findings demonstrate that greater than 90% of normal tissue samples show a predominant nuclear localisation of Bcl-3 while the majority of the cancer tissue samples showed a predominant cytoplasmic localisation. Cytoplasmic Bcl-3 was associated with tumour stage and the proliferation marker Ki67 but not caspase-3 positive cells. The findings are an important contribution to the association of Bcl-3 with cancer and suggest that subcellular distribution of Bcl-3 may be more important than total levels of Bcl-3 protein. In addition the findings suggest that cytoplasmic Bcl-3 may be an early diagnostic marker of colorectal cancer. The study is well written and the data supports the conclusions. I only have minor comments as follow:

1. The authors stain for caspase-3 (Figure 4) which they use as a proxy for cell death. I am presuming that the antibody is specific for active caspase-3 rather than total caspase-3. The authors need to clarify this and provide specific details for the antibody used including supplier, clone and catalogue number.

2. Anti-bodies against Bcl-3 have been notoriously unreliable and so the use of the Bcl-3 blocking peptide in Figure 1 is welcome. However, the authors need to provide more details on the antibody used in this study including the clone and catalogue number.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.