Reviewer's report

Title: Tumour Selective Nuclear Targeting In A Tumour Progression Model

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Reviewer: Jose Teodoro

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The manuscript by Nastasie et al presents the properties of chimeric proteins in which the nuclear targeting sequence (NTS) of the Chicken Anemia Virus VP3 protein (Apoptin) have been fused to the nuclear proteins H2B and H3. The NTS of apoptin has been suggested to act in a tumour specific manner and to augment the nuclear accumulation of apoptin in transformed cells. In this study, the NTS of apoptin is fused to bona fide nuclear proteins (histones) and the ability of the NTS to alter the localization in cell systems mimicking transformed and non-transformed states has been examined. I have the following comments regarding the manuscript.

Major compulsory revisions

1. In general, the experiments have been performed and quantitated carefully and the data certainly supports that argument that the NTS of apoptin can slightly alter the localization of the histones in a transformed cell-specific manner. However, the language used in the title “transformed selective nuclear targeting” suggests there are black and white differences in localization between the localization of NTS-fused histones in transformed and non-transformed cells. The differences are in fact quite subtle and only apparent after careful quantitation. All the fusion proteins presented display strong nuclear localization with the NTS fused proteins showing slight cytoplasmic retention in non-transformed cells. I would suggest the language in the title and main text be toned down to reflect the subtlety of the observations.

2. In the final experiments showing direct transduction of the fusion proteins, the images are of much lower magnification that those in earlier figures. Moreover, the localization appears much different than in transfected proteins with more punctate and possibly cytoplasmic foci. It is difficult to tell from the images in figure 5 if the protein is behaving as expected. Higher magnification images should be provided or other evidence (as suggested in point 3 below).

Minor essential revisions

3. The authors should consider adding a biochemical experiment in which nuclear and cytoplasmic extracts are analyzed by western blot to determine the % of total protein that is present in the nucleus in the transformed and non-transformed states.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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