Reviewer's report

Title: Nuclear expression of Rac1 in cervical premalignant lesions and cervical cancer cells: implications for cell proliferation

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Reviewer: Margaret E McLaughlin-Drubin

Reviewer's report:

The expression of some Rho-GTPases is altered in a number of human cancers. Specifically, RhoC regulates invasion and motility of cervical cancer cells. Moreover, RhoC is over-expressed in biopsies from squamous carcinoma of the cervix (SCC) and cervical intraepithelial neoplasia (CIN) II/III when compared to normal cervical epithelium and CIN I. However, expression of additional Rho-GTPases has not been investigated in cervical cancer or its precursor lesion. The authors of “Nuclear expression of Rac1 in cervical premalignant lesions and cervical cancer cells: implications for cell proliferation” have investigated the expression of the GTPases Rac1, RhoA, Cdc42, and the Rho-GEFs Tiam1 and beta-Pix in cervical pre-malignant lesions and cervical cancer cell lines and found that immunoreactivity for Rac1, RhoA, Tiam1, and beta-Pix was significantly associated with the histological diagnosis. Moreover, they conclude that Rac1 is expressed in the nucleus of epithelial cells in SILs and cervical cancer cell lines, and chemical inhibition of Rac1 reduces cellular proliferation.

Major Compulsory Revisions:

1) The authors of J Cell Biol. 2008 May 5;181(3):485-96. Epub 2008 Apr 28. Rac1 accumulates in the nucleus during the G2 phase of the cell cycle and promotes cell division conclude that none of the commercially available antibodies reliably reports the subcellular localization of endogenous Rac1 in fixed cells. Given this major limitation, the authors should perform subcellular fractionation and western blotting to determine the localization of Rac1.

2) HaCaTs (or preferably a normal cell type) should be treated with the Rac1 inhibitor to determine if the observations are merely a general effect of the inhibitor.

3) The authors of British Journal of Cancer (2011) 104, 324–331. doi:10.1038/sj.bjc.6606026 www.bjcancer.com Published online 7 December 2010 The HPV16 E6 binding protein Tip-1 interacts with ARHGEF16, which activates Cdc42 found that cells expressing HPV16 E6 had higher levels of Cdc42 activation. Is it possible that the overall expression levels of the GTPases and Rho-GEFs might not change while the activation level does change? This should be experimentally addressed.
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.