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:** Luis F. Jave-Suarez

**Reviewer's report:**

In this work Mendoza-Catalán and col. evaluated the expression of RAC1, RHOA, CDC42, TIAM1 and Beta-PIX in 20 cervical samples of women without lesions and 82 samples of patients with premalignant lesions (L-SIL and H-SIL). Additionally, they look for the expression of RAC1 in cervical cancer cell lines (SiHa and C33).

Interestingly, overexpression of RAC1, TIAM1, RHOA and Beta-PIX were preferentially detected in samples of patients with L-SIL and H-SIL, the incidence rate being higher than that in samples without SIL. In addition, blocking of RAC1 was associated with decreased proliferation of cancer derived cervical cell lines.

Despite of the interesting data that the authors shown, there are some points that need to be addressed.

**Major compulsory revisions**

Is the overexpression of RAC and TIAM1 also observed in cervical derived cell lines compared with control cells? Authors could address this question by utilizing westernblot assays.

The nuclear localization of RAC1 in SiHa cells described by the authors is unclear. Authors should demonstrate the nuclear localization of RAC1 in cell lines (HaCat, SiHa and C33) by westernblot.

The most important event during the development of cervical cancer is the infection with HPV, in this regard, overexpression of Rho-GTPases and RhoGEFs should to be a posterior event induced or not by the HPV oncoproteins. The authors demonstrate the overexpression of RAC, TIAM1, RHOA and Beta-PIX, but did not observe a relation with HPV infection. However, they only looked for infection with high risk –HPVs. It is adventurous to conclude that HPV infection doesn’t play any role in the overexpression of these proteins. If that is true, what are the mechanisms that are inducing the overexpression of these proteins in L-SIL and H-SIL?

How the authors could demonstrate that HPV oncoproteins are not playing a role in the expression of Rho-GTPases and RhoGEFs?. If HaCaT cells express low levels of RAC1, what would happen with RAC1 if the expression of E6 or E7 is induced in these cells?

HaCaT cells are non-tumorigenic, however, the exogenous expression of HPV16 E6 protein turn these cells into tumorigenic. Would induce the overexpression of
RAC1 the same effect in these cells?
How explain the authors, why some samples without SIL showed moderate to strong immunoreactivity?

Discretionary Revisions
Are the samples with RAC1 overexpression the same that those with TIAM1 overexpression? ... Are these events related?

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.

Declaration of competing interests:
I declare that I have no competing interests