Reviewer’s report

Title: Knocking down CDK4 mediates the elevation of let-7c suppressing cell growth in nasopharyngeal carcinoma

Version: 2 Date: 11 October 2013

Reviewer: Konstantinos Mavridis

Reviewer’s report:

The authors have answered the majority of the criticisms raised by the reviewers. In two cases, i.e. i) assessment of let-7c expression in all NPC tissues and ii) proof whether E2F1 binds to the promoter of let-7c) the authors could not fulfill the reviewers’ suggestions, but provided reasonable explanations for doing so. Nonetheless, few additional issues, which need to be addressed before this article is suitable enough for publication, have arisen from the authors’ responses. These issues are described below:

Major Compulsory Revisions

1. The authors have included T classification, N classification, M classification and at the same time TNM stage at their multivariate logistic regression models. By definition, these variables are bound to present significant correlations between them. It is known that this approach introduces collinearity and multicollinearity in the regression models and can seriously affect the interpretation of a model. I suggest that the authors include the TNM stage variable instead of separately including T classification, N classification and M classification.

2. Taking into consideration that radiotherapy-treated patients present a statistically significant difference in overall survival, the authors should proceed with subgroup survival analysis in radiotherapy treated and non-treated subgroups of patients, with the perquisite that the sample size for these subgroups is adequate.

3. The treatment plans that were followed should be described. The numbers of radiotherapy and chemotherapy treated patients should be included in the clinicopathologic characteristics table (Table 2).

Minor Essential Revisions

1. It should be made clear throughout the manuscript that let-7c expression analysis was made in fresh NPC and NP samples and not in the FFPE tissues.

2. In order to use the “2 –##Ct” method for the calculation of gene expression the same sample, usually referred to as the “calibrator” should be included in each run, in order to be used for normalizing the expression units of samples assessed in different runs/plates. It is not clear wether this approach has been followed here. Did the “the sample with the maximal #Ct value” play the role of the calibrator by being included in each run? Also, “2 –##Ct” should be corrected to “2 –##Ct”.
Discretionary Revisions
None

**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.