Reviewer’s report

Title: Increased IR-A/IR-B Ratio in Non-small Cell Lung Cancers Associates with Lower Epithelial-Mesenchymal Transition Signature and Longer Survival in Squamous Cell Lung Carcinoma

Version: 1 Date: 16 August 2013

Reviewer: Roger Moorehead

Reviewer’s report:

The article submitted by Jiang et al describes the expression of IR-A and IR-B in lung cancer tissue. This manuscript shows that the expression of IR-B is reduced in NSCLC and this leads to an increase in the IR-A/IR-B ratio in NSCLC. Patients with a high IR-A/IR-B ratio showed significantly better survival than patients with a low IR-A/IR-B ratio. Although I found the manuscript interesting and reasonably well written I do have some suggested revisions.

Minor Revisions
1. Abstract, line 9, sentence starting with “Notably…” needs to be modified with correct grammar

2. The authors should keep the color-coding consistent in the panels of Figure 2 (ie use red for all LUAD samples)

3. In the results the ECM gene signature is referred to as Figure 4C and the EMT gene signature as Figure 4B however in Figure 4, panel B refers to ECM and panel C refers to EMT

Major Revisions
1. I think the authors should explain why IGF-IR expression was not evaluated in this study as there may be some interesting correlations between IGF-IR expression and IR expression. If IGF-IR expression has already been evaluated in these samples, this information should be provided and discussed.

2. Since the article is trying to relate the expression of IR-A, IR-B and the IR-A/IR-B ratio to the ineffectiveness of anti-IGFIR therapy in lung cancer, it would have been more useful to measure the levels of IR-A and IR-B in patients that either responded or did not respond to anti-IGFIR therapy. The levels in IR-A and IR-B in lung cancer and their association with prognosis is very interesting but there is no data linking the susceptibility of individuals with different IR expression to their response to anti-IGFIR therapy. If data linking IR and IGF-IR is not provided, I think the manuscript needs to be re-written to simply focus on the importance IR expression (ie remove paragraph in introduction and discussion talking about resistance to anti-IGFIR agents). I kept looking for data linking IR expression to IGF-IR therapy resistance.
3. On the bottom of page 14 and top of page 15, the author is trying to correlate the HIR observed in luminal B breast cancer with EMT. I don’t think this is an accurate comparison. The main difference in luminal A and luminal B breast cancers is the higher level of markers associated with proliferation in luminal B breast tumors. Basal-like and claudin-low breast cancers express markers of EMT however luminal A and luminal B tumors primarily express luminal markers. Therefore, the poorer survival of patients with luminal B tumors compared to those with luminal A tumors in not typically associated with EMT.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

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