Reviewer's report

Title: Autoantibodies to Tumor Associated Antigens as Early Detection Biomarkers for Lung Cancer or Noncalcified Nodules

Version: 2 Date: 15 December 2009

Reviewer: Caroline Chapman

Reviewer's report:

1. Many of the comments to the referees need adding into the text of the paper and are not.
   The revised manuscript for instance does not state ELISA controls etc - despite assurances in the letter. This needs addressing.
   Cut off used, western analyses etc etc are not included in the paper.
   Material and methods do not state if the protein is purified using native, or denatured technology or if it was refolded.
   They do not note if they corrected their signal for any background binding – ie subtracted any control to account for Non-specific binding.
   Response to comment 3 states that they address many of these things with a sentence at the bottom of page 8 – but it is not included in the manuscript that I can find.
   “Also see page 8 bottom paragraph, “In every microtiter plate, there were a number of internal controls including a blank, a negative control, one high-positive control and one low-positive control to ensure equivalency of results from one plate to another. The cut-off delineating abnormality was the mean of 36 healthy non-smokers plus 3 standard deviations. In this study, we performed only enzyme immunoassay to detect autoantibodies to TAAs since previous studies with these antigens had shown EIAs at this cut-of level were specific and more sensitive than Western blotting (24, 25, 26).”
   Is not included

2. They state that : Kruskal-Wallis nonparametric analysis of variance Chi Square tests were used to assess the differences in the distributions of individual biomarker measurements by classification group. These analyses were conducted to compare the four groups of lung cancer patients, GGOs, solid nodules, and nodules and for all five groups of subjects including the healthy controls.
   There are not 4 groups of lung cancers.
   This reads badly and should state .................. These analyses were conducted to compare 5 groups which consisted of lung cancer patients, patients with GGOs, solid nodules, and smokers with no nodules as well as healthy non smokers.
3. Point 6 in the original review was only addressed in the response to the reviewer but not in the text. It is not clear if they are ‘at diagnosis samples’. It needs stating that there were 2 advanced SCLC and 20 NSCLC (4 squamous and 16 adenocarcimonas, 4 with advanced disease).

The author need to address the referees comments in the text or state why they cannot.

**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:**

as stated previously