Reviewer's report

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

Version: 1 Date: 1 September 2009

Reviewer: Iver Petersen

Reviewer's report:

General
Rom et al. studied tumor-associated autoantibodies as potential biomarkers for early detection of lung cancer and in particular for the differentiation of patients with CT abnormalities that may be associated with lung cancer. In total 10 recombinant proteins were generated (p53, c-myc, cyclin A, cyclin B1, cyclin D, CDK2, survivin and 3 directed against the insulin-like growth factor 2 mRNA binding protein) to establish an ELISA for autoantibody detection. The ELISA was applied to serum samples from individuals of 5 different groups: lung cancer patients (n=22), patients with no CT nodules (n=35), solid nodules (n=55), ground glass opacities, GGOs (n=46) and finally normal, healthy non-smokers (n=36). The later group of samples originated from the Scripps General Clinical Research Center while the others came from the New York University Lung Cancer Biomarker Center (NYU LCBC).

The results indicate that cancer patients can be separated from the non-cancer patients with a considerable sensitivity and specificity by applying the panel of autoantibodies.

Overall, this is an interesting study. The paper is well written, the data is comprehensively presented in 5 tables and 4 figures.

However, there are some fundamental, methodology related issues that need further clarification and discussion.

Specific
Unfortunately there is no data on the specificity of the recombinant proteins that have been generated for the ELISA. This may be determined by performing Western Blot analysis with commercially available antibodies against these proteins. At least the size of the proteins should be determined for comparison with expected protein size.

There is no data on the concentrations of the autoantibodies in the serum. What are the units provided for the different genes in Figure 1? Are these relative optical densities provided by the ELISA analysis? The values seem to have a considerable variability and overlap between the groups. By looking at these graphs the high p-values of the statistical analysis are astonishing. The authors should provide a judgement of the amount/concentration of the autoantibodies and relative differences between the sera.
In addition, they should provide data on the intra-individual variations when several measurements per serum sample are performed. In addition they should analyze or at least comment on the potential influence of the methodology for serum generation. It is conceivable that this may have a profound impact on the results. The different origin of the sera (New York, Scripps) should be considered in this context.

1. Is the question posed by the authors well defined? yes
2. Are the methods appropriate and well described? yes
3. Are the data sound? not fully judgable.
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? yes.
5. Are the discussion and conclusions well balanced and adequately supported by the data? yes.
6. Are limitations of the work clearly stated? no (see reivew).
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? yes.
8. Do the title and abstract accurately convey what has been found? yes.
9. Is the writing acceptable? yes