Reviewer’s report

Title: Serum p53 antibody detection in patients with impaired lung function

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Reviewer: Virginie Marcel

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The manuscript of Mattioni et al entitled “Serum p53 antibody detection in patients with impaired lung functions”, evaluated the association between detection of p53 antibodies in human serum and smoking status as well as lung impairment, two well known risk factors of lung cancer. Using a series of 675 human serums, they showed a statistical association of p53 antibodies detection with smoking status (i.e. number of cigarettes per days and pack-year) and with high levels of LFT impairment. These data are of interest for future development of early detection/diagnosis of lung cancer.

MAJOR COMMENTS

1- (Table 1) The authors reported that no difference in p53 Ab was observed between group 1 (399 normal people) and group 2 (275 patients with impaired lung function), since in group 2, three groups have been determined (including 2% with mild impairment). However, a difference in sex/smoking habits distribution between the 2 groups can be observed. Is this difference significant? If a significant difference is observed, it would be interesting to adjust p53 Abs detection to sex and/or smoking habits to determine whether a statistical difference exist between normal and cases group in term of p53 Abs detection (results section, paragraph 2, lines 2-4).

2- In addition to statistical analysis of p53 Abs detection on the series of 675 subjects, the authors should investigate whether there is any difference of p53 Abs detection for the 2 different groups (399 normal peoples and the 275 cases) in regard to age, sex, no of cigarettes per days and pack-year. In addition to compare “negative” vs “positive” p53 Abs detection (ie. qualitative detection), it would be important to compare the median p53 Abs levels for each group presented in Table 2, to determine whether quantitative p53 Abs levels is corrrelated to smoking status and/or lung impairment.

3- The ex-smokers have been defined as people that had quit smoking at least 6 months before lung function tests. Is there any benefit of quitting (ie. reduction of p53 Ab throughout time?). If so, the analyses based on number of cigarettes smoked per days and pack-year should also be performed in ‘current smokers only’ or ‘current smokers and recent ex-smokers’.

MINOR COMMENTS

1- Methods complement: Does the cut-off of p53 Abs levels used to determine the positivity, correspond to commercial cut-off or to authors’ experienced-based
cut-off? Is this cut-off accurate to other studies? The authors should give this information. The authors should also indicate that ELISA has a low sensibility for serum antibody detection and that novel and more sensitive methods have been developed.

2- In ELISA detection assays, human recombinant WTP53 protein was used to evaluate p53 Abs in human serum produce by patients over-expressing MT p53 protein, as explained by the authors (background section, lines 5-7). This method is a conventional method for such analysis, however is it possible that p53 Abs produced by patients can only recognise MT p53 conformation and not the one of WT p53, thus introducing false-negative results? Has this method been evaluated by testing conformational p53 antibodies in ELISA assays (ie. PAb 240 specific of MTp53 conformation and PAb 1620 specific of WTp53 conformation)?

3- Methods complement: In which circumstances, and where, subjects have been recruited (ie. hospital, physicians, normal consultation...). This might determine in which extent the 675 subjects come from normal or case population. For the follow-up, nothing is said about development of cancer development different from lung cancer.

3- Table 1: percentage should be given. This table can be clarified by placing side by side the 2 distinct groups in columns.

There are some missing data (Normal LFT – no of cigarettes smoked per days and pack-years = 355 subjects / 357 current and ex-smokers; Impaired LFT – no of cigarettes smoked per days and pack-years = 276 cases / 277 current and ex-smokers), however that did not affect the statistical analyses (Same in table 2, age).

4- Table 2: percentage should be given. Statistical tests used to obtain p-value should be indicated at the bottom for each individual analysis.

5- The authors showed that 2 of 44 non-smokers (4.6%) patients with impaired tests are positive for p53 Abs expression. The authors said that p53 mutation, due to smoke exposure, promotes over-expression of p53 leading to increase in p53 Abs production in serum. How the authors explain that non-smokers are positive for p53 Abs?

6- It would have been interesting to analysed other well-defined markers of lung cancer, such as K-Ras or EGF-R expression by ELISA, or at least mention them in the discussion.

**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.