**Reviewer's report**

**Title:** Combined immunohistochemistry of beta-catenin, cytokeratin 7, and cytokeratin 20 is useful for differential diagnosis between metastatic lung cancer from colorectal cancer and primary lung adenocarcinoma tubular type

**Version:** 1  **Date:** 24 April 2005

**Reviewer:** Tibor Tot

**Reviewer's report:**

**General**

This is an interesting, although not very original manuscript, aiming to provide further evidence for the value of immunophenotyping of lung adenocarcinomas in order to discriminate them from lung metastases of colorectal cancer. The problem is of paramount clinical relevance, the topic has already been a subject of many publications in the current literature. Although dealing with a limited segment of this topic, the manuscript is potentially acceptable for publication, but only after substantial corrections and thorough language editing.

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**Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)**

1. The methodology of the immunostaining and the interpretation of the result is correct. However, the patient groups are small, bordering the limit of an acceptable sample. A single needle biopsy should not be mentioned as a separate category, but should be included into the group of metastasis. Make a comment on the operation statistics on your department; how many lung (and colorectal) operations are performed yearly, which percentage of these lung tumors corresponds to "LAT", how long period is needed to collect 11 such cases ? This may influence the readers to accept 11 cases as a representative sample.

2. "Lung adenocarcinoma of tubular type" has to be introduced by stating the Classification system it belongs to. It would be of value to describe shortly the other subtypes of lung adenocarcinoma and their beta-catenin - CK20/7 phenotype, as there are considerable differences between them. Especially, primary lung adenocarcinomas similar in their CK phenotype to colorectal cancer, have to be discussed.

3. The results are not unexpected, rather surprisingly straightforward. The 100% positivity on beta-catenin among primary and metastatic colorectal carcinomas contrasts to the results of some other studies (e.g. Hugh TJ et al, Int J Cancer 1999;82:504-11, Chiang JM et al Br J Cancer 2002;86:1124-9 or Resnick MB et al Clin Cancer Res 2004;10:3069-75) reporting a reactivity far under 100% in these tumor categories. These differences, which are probably related to the low number of analyzed cases in the present study, have to be included into the Discussion, in addition to the single reference (8) already discussed in the manuscript.

4. A better balance is needed in the Discussion between comparing the own findings with the relevant data from the literature and the molecular pathology details (not a subject of the present study) from references.
4. To mention TTF-1 in the Discussion is correct, but there is no reason for mentioning it in the Conclusions (in fact, it is a serious formal mistake), as expression of this marker was not analyzed in the present study.

5. The illustrations: there is no reason to repeat the illustrations of the staining pattern of metastatic colorectal cancer already shown in Fig 1. Thus, Fig 2 is unnecessary. The illustrated reactions to beta-catenin have a kind of cytoplasmic background stain, also in Figs 1a and 1c.

6. A thorough, preferably external, language editing is mandatory, as minor errors are present throughout the text and there are sentences, which are hard to understand. Even more importantly, the used terminology has to be adopted to the international standards (see the comments below).

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The Title of the manuscript is too long and complicated.

2. "Metastatic lung cancer" is a term inadequately used throughout the text as it means for many of the readers metastases of primary lung carcinoma. Replace it with "lung metastasis of colorectal cancer" or "colorectal cancer metastatic to the lungs".

3. Abbreviations, such as "CK" are well-established in the literature, however, "MLC", "CRC", "LAT" are not and are only disturbing. As the manuscript is not too long, I suggest not to use the last three abbreviations at all.

4. The first sentence in the Background: it is difficult to understand whether the authors comment on intraoperative findings (frequent appearance of lung metastases in patients in addition to liver metastases of colorectal cancer) or on cancer epidemiology (the most frequent metastatic site of colorectal cancer is the liver, the next frequent are the lungs).

5. "...cell proliferation, morphology and fate." is also a rather unusual combination of terms.

6. Results, para 1, line 3 "gland cells": possibly the cells of bronchial glands? And "normal methotherial" cells in line 12???

7. Discussion, para 1, the last line "these two states." - rather these two clinical situations.

8. Authors' contribution: "experimental....analysis": there were no experiments reported in this study.

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Discretionary Revisions (which the author can choose to ignore)

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What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions.

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

Quality of written English: Not suitable for publication unless extensively edited.

Statistical review: No.
Declaration of competing interests:

I declare that I have no competing interest.