Reviewer’s report

Title: Diagnosis of lung cancer in individuals with solitary pulmonary nodules by plasma microRNA biomarkers

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Reviewer: Heidi Schwarzenbach

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In a testing set miR-21, miR-210 and miR-486-5p were quantified in 76 patients with malignant SPNs and 80 patients with benign SPNs by quantitative RT-PCR. The miRNA panel had diagnostic value to differ benign and malignant disease.

Overall, the manuscript is well structured, and the statistics describes detailed the data.

Major Compulsory Revisions

In the Results (page 8), the feasibility of measuring endogenous miRNAs in plasma of lung cancer patients by quantitative RT-PCR has already been shown by several other laboratories. Therefore, the sentence “The observations are consistent with our previous finding that demonstrated the feasibility of measuring endogenous miRNAs in plasma by qRT-PCR.“ should be cancelled.

On page 8-9, the sentence “….although miR-486-5p expression was reduced in patients with benign SPNs compared to healthy smokers (P< 0.0001), it exhibited higher expression level in patients having malignant SPNs compared to patients with benign SPNs (P=0.0048) (Table 3 and Fig 1).” is not correct. Table 3 and Fig 1 show, that miR-486-5p expression levels were reduced in both (benign and malignant) groups compared to the cohort of healthy individuals.

In the discussion, the paragraph on CT (page 13 and 14) should be cancelled or moved in a shortened version to the introduction. Instead, the authors should refer more their findings to the numerous articles which already exist on circulating miRs in plasma of lung cancer patients. Cancer-specific miRs in blood of lung cancer patients, which discriminate between malignant and benign lung disease, have already been detected by other laboratories. For example, miR10b, miR34a etc. were significantly elevated in only lung cancer patients, but not in benign patients and healthy individuals (Roth et al., Mol. Oncol. 2011 or see other articles). Explain also, what is better for the diagnosis: circulating miR levels which are significantly decreased/increased in only lung cancer patients in comparison with benign lung tumor patients and healthy individuals, or circulating miR levels which are significantly decreased/increased in both (malignant and benign) groups compared to each other.

Moreover, explain in the discussion, why the miR-486-5p levels were in cancer patients decreased (page 12), although cancer patients have an increased cell
turnover and RNA levels in their blood.

Minor Essential Revisions

In the abstract the technique which was performed for the quantification of the miRs should be mentioned (quantitative RT-PCR).

In Fig. 1, the p values should be entered.

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.