Reviewer's report

Title: Expression of the Na+/I- symporter (NIS) is markedly decreased or absent in gastric cancer and precancerous lesions

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Reviewer: Sebastiano Filetti

Reviewer's report:

General
In this manuscript Altorjay et al. describe the reduction/loss of the NIS protein expression in gastric cancer and precancerous lesions. They used immunoblot and immunohistochemistry analysis to expand their previous research in which tissue microarrays were used. The question is well defined but not new, methods are appropriate and data sound and well controlled. More caution is suggested both in the abstract and in the conclusion session regarding a putative role of the NIS as a marker for diagnosis and prognosis of gastric neoplastic lesions, as detailed in the specific points.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
No major compulsory revision is required

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. Abstract, last sentence and Conclusions:
   I would suggest more caution on assigning a putative role to the NIS as a marker for diagnosis and prognosis of gastric neoplastic lesions. In fact, only 17 samples were examined by immunoblot: 5 were weakly positive, 7 examined with IHC and 3 positive in the border. Moreover, previous data by Wapnir et al reported 59% of 27 tissues examined weakly positive for the NIS. Thus, considering that immunohistochemistry is not quantitative, such analysis may produce false results.

2. Introduction, page 3 line 11: Among the tissues which transport iodide and express the NIS, it should be mentioned the placenta, as detected by Bidart et al. (J Clin Endocrinol Metab 2000) and confirmed by other reports.

3. Introduction, page 3 line 16: A recent report by Bruno et al. (J Endocrinol Invest 2004) detected 131I uptake in stomach and salivary glands in 78% and 39% respectively of 302 patients who underwent total body scintiscan in the follow up of thyroid carcinomas. This work or others should be cited, while Figure 1A is unnecessary.

4. Introduction, page 4 line 19: there is at least one report of radioiodide uptake in gastric adenocarcinoma by Wu et al. J Nucl Med 1984, who also revised the previous literature on this field.

5. Results, page 9: please, specify whether the samples examined by immunoblot and those analyzed by immunohistochemistry come from the same patients; if so, was a correspondence found between the weak positivity in immunoblot and the focal staining by immunohistochemistry?

Discretionary revision

6. Discussion, page 11 2nd paragraph: Beside the generation of NO, a possible protective role of iodide may be related to its antioxidant action, as hypothesized by Venturi et al. (Adv Clin Pathol 2000)

7. Discussion, page 9 3rd paragraph: the whole paragraph, which reports well known data on the NIS expression in thyroid and breast cancer, may be amended.

Discretionary Revisions (which the author can choose to ignore)
What next?: Accept after minor essential revisions

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

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests