Reviewer’s report

Title: PI3K Activation is Associated with Intracellular Sodium/Iodide Symporter Protein Expression in Breast Cancer

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Reviewer: Jean-Michel Bidart

Reviewer’s report:

General
The sodium/iodide symporter (NIS), a membrane glycoprotein mediating the active transport of iodide in the thyrocyte, is also expressed in the lactating mammary gland. Several studies demonstrated that NIS expression is detected in breast carcinomas but few tumors display iodide uptake ability. The authors previously showed that PI3K and cAMP pathways are associated with NIS expression (Knostman et al., 2004). In this context, the aim of the present study was to further investigate the role of PI3K using the MCF-7 in vitro model. Their results clearly demonstrate that PI3K activation increases the expression of underglycosylated NIS protein but interferes with NIS cell surface trafficking, and thus on the iodide uptake. This observation could explain the low uptake by tumors. Overall, this is an elegant piece of work, in the continuation of their previous studies, with well-defined questions and appropriate methods that contributes to the basic knowledge on NIS expression and function. The clinical interest of these observations is less evident when comparing to new molecular targeted therapeutic and imaging strategies.

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

Concerning the immunohistochemical (IHC) study:
1- the exact number of tissues analysed for NIS interpretation should be precised (page 10: n=36; table 1: n=33).
2- the sentence " There was a 3-fold increase in Akt phosphorylation …" (page 13, line 17) is somewhat misleading. IHC is not a quantitative method and no data are given in term of signal intensity. It is also difficult to conclude on the sub-cellular localization of NIS due to the low number of samples (n=2 for membranous NIS). This sentence should be modified.

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

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

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