Reviewer's report

Title: Recovery of NIS expression in thyroid cancer cells by overexpression of Pax8 gene

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Reviewer: Ferruccio Santini

Reviewer's report:

General
This study describes the effects of Pax8 transfection in a cell line from human thyroid anaplastic cancer (ARO cells). Results clearly demonstrate that Pax8 expression is associated with recovery of mRNA expression of various markers of thyroid differentiation (i.e. NIS, pendrin, TPO, thyroglobulin and TTF1). Following Pax8 transfection, abundant NIS protein was demonstrated by Western blot analysis and immunofluorescence whereas NIS activity was only slightly increased as compared with control cells. The Authors conclude that overexpression of thyroid-specific transcription factors may be a first step to recover the iodide uptake ability in poorly differentiated thyroid cancers, in order to administer radioiodine for therapeutical purposes. I liked very much the discussion that clearly explain purposes and results of the study, without neglecting limitations and unresolved issues that remain before applying the treatment to humans.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1) Results, Figure 4. It is unclear how it was demonstrated that only few amount of NIS protein reached the plasmamembrane, since immunofluorescence was performed in fixed (permealized) cells.
2) Results, Figure 5. Both the text and the figure legend report that the efflux rate was measured in FRTL-5 cells, but these results do not appear in the figure.

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. It should better explain that in spite of abundant NIS protein synthesis, recovery of NIS activity was poor.
2) Background, last paragraph. ARO cells..were chosen because they lost iodide uptake function. This is not correct since ARO cells retain some iodide uptake activity as shown in Figure 5 and Table 2. That sentence also has grammar problems.

Discretionary Revisions (which the author can choose to ignore)
1) Western blot analysis for the other markers of thyroid differentiation (beside NIS) would strengthen the study.

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published
Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.