Reviewer's report

Title: Reduced expression of N-Myc downstream-regulated gene 2 in human thyroid cancer

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Reviewer: Salvatore Sciacchitano

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Zhao and collaborators report their findings on the analysis of the expression, both at mRNA and protein levels, of NDRG2 gene in thyroid tumors. This gene was previously found to be down regulated in many other human cancers. Although additional functional studies are required, it has been postulated that it may function as a new tumor suppressor gene.

The study appears generally well designed and appropriately reported. The findings are novel and the number of sample examined (40 adenomas and 35 carcinomas, with their matching adjacent tissues) is adequate to support the conclusions. However, it deserves only some minor comments.

Discretionary Revisions:

1. The reduction was mostly observed in carcinomas, with no difference regarding their specific histotype. The expression of NDRG2 is only slightly reduced in thyroid adenomas, suggesting that this genetic alteration may be specifically associated with thyroid malignant transformation. What is the behavior of the 40 lesions examined? They were all expressing slightly reduced levels of NDRG2 mRNA and protein or reduction affected only few of them? Considering the difficulty encountered by many experienced pathologists in diagnosing some adenomas, it would be of interest to know the specific histological features of those adenomas that showed reduced expression of NDRG2. Were they true adenomas or atypical adenomas or follicular thyroid lesion with uncertain malignant potential? Did another pathologist review the diagnosis of these adenomas?

2. The fact that NDRG2 is downregulated in papillary and follicular carcinoma tumors and also in anaplastic carcinoma may indicate that this is a feature of the whole spectrum of differentiation in follicular derived thyroid tumors. However, the occurrence of down-regulation of this gene also in medullary thyroid cancer indicate that this alteration is not specific for tumors derived from the thyroid follicular epithelial cells. The author should add some comments about this in the manuscript.

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.

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