

Peer Review File

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Round 1

Reviewer A

This study mainly distributed to 4 aspects: Prognostic/diagnostic prediction, functional characterization, immunological/therapeutic target and ceRNA network to explore the potential roles of COL26A1 in THCA. This analysis is comprehensive and verified by experiment, which is very well.

Please cite relevant literature, such as

1. DOI: 10.3390/cancers14051353;
2. DOI: 10.3389/fcell.2021.719820;
3. DOI: 10.21037/atm-21-383.

Reply: Thanks for comments made by the reviewer. We have made corresponding modifications in the text.

Changes in the text: Please see P19 L735, P18 L723, and P17 L658.

Reviewer B

-The abstract should be revised in order to better summarize the results, such as the exact numbers, and 95% CI.

Reply: We totally agree with this beneficial advice which renders the abstract more informative. We have the abstract re-wrote as suggested.

Changes in the text: Please see P3 L72-91.

-The introduction suggested be revised: the disease always comes first, followed by the molecular, the study gap, and purpose of the present research.

Reply: We take this suggestion into absolute consideration and the introduction section has been re-structured.

Changes in the text: Please see P3 L97-P4 L134.

-The framework should be moved to part of the Materials and methods.

Reply: Thank you for noticing that and we totally agree with this comment.

Changes in the text: Please see P4 L137.

-Inclusion/exclusion criteria should be better clarified.

Reply: Thank you for raising this comment which makes the study design more clear.

Changes in the text: Please see P4 L148-149.

-The author should clarify the cutoff of expression level to determine the high/low COL26A1 samples.

Reply: Thank you for pointing out this detail for us and we will complete it.

Changes in the text: Please see P4 L151-153.

-Give that the KM curves of Fig 5B-D indicated no significant differences, so it's pointless to involve these endpoints (DSS, DFI and PFI).

Reply: Thank you for spotting this detail in Figure 5. We have renewed the figure which was attached in the file zip. Corresponding text has also been revised.

Changes in the text: Please see P9 L321-342 and the revised Figure 5.

- Did the research performed with two versions of R software (L144, 3.6.3 and L242 4.0.3) ? If so, please state the reason.

Reply: Thank you for discovering this mistake caused by our carelessness. We use the R 4.0.3 throughout the study. Perhaps due to different authors wrote the two parts respectively, the mistake occurred. We truly apologize for our carelessness, please kindly understand.

Changes in the text: Please see P5 L158.

-I also suggest authors to better organize the discussion section following this ideal structure: main findings of the study, implications and comparison with literature, and limitations of the study.

Reply: Thank you for raising this helpful suggestion. We added the part of limitations to the end of the Discussion part, please kindly check.

Changes in the text: Please see P16 L629-633.

Round 2

Reviewer Comments

In this paper the Authors analyzed the New insights into COL26A1 in thyroid carcinoma: It is a debated and novel topic. A comprehensive and extensive literature review of the NCBI database PubMed was also carried out. The article was well conducted and it is interesting in its fields. It is a well-structured paper, written in good English and the References are up dated. Minor issues:

In more demolitive surgery, interventions are affected by more severe complications. In the "discussion" section I suggest to better analyze this topic. Therefore, the following paper should be considered:

"Gambardella C, Offi C, Romano RM, De Palma M, Ruggiero R, Candela G, Puziello A, Docimo L, Grasso M, Docimo G. Transcutaneous laryngeal ultrasonography: a reliable, non-invasive and inexpensive preoperative method in the evaluation of vocal cords motility-a prospective multicentric analysis on a large series and a literature review. Updates Surg. 2020 Sep;72(3):885-892. doi: 10.1007/s13304-020-00728-3. Epub 2020 Mar 2. PMID: 32124271."

"Marotta V, Sciammarella C, Capasso M, Testori A, Pivonello C, Chiofalo MG, Gambardella C, Grasso M, Antonino A, Annunziata A, Macchia PE, Pivonello R, Santini L, Botti G, Losito S, Pezzullo L, Colao A, Faggiano A. Germline Polymorphisms of the VEGF Pathway Predict Recurrence in Nonadvanced Differentiated Thyroid Cancer. J Clin Endocrinol Metab. 2017 Feb 1;102(2):661-671. doi: 10.1210/jc.2016-2555. PMID: 27849428."

"Gambardella C, Offi C, Patrone R, Clarizia G, Mauriello C, Tartaglia E, Di Capua F, Di

Martino S, Romano RM, Fiore L, Conzo A, Conzo G, Docimo G. Calcitonin negative Medullary Thyroid Carcinoma: a challenging diagnosis or a medical dilemma? BMC Endocr Disord. 2019 May 29;19(Suppl 1):45. doi: 10.1186/s12902-019-0367-2. PMID: 31142313; PMCID: PMC6541563.”

Reply: Thanks for the reviewer’s beneficial advice. We have added the three references into our text. Please kindly check.

Changes in the text: P17 L660, P18 L717/L725.