Author’s response to reviews

Title: Indirubin inhibits Wnt/β-catenin signal pathway via promoter demethylation of WIF-1

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Author’s response to reviews:

Dear editor,

Thank you for your careful review and the two reviewers’ comments on the manuscript.

The following is our response:

Reviewer 3:
The authors have mostly satisfied all my concerns and made the necessary changes to the manuscript.

Reply:
Thank you reviewer 3 for agreeing our work and the revision of the article. We will treat every research and manuscript writing in the future with a more rigorous attitude. We still apologize for the confusion this article caused to reviewer 3 previously, and sincerely thank reviewer 3 for their comments, which give our article a chance to be published in the magazine.

Reviewer 4:
However, there is still one problem concerning the HaCaT cell line.
Balato A et al showed that in HaCaT cells, TNF-α was able to induce IL-6, MCP-1 and VEGF, and the addition of IL-33 reinforced these increases. TNF-α + IL-33 combination showed similar results in primary KCs and ex vivo skin organ culture. This means that after the stimulation HaCaT cells became a model for psoriasis like keratinocytes. However as the focus is no longer on psoriasis in the paper this point is not relevant anymore.

Reply:
Thanks to reviewer 4 for his suggestions on the application of cell lines.
In the next step, we will use this type of cell line to build a model of psoriasis keratinocytes to study the pathogenesis of psoriasis.
However, I have still the note that HaCaT cells cannot be ordered by ATCC. ATCC has only primary epidermal keratinocytes; Normal, Human, Adult (HEKα) (ATCC® PCS-200-011™). And Cell lines services (CLS) sell HaCaT cells (https://www.clsgmbh.de/p800_HaCaT.html). I know that in some publications it is mentioned that the HaCaT cells are obtained from ATCC but this is nevertheless wrong. Therefore, it should be corrected.

Reply:
We consulted the purchasing agent and consulted the HaCaT cell instructions. HaCaT cells are derived from Cell lines services (CLS). We have made changes in the corresponding positions （Methods section -Cell culture, line 12-13, page 5）.

Thank you reviewer 4 for your suggestions on our previous work and correcting our mistakes. In future research, we will pay more attention to every detail to ensure that it is correct. Thanks again to reviewer 4 for the comments.

Finally, thanks again for the hard work of the editor.