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 very much for you patiently review and comments from the two reviewers. In order to better display our research results, we have made detailed and comprehensive amendments to the manuscript.

The location of the revised manuscript is as follows:
1. Results section: This part consists of seven small units. According to the comments of reviewer 2, we have provided detailed supplementary explanations for each small unit. page10-13.
2. Discussion section: At various places we explain our scientific findings through comprehensive literature and our research results based on the comments of Reviewer 2. page14-17.
3. Conclusions section: We revisited the manuscript and partially revised the conclusions. page17.
4. References section: We have added three references. page23. The location of literature :23,24,25. Literature position in manuscript: line 12, page 16.
5. Figure Legends section: According to the comments of reviewer 2, we have illustrated the figure in detail. Figure 1: page 24-25. Figure 2: page27. Figure 3: page29. Figure 4: page31.

According to reviewer 1, our response is as follows:
1. We observed that the phosphorylation level of β-catenin by the western blot in the experiment, and we marked Human Phospho-β-Catenin (Ser33 / 37 / Thr41) Antibody (1: 1000, # 9561, CST, Boston, MA, USA) in Methods-Chemicals in the original manuscript, but we did not explain the phosphorylation site of β-catenin in Figure 1. In the returned manuscripts, we complement the omission. In addition, we have made corresponding explanations in the results and discussion.
2. By consulting the literature, Wnt antagonists (WIF-1 and sFRPs) promote the accumulation of nuclear β-catenin and generate a functional transcription factor complex and the expression of downstream target genes when the Wnt signaling pathway is activated, we speculate that β-catenin enter the nucleus to complete transcription of downstream genes so we have not determined the nuclear transcription level of β-catenin, We have only detected the expression of β-catenin phosphorylated by western blotting to show that indirubin inhibit the wnt signaling pathway by inhibiting β-catenin expression. In the next stage, exploring downstream genes of the wnt signaling pathway, we will explore problem of the β-catenin nucleus translocation.

3. Thanks to the suggestion of reviewer 1, we may research long non-coding RNAs in the next assay to probe the epigenetics-associated machinery in psoriasis, but in the assay, we did not explore whether long non-coding RNAs played role in inactivation.

Based on the comments of Reviewer 2, our response is as follows:
1. We made a more complete description of the documented results. In the discussion section, we also rewritten to interpret the work that we did in the experiment.
2. We re-explained legends of figures to illustrate our scientific findings.

We hope that our response will be accepted by the editors and two reviewers, and we look forward to your good news.

Yours sincerely