Peer Review File

<mark>Reviewer A</mark>

1. **Comment 1:** English language of the paper needs extensive editing.

   Reply 1: Taking the reviewers' comments into consideration, we have revised our manuscript to improve the language, and marked the changes in tracking in the paper. In addition, as suggested, we sought assistance from a professional English language editing service (AME Editing Service) to ensure that our manuscript meets the required language standards and to improve its clarity.

   Changes in the text: The English Editorial Certificate is at the end of this article.

2. **Comment 2:** Abstract. The authors need to provide detailed figures and corresponding statistics to support the main findings. They also need to briefly describe the clinical significance of the current research topic.

   Reply 2: We have modified our text as advised (see Abstract).

   Changes in the text: Please see Abstract.

3. **Comment 3:** Background. First, please explain why a focus on the adding manner of IL-2, i.e., the clinical significance. Second, the authors need to have a brief review on known adding methods of IL-2 and comment on their limitations to indicate the why the current topic is needed.

Reply 3: We have modified our text as advised (see Introduction).

Changes in the text: Please see Introduction.

4. **Comment 4:** Methodology. The authors may consider to have an overview on the procedures of the experiment at the beginning of this part. Second, please consider the quality control measures of this experiment.

Reply 4: Each experiment was repeated 3 times, and the results were expressed as X±S. We have modified our text as advised (see Methods).

Changes in the text: Please see Methods.

5. **Comment 5:** Statistics. Please indicate the dependent and independent variables in the linear regression analysis. For ANOVA, please specify the groups to be compared. Please indicate the test of normality of continuous variables and whether $P<0.05/0.01$ is two-sided.

Reply 5: In linear regression analysis, growth days was the independent variable and proliferation was the dependent variable. Multiple comparisons were carried out using Dunnett's multiple comparisons tests (multiple comparisons were performed between the group that had the highest CD3+ CD56 + ratio, the highest IFN-γ production, the best cytotoxicity and the other groups). *P*-values were one-sided. We modified our text as advised (see Statistical analysis).

Changes in the text: Please see Statistical analysis.

6. **Comment 6:** Discussion. Please use a separated paragraph to discuss the limitations of this study. Further, please have some comments on the implications of the main findings.

Reply 6: We modified our text as advised (see Discussion).

Changes in the text: Please see Discussion.

1. **Comment 1:** Please add the original reference on CIK cells of Schmidt-Wolf et al., J Exp Med., 1991.

   Reply 1: We added this reference under " Introduction" and " References 2".

   Changes in the text: "Introduction" and "References 2".

2. **Comment 2:** Please add the reference on the CIK cell registry of Y. Zhang et al, 2020.

   Reply 2: We only found the following article: "Zhang Y , Zhang X , Liang Z , et al. Interleukin-17 suppresses grass carp reovirus infection in Ctenopharyngodon idellus kidney cells by activating NF-κB signaling[J]. Elsevier Public Health Emergency Collection, 2020, 520." However, this article relates to "ctenopharyngodon idellus kidney cells (CIK)", not "cytokine-induced killer cells (CIKs)", and therefore we did not include it.

   Changes in the text: There is no change.