

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The title is suitable.

1. The section of "Methods" in abstracts should be rewritten and what is Elisa? You mean ELISA.

Response: Thank you for your suggestion. We have rewritten what is Elisa as Enzyme-linked immunosorbent assay and marked it in blue.

2. The abbreviation should be clarified in the whole manuscript.

Response: Thank you for your suggestion. We have added the full titles of all abbreviations in the section Abstract, Introduction, and Discussion and marked them in blue.

3. The name of the different groups of animals is not clear and should be clarified in "Methods".

Response: We accepted the reviewer's advice and revised this part in the Methods section and marked them in blue. The revised part is as followed:

Mice for the experiment were divided into 5 groups (n=9, total=45): SD, HFD-WT, HFD-KO, Con, and AAV group. VEGFB^{+/+} mice and VEGFB^{-/-} mice were selected randomly for the experiment. Nine VEGFB^{+/+} mice fed with a standard diet were named the standard diet (SD) group. Twenty-seven VEGFB^{+/+} mice and nine VEGFB^{-/-} mice were fed with a high-fat diet (HFD) for 20 weeks. (Fig. 1C). Nine VEGFB^{+/+} and nine VEGFB^{-/-} mice with HFD were defined as the HFD-WT and HFD-KO groups. Nine VEGFB^{+/+} mice injected with targeting VEGFB¹⁸⁶ adeno-associated virus (AAV) were named as AAV group, and nine VEGFB^{+/+} mice injected with the non-targeting AAV were defined as the Con group.

4. The authors have to present a small introduction about VEGF and its subtypes.

Response: We have added a small introduction about VEGF and its subtypes in the Discussion section and marked them in blue. The revised part is as followed: Seven members of the vascular endothelial growth factor (VEGFs) have been identified, including VEGFA, VEGFB, VEGFC, VEGFD, VEGFE, VEGFF, and placental growth factor (PIGF). These subtypes play different roles in many biological functions. The deletion of VEGFA and VEGFC genes can cause pathological changes and biological function loss. VEGF-C and VEGF-D mainly work on the regulation of lymphangiogenesis.

5. Many methods should be reference-cited, especially the assay of glucagon and western blotting. The results are good and Figure 8 is very important to reflect the results. The discussion and conclusion are fine.

Response: We have added the relative reference at the end of each method and marked them in blue.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Accept in present form.

Response: Thank you for your recognition.