

Supplemental information

Bempedoic acid directly binds and activates PPAR α

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Supplemental Material to:

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Supplemental Figures

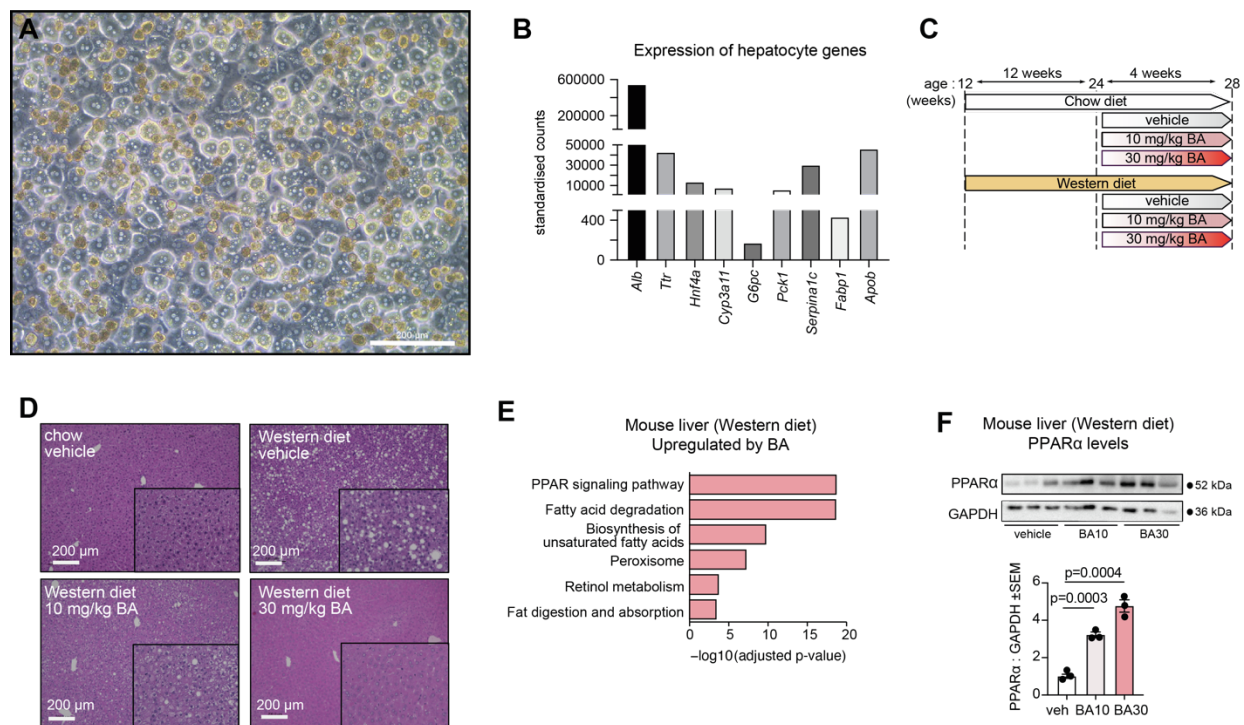


Figure S1 – Bempedoic acid activates PPAR α

Related to Figure 1

(A) Exemplary image of primary mouse hepatocytes used in this study. Bi-nucleated hepatocytes were commonly observed. Scale bar equals 200 μ m.

(B) Expression of genes typically used as markers of primary mouse hepatocyte [S1,S2]. Data were extracted from RNA-seq analyses of primary mouse hepatocytes, and are averaged across 8 biological replicates. The normalized expression levels are provided, which standardizes for overall sequencing depth.

(C) Experimental design of the in vivo study. Male C57BL/6N mice were fed with chow or Western diet for 12 weeks. Randomized animals under different diets were grouped to receive either vehicle, 10 mg/kg body weight BA (BA10) or 30 mg/kg body weight BA (BA30) daily via oral gavage. After 4 weeks of diet and treatment, animals were sacrificed and livers were collected for further analysis.

(D) Histology of livers from chow and Western diet-fed animals treated with vehicle, BA10 and BA30. Western diet: n = 6 animals per group; chow: n = 5 animals per group.

(E) KEGG-annotated pathways significantly upregulated in livers of Western diet-fed mice treated with BA30. List of significantly upregulated genes (Benjamini-Hochberg adjusted p-value < 0.05, log2 fold change > 0.5) was used for these analyses. n = 4 mice per group.

(F) Top: Western blot for PPAR α and GAPDH proteins following BA treatment of Western diet-fed mice. Bottom: Signal quantification analysis of PPAR α : GAPDH signal. Data are provided as mean \pm SEM, and were analysed via a two-tailed Student's t-test. n = 3 animals per group.

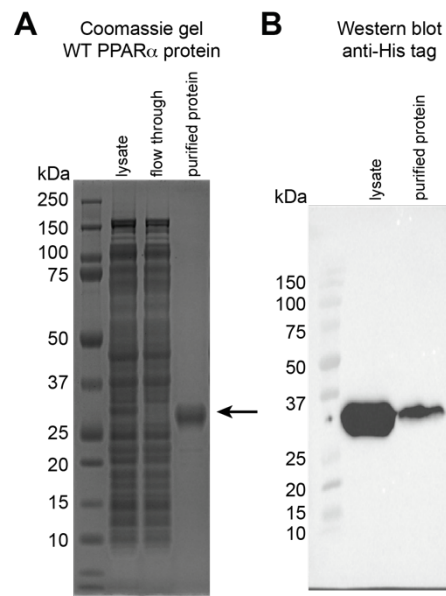


Figure S2 – Expression and purification of the ligand binding domain of PPAR α

Related to Figure 2

(A) Coomassie-stained gel showing the initial bacterial lysate, the flow through from the Ni₂NTA column, and the purified protein following size-exclusion chromatography.

(B) Western blot using antibodies raised against the His-tag.

Supplemental References

- S1. Ardisasmita, A.I., Schene, I.F., Joore, I.P., Kok, G., Hendriks, D., Artegiani, B., Mokry, M., Nieuwenhuis, E.E.S., and Fuchs, S.A. (2022). A comprehensive transcriptomic comparison of hepatocyte model systems improves selection of models for experimental use. *Commun Biol* 5, 1094. [10.1038/s42003-022-04046-9](https://doi.org/10.1038/s42003-022-04046-9).
- S2. Franzen, O., Gan, L.M., and Bjorkegren, J.L.M. (2019). PanglaoDB: a web server for exploration of mouse and human single-cell RNA sequencing data. *Database (Oxford)* 2019. [10.1093/database/baz046](https://doi.org/10.1093/database/baz046).