Scientific Reports December 1st, 2015 SREP-15-20951B

Targeting arginase-II protects mice from high-fat-diet-induced hepatic steatosis through suppression of macrophage inflammation

Chang Liu¹, Angana G. Rajapakse¹, Erwin Riedo², Benoit Fellay², Marie-Claire Bernhard³, Jean-Pierre Montani^{1,4}, Zhihong Yang^{1,4*} and Xiu-Fen Ming^{1,4*}

¹Vascular Biology, Department of Medicine, Division of Physiology, University of Fribourg, Chemin du Musée 5, CH-1700 Fribourg, Switzerland

² Laboratory HFR, Hospital Fribourgeois, Chemin des Pensionnats 2, 1708 Fribourg,

Switzerland

³ Promed Medical Laboratory SA, Fribourg, Switzerland

⁴National Center of Competence in Research "Kidney.CH", Switzerland

Address for correspondence:

Zhihong Yang, MD or Xiu-Fen Ming, MD, PhD Laboratory of Vascular Biology Department of Medicine Division of Physiology University of Fribourg Chemin du Musée 5 CH-1700, Fribourg Switzerland Tel: 0041-26-300 85 93 Fax: 0041-26-300 97 34 Email: <u>zhihong.yang@unifr.ch</u> or <u>xiu-fen.ming@unifr.ch</u>



Fig. S1. The increase in plasma ALT and AST tends to be smaller in obese Arg-II^{-/-} mice as compared to obese WT mice, but does not reach statistical significance. Liver injury was assessed by measuring plasma ALT (A) and AST (B). n=9 (NC) and n=18 (HFD).

A



Fig. S2. Arg-II is not detectable in liver lysates, whereas Arg-I expression and total arginase activity in liver of obese mice are not significantly affected by Arg-II-deficiency. Liver lysates from obese WT and Arg-II^{-/-} mice were prepared and subjected to immunoblotting analysis of (A) Arg-II expression. Mice kidney lysate was used as positive control (P). (B) Arg-I expression. Tubulin served as loading control. (C) Arginase activity assay.



Fig. S3. There is no significant difference in epididymal fat weight between wt and Arg-II^{-/-} mice fed HFD.





Fig. S4. All the macrophages in liver are Kupffer cells. (A) Liver sections from WT and Arg-II^{-/-} mice fed NC or HFD were stained with pan-macrophage marker F4/80 (green) and Kupffer cell specific marker CLEC4F (red) followed by nuclei counterstaining with DAPI (blue). (B) Quantification of the fluorescence signals.