Supplementary information

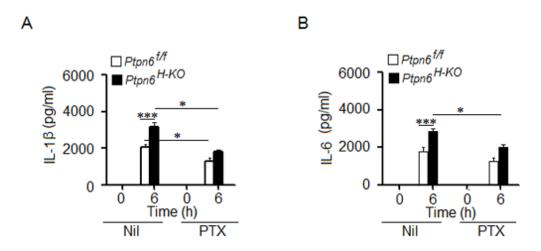
Hepatocyte SHP-1is a Critical Modulator of Inflammation During Endotoxemia

Anupam Adhikari^{1, 2}, Caroline Martel^{1, 2}, André Marette³ and Martin Olivier^{1, 2}*

¹Department of Medicine, Microbiology and Immunology, Faculty of Medicine, McGill University, Montréal, Québec, Canada; ²The Research Institute of the McGill University Health Centre and Infectious Diseases and Immunity in Global Health Program, Montréal, Québec, Canada; ³Heart and Lung Institute (Laval Hospital), Université Laval, Québec, QC, Canada.

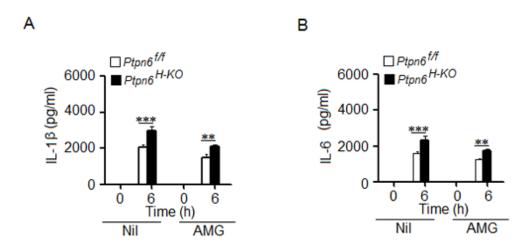
*<u>Corresponding author</u>: Martin Olivier, Ph.D. 1001 Boul. Décarie The Research Institute of the McGill University Health Centre Site Glen, Pavillon E/Block E Montréal, Qc, H4A 3J1, Canada E-mail: <u>martin.olivier@mcgill.ca</u>

Supplementary Figure 1.



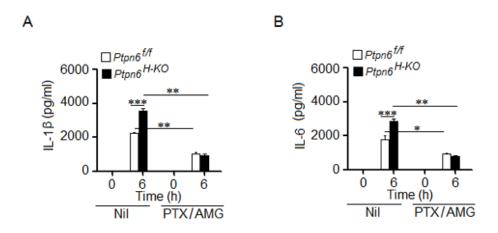
Supplementary Figure 1. TNF- α inhibitor pentoxifylline treatment reduced proinflammatory cytokines in *Ptpn6^{H-KO}* challenged with LPS. Serum levels of (A) IL-1 β and (B) IL-6 in *Ptpn6^{H-KO}* and *Ptpn6^{f/f}* mice treated with pentoxifylline, during LPS challenge (30 mg/kg body weight). Data are presented as mean ± SEM, n = 6. * P ≤ 0.05, and ***P ≤ 0.001.

Supplementary Figure 2



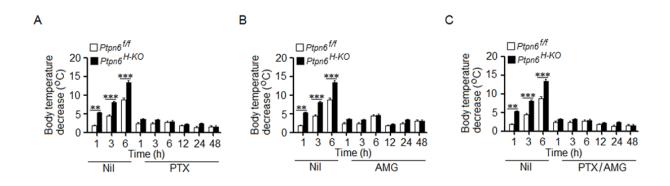
Supplementary Figure 2. Effect of iNOS/NO inhibitor aminoguanidine treatment on proinflammatory cytokines in *Ptpn6^{H-KO}* challenged with LPS. Serum levels of (A) IL-1 β and (B) IL-6 in *Ptpn6^{H-KO}* and *Ptpn6^{f/f}* mice treated with aminoguanidine, during LPS challenge (30 mg/kg body weight). Data are presented as mean ± SEM, n = 6 ***P ≤ 0.001.

Supplementary Figure 3

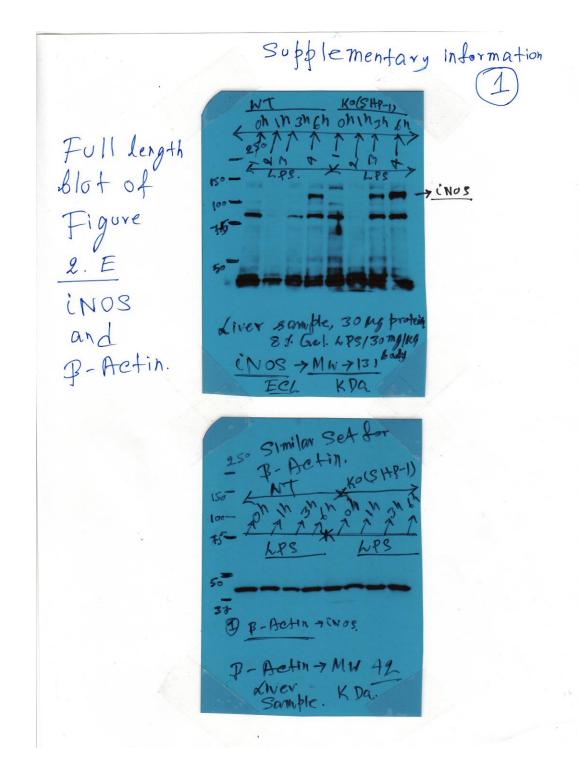


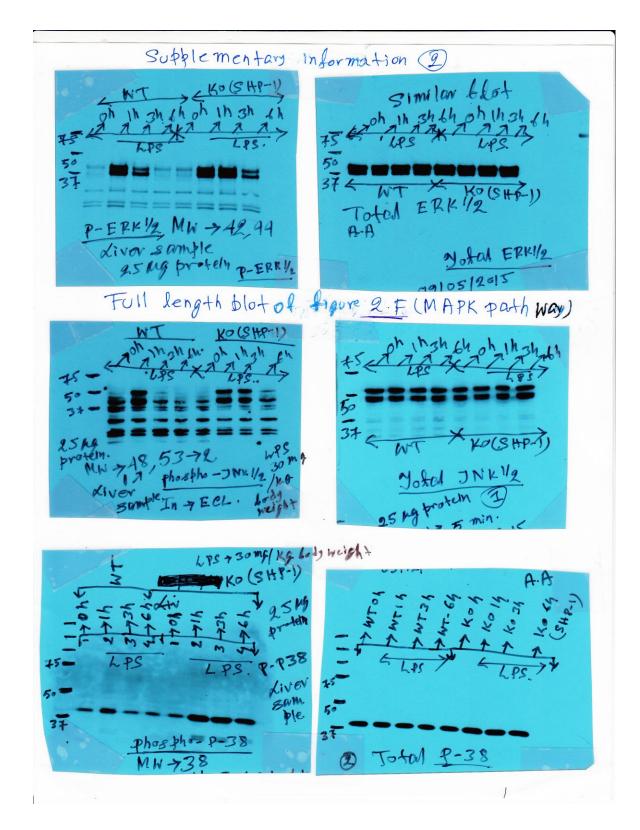
Supplementary Figure 3. Combination of TNF- α and iNOS/NO inhibitors treatment reduced pro-inflammatory cytokines in *Ptpn6^{H-KO}* challenged with LPS. Serum levels of (A) IL-1 β and (B) IL-6 in *Ptpn6^{H-KO}* and *Ptpn6^{ff}* mice treated with aminoguanidine plus pentoxyfyline during LPS challenge (30 mg/kg body weight). Data are presented as mean \pm SEM, n = 6. * P ≤ 0.05 , **P ≤ 0.01 and ***P ≤ 0.001 .

Supplementary Figure 4.



Supplementary Figure 4. Effect of TNF- α or NO inhibitors on body temperature of *Ptpn6^{H-KO}* and *Ptpn6^{f/f}* mice Body temperature decrease in *Ptpn6^{H-KO}* and *Ptpn6^{f/f}* mice treated with (A) pentoxyfyline (B) amino guanidine and (C) their combination during LPS challenge (30 mg/kg body weight). No significant differences in body temperature reduction between *Ptpn6^{H-KO}* and *Ptpn6^{f/f}* mice at the indicated time points. Data are presented as mean \pm SEM, n = 6. **P ≤ 0.01 and ***P ≤ 0.001 .





Supplementary information 3 7 MW 736 K Da. SAA * MUS ADOE D 'U M 5 W 107. Gel Full length blot of figure 2. G. (SAA, ApoE, 1. 2. G. (BP, Albumin) In Berum 37 Albumin 767KB

Supplementary information (A) EN: +5 se protein Intern 17 ECL 25/19 250 L-85 1 hg/m 150 Cel. 30 AS 75 EPKY KO (SHP-1) MW7A2, PK 37 AA K-Da WT Ko (SHP2) Ing/m Full length blot of figure MAPK Path Way in Helato rotein ente) 50 KO (SHP-I) Ko (3HP-1) P-JNK1/9->MW Jotal) + PJNK 1/2 Ko (SHP P-38 Hebatocyte (primany) e thes thes. ing/mi

Supplementary Information (5) 31 Ko (SHP-1) P-ERK1/2 otal ERK% Maerophages + LPS blot of Full length figure 5 (MAPK pathway in macrophages) 25 14 protein. 37 LIT Total-JNK12 Macropha fig(mi) A.H 5#8-1 50 MW-> P-938 38 Maers pha