

1 **Supplemental Material**

2

3 **Hepatic dysfunction and thrombocytopenia induced by excess**
4 **sFlt1 in mice lacking endothelial nitric oxide synthase**

5

6

7 Yuji Oe^{1,5}, Mieko Ko², Tomofumi Fushima², Emiko Sato^{2,3}, S Ananth Karumanchi⁴, Hiroshi
8 Sato^{2,3}, Junichi Sugawara¹, Sadayoshi Ito³, and Nobuyuki Takahashi^{2,3*}

9

10 ¹ Division of Feto-Maternal Medical Science, Department of Community Medical Support, Tohoku
11 Medical Megabank Organization, Tohoku University, Sendai 980-8574, Japan.

12 ² Division of Clinical Pharmacology and Therapeutics, Tohoku University Graduate School of
13 Pharmaceutical Sciences & Faculty of Pharmaceutical Sciences, Sendai 980-8578, Japan.

14 ³ Division of Nephrology, Endocrinology, and Vascular Medicine, Tohoku University Graduate School
15 of Medicine, Sendai 980-8574, Japan.

16 ⁴ Department of Medicine and Center for Vascular Biology Research, Beth Israel Deaconess
17 Medical Center and Harvard Medical School, Boston, MA 02215, USA.

18 ⁵ Research Fellow of Japan Society for the Promotion of Science.

19

20

21

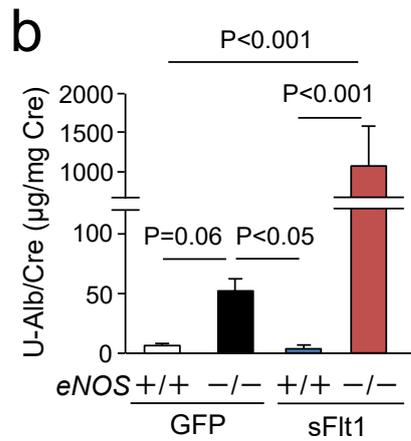
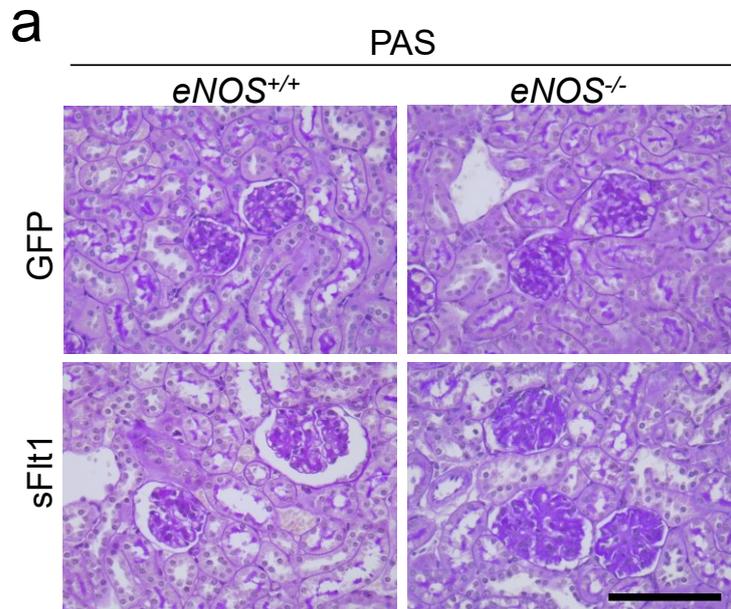
22

23

24

25

1
2



3
4
5
6
7
8
9
10
11

Supplementary Figure 1. Glomerular injury and urinary albumin excretion in *eNOS*^{-/-}; sFlt1 mice.

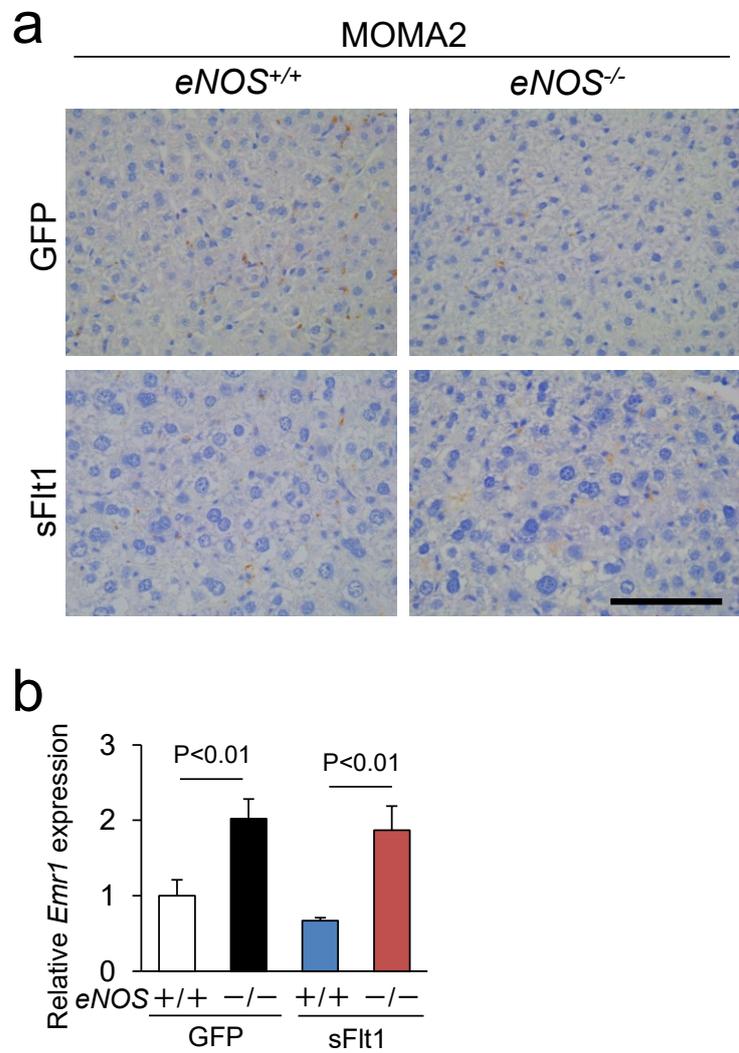
(a) Representative photomicrographs of Periodic acid-Schiff (PAS) stain in the kidney. Severe

endotheliosis accompanied by mesangial expansion is shown in glomeruli from *eNOS*^{-/-}; sFlt1 mice.

Scale bar indicates 100 µm. (b) The level of urinary albumin/creatinine ratio (U-Alb/Cre) in each group.

n=6-8. Data are shown as mean ± s.e.m. ANOVA.

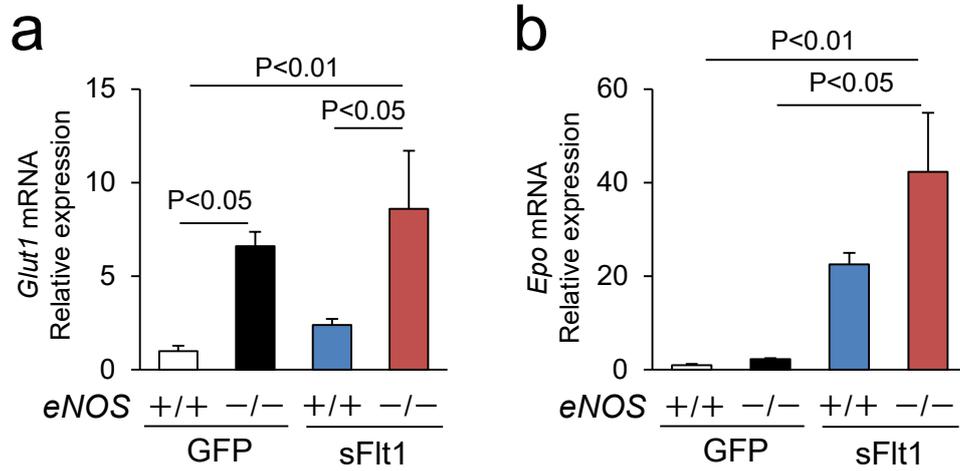
1
2
3
4
5
6
7
8
9
10
11



Supplementary Figure 2. Excessive sFlt1 do not affect macrophage infiltration.

(a) Representative photomicrographs of MOMA-2, a macrophage marker, in the liver. Scale bar indicates 100 μ m. (b) Expression of *Emr1* mRNA in the liver. n=7-8. Data are shown as mean \pm s.e.m. ANOVA.

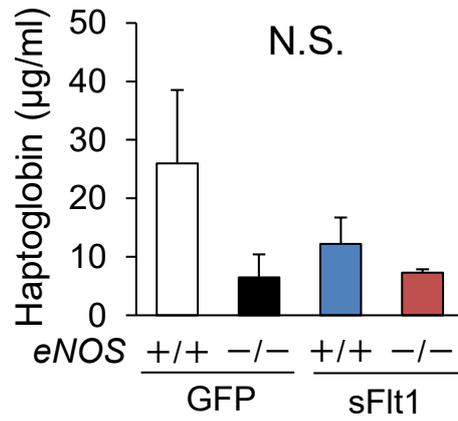
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16



Supplementary Figure 3. Expression of *Glut1* and *Epo* mRNA in the liver

(a-b) the levels of *Glut1* and *Epo* mRNA in the liver. n=7-8. Data are shown as mean \pm s.e.m. ANOVA.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

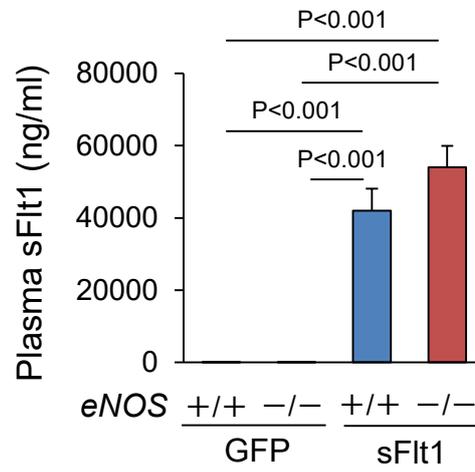


Supplementary Figure 4. The level of plasma haptoglobin in each group. n=7-8. Data are shown as mean \pm s.e.m.

1

2

3



4

5

6 **Supplementary Figure 5.** The level of plasma sFlt1 in each group. n=7-8. Data are shown as mean ±
7 s.e.m. ANOVA

8