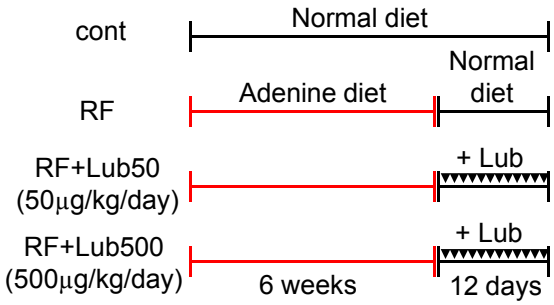
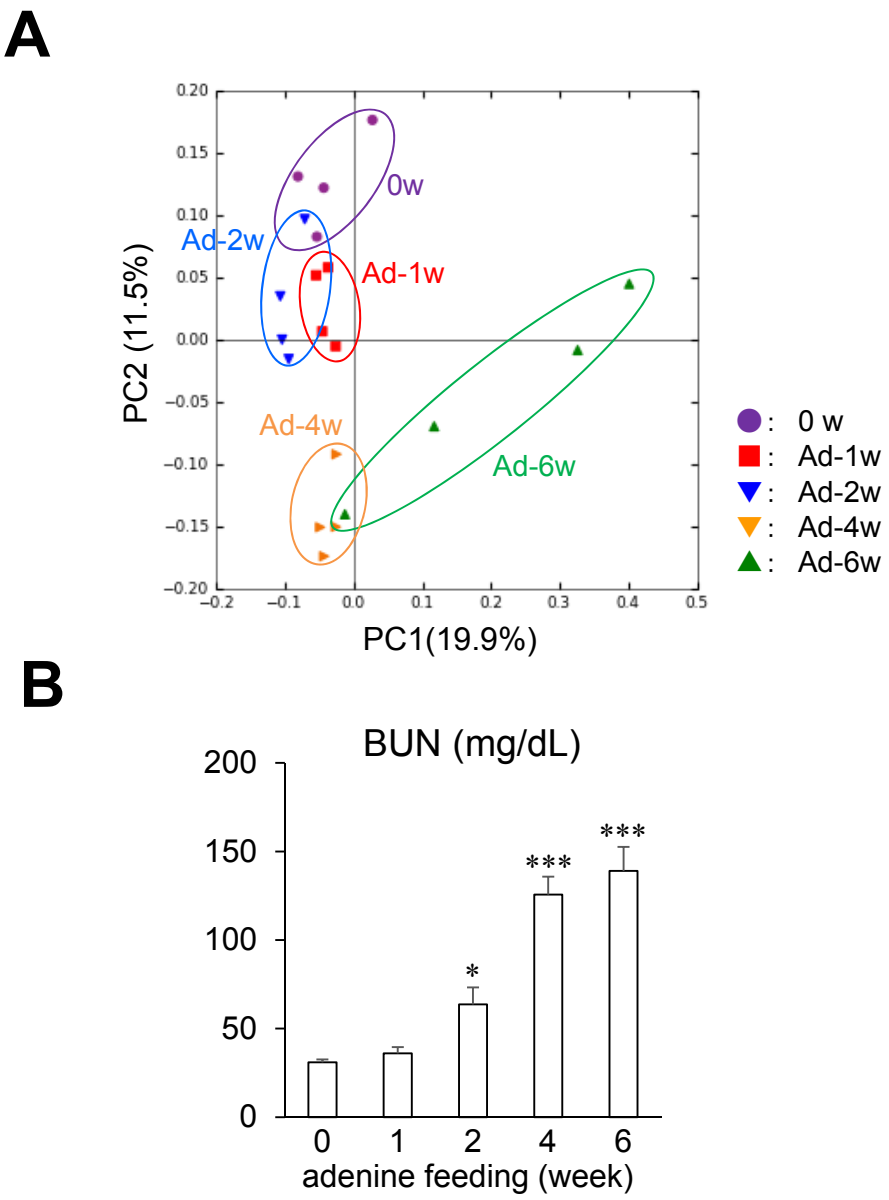
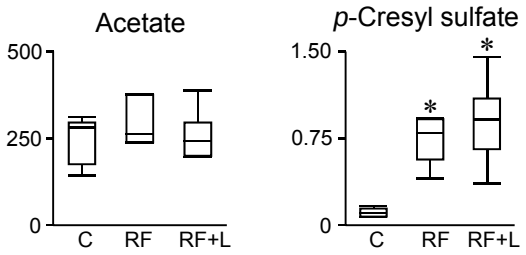


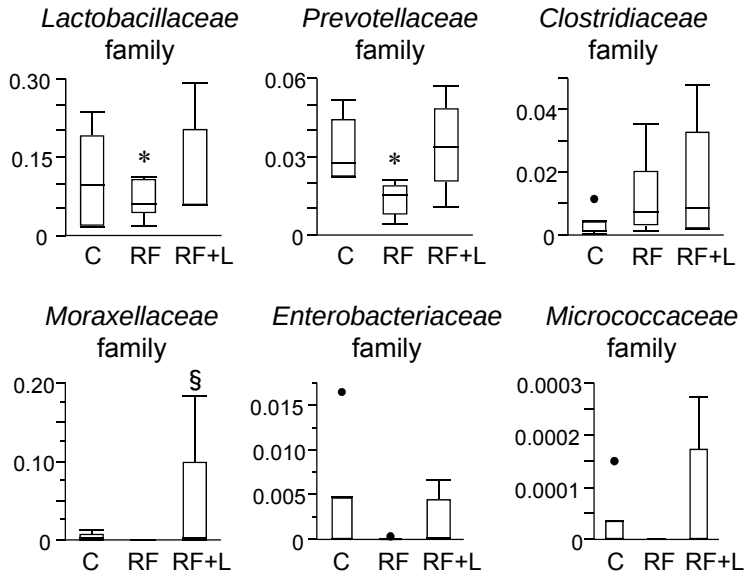
Supplementary Figure 1. Experimental design.
Mice were divided into four subgroups: 1) a control normal diet group (cont), 2) an adenine-induced uremic renal failure group (RF), 3) a lubiprostone (50μg/kg/day)–treated RF group (RF+Lub50), 4) a lubiprostone (500μg/kg/day)–treated RF group (RF+Lub500).



Supplementary Figure 2. The changes of gut microbiota and BUN after adenine feeding.
(A) Unweighted unifrac distance analysis of gut microbiome after adenine feeding. n=4 for each group. *Ad*, adenine feeding for 1, 2,4 and 6 weeks.
(B) The level of blood urea nitrogen (BUN) during adenine feeding.
*P < 0.05 and ***P< 0.001 versus 0-week group (ANOVA).
n=3 for each group.



Supplementary Figure 3. Plasma acetate and *p*-cresyl sulfate levels.
Plasma acetate (μM) and p-cresyl sulfate (relative levels) were measured as descried in supplemental methods.
C, control; RF, renal failure; RF+L, lubiprostone 500μg/kg/day treated renal failure. *P<0.05 versus the control group. n=6



Supplementary Figure 4. Change of microbiota at the family level
The proportional change of fecal microbiota at the family level. Microbial families shown in this figure were reported to be changed in ESRD patients and to possess urease, uricase, and butyrate-, indole- and *p*-cresol-forming enzymes in the previous *in silico* study.[27] The other microbial families enriched in ESRD patient in the previous study, *Alteromonadaceae*, *Cellulomonadaceae*, *Dermabacteraceae*, *Halomonadaceae*, *Methylococcaceae* and *Polyangiaceae*, were not detected in the present analysis. The y-axis indicates the abundance of each microbe (%). *P<0.05 versus the control group, § P<0.05 versus the RF group (Steel-Dwass).

Supplementary Table 1. Metabolic and biochemical parameters of mice
Parameters were measured at the one day prior to killing (metabolic parameters) or when killed (body weight and biochemical parameters). SBP, systolic blood pressure. *P<0.05 versus control group, § P<0.05 versus RF group. n=6-7

		control	RF	RF+Lub50	RF+Lub500
Body weight	(g)	24.8±1.2	21.1±1.1*	21.4±1.1*	21.6±1.0*
Water intake	(mL/day)	2.5±1.0	8.6±4.0*	8.9±1.7*	9.1±1.9*
Food intake	(g/day)	2.7±0.7	2.2±1.1*	2.2±0.9*	2.3±0.7*
Urine volume	(mL/day)	1.5±0.3	9.4±1.6*	8.3±1.0*	7.8±1.3*
Fecal wet weight	(g/day)	1.9±0.3	1.2±0.5*	1.3±0.1*	1.5±0.2*
Fecal number	(/day)	107.0±24.1	79.8±29.6*	76.3±8.4*	70.0±10.4*
SBP	(mmHg)	106.9±6.7	88.9±3.9*	91.1±12.2*	82.0±7.6*
Na	(mEq/L)	151.8±2.7	153.0±2.1	148.3±3.2*§	146.7±0.8*§
Cl	(mEq/L)	119.2±2.2	118.7±3.0	116.6±3.0	117.0±1.7
K	(mEq/L)	4.9±0.7	5.1±0.9	5.3±0.6	5.5±1.9
iCa	(mg/dL)	1.2±0.1	1.1±0.1	1.2±0.1	1.2±0.1
Glucose	(mg/dL)	182.5±41.0	163.1±20.1	188.9±58.0	192.7±9.0
Ht	(%)	45.5±2.4	26.1±2.7*	25.8±3.8*	28.2±3.5*
Hb	(g/dL)	15.5±0.8	8.9±0.9*	8.8±1.3*	9.6±1.2*

Supplementary Table 2. Primers used in PCR analysis

Taqman Gene expression assays	
Tnfa	Mm00443260_g1
Il6	Mm00446190_m1
Pai1	Mm00435860_m1
Ccl2	Mm00441242_m1
Col1a1	Mm00801666_g1
Col3a1	Mm01254476_m1
Acta2	Mm00725412_s1
Tgfb1	Mm01178820_m1
Gapdh	Mm99999915_g1