Table of Contents for the Supplementary Materials:

Supplemental Methods:

Additional patient exclusion criteria and clinical variables: Exclusion criteria consisted of pregnancy, institutionalized individuals, chronic medical conditions, a known immunodeficiency, chronic inflammatory conditions, malignancy, immunosuppressant medications, indwelling hardware, comorbid urinary tract anomalies (including hydronephrosis, solitary kidney, pelvic kidney, renal dysplasia, cystic kidney disease, urinary tract obstruction, ureterocele, or neurogenic bladder), high-grade VUR, chronic kidney disease stage 2-5, intermittent catheterization, history of urinary tract surgery, chronic antibiotic use, or antibiotic use within 1 week of enrollment (i.e. all patients were off antibiotic therapy at time of urine sample collection).

UPEC isolates: UTI89 is a type I-piliated UPEC strain isolated from a patient with cystitis.[1] UTI89Δ*fimH* does not produce adhesive type 1 pili.[2] MDR-UPEC isolates were collected from pediatric patients with UTI and no evidence of structural urinary tract disorders or high-grade VUR (**Supplementary Table 2**).

LDH *in vitro* cytotoxicity assay: UROtsa cells were cultured to confluency in antibiotic-free RPMI media containing 10% fetal bovine serum. Confluent cells were cultured in fresh media for 16 hours and then infected with $2x10^6$ CFU/well UPEC for four hours at 37°C. LDH release into the culture media was measured using the LDH Cytotoxicity Detection Assay (Takara Bio, Kyoto, Japan) as previously described.[3]

RNase 7 transgenic mouse PCR genotyping: PCR assays were designed with primers specific to the 5' and 3' ends of the *RNASE7* gene. The 5' end of the *RNASE7* gene was identified by the

presence of a 266 bp product generated using the sense primer 5'-TAACACCACAGTGATTGACTCTTC-3' and the antisense primer 5'-GTTCATGCCTCTCCACTTACAT-3'. The 3' end of the *RNASE7* gene was identified by the presence of a 289 bp product generated with the sense primer 5'-TGCGCAAGAAAGAAGTCACT-3' and the antisense primer 5'-CACTCCCTTTACCTTATGTCTTCAG-3'. The identity of the PCR products and was confirmed with sequencing.

Mouse serum chemistries and complete blood counts: Serum chemistries were measured using the Alfa Wassermann VetACE chemistry analyzer (Diamond Diagnostics, Holliston, MA, USA) at The Ohio State University Comparative Pathology and Mouse Phenotyping Shared Resource. Mouse complete blood counts with differential were measured using the Hemavet 950FS Hematology Analyzer (Drew Scientific, Miami Lakes, FL, USA).

RNA isolation and qRT-PCR: RNA was isolated from murine tissues with TRIzol (Invitrogen, Carlsbad, CA, USA). cDNA synthesis and qRT-CR was performed as previously described.[4] Relative expression changes were calculated using the $2^{-\Delta\Delta CT}$ method.

Primer sequences used include:

RNASE7: 5'-GATCTGACAGCCTAGGAGTGC-3'(forward) and

5'-GGGGTCGCTTTGCGCTTG-3' (reverse).

Gapdh: 5'-CTGGAGAAACCTGCCAAGTA-3' (forward) and

5'-TGTTGCTGTAGCCGTATTCA-3' (rev).

SDS-PAGE Western blot and ELISA: Protein extraction and Western blot on murine tissues and cell culture lysates was performed as previously described.[3, 5] Primary antibodies included: monoclonal mouse anti-RNase 7 (clone CL0223, Sigma-Aldrich), polyclonal rabbit anti-uroplakin 2 (N-18, Santa Cruz Biotechnology, Dallas, TX), goat polyclonal anti-uroplakin 3a (Santa Cruz Biotechnology), mouse monoclonal anti-cytokeratin 14 (ThermoFisher Scientific), and rabbit polyclonal anti-GAPDH (Cell Signaling). The RNase 7 ELISA was performed as previously published.[4]

Histopathology and Immunostaining: Immunohistochemical and immunofluorescent staining in mouse bladder and kidneys was performed as previously described.[4-5] The kidney's principal cells were labeled with a polyclonal goat aquaporin 2 antibody (Santa Cruz Biotechnology) and RNase 7 was labeled with a mouse monoclonal antibody (Sigma Aldrich). Alexa Fluor® 488 AffiniPure Donkey Anti-Goat IgG (Jackson ImmunoResearch Laboratories, West Grove, PA) and Cy™3 AffiniPure $F(ab')_2$ Fragment Goat Anti-Mouse IgG (Jackson ImmunoResearch) served as the secondary antibodies.

Mouse cytokine profiles: The expression of 84 cytokines, chemokines, and their receptors were analyzed in murine kidney using RT2 Inflammatory Cytokine and Receptor array (PAMM-011Z, SABioscience, Frederick, MD) according to the manufacturer's protocol. cDNA was synthesized from 1 μg of total RNA using a First Strand cDNA synthesis kit (Qiagen). The concentrations of 23 mouse cytokines in sera of bladder homogenates were measured with a multiplex bead array platform (Bio-Plex, Bio-Rad, Hercules, CA) as previously described.[6-7]

Gastrointestinal microbiota profiles: *DNA extraction and sequencing:* DNA was extracted from the stool samples and ileum contents (~10 mg each) using a QIAamp Fast DNA Stool Mini Kit following manufacturer's instructions, with slight modifications. Briefly, stool was incubated for 45 min at 37˚C in lysozyme buffer (22 mg/ml lysozyme, 20 mM TrisHCl, 2 mM EDTA, 1.2% Triton-x, pH 8.0). After the addition of 300 mg of 0.1 mm sterile zirconia beads, samples were bead-beat for 150 s. Samples were incubated at 95˚C for 5 min with InhibitEX Buffer, then incubated at 70˚C for 10 min with Proteinase K and Buffer AL. Following this step, the QIAamp Fast DNA Stool Mini Kit isolation protocol was followed, beginning with ethanol precipitation. DNA was quantified with the Qubit 2.0 Fluorometer (Life Technologies, Carlsbad, CA) using the dsDNA Broad Range Assay Kit and submitted for sequencing. DNA was sent to Argonne National Laboratory (Lemont, IL) for library preparation and sequencing using the Earth Microbiome Project protocols.[8] Amplified PCR libraries were bi-directionally sequenced using an Illumina MiSeq (Illumina, San Diego, CA). *16S rRNA gene analyses:* Raw sequencing reads were trimmed to a uniform length of 139 bp for the forward reads and 160 bp for the reverse reads as determined by quality drop off below a phred score of 20. Forward and reverse reads were joined with a minimum of 20 bp identical overlap and then de-replicated using the DADA2 plug-in using Quantitative Insights into Microbial Ecology [QIIME] 2.0 software.[9] Reads were taxonomically assigned using the ribosomal RNA database SILVA version 132.[10] Features with less than 10 total reads across the dataset were removed from analyses resulting in a total of 319 features. Relative abundance values and bray-curtis dissimilarity metric was calculated in R using the vegan package.

Transurethral UTI: Experimental UTI was performed as previously described.[11,12] Briefly, six to eight-week-old female mice were anesthetized and transurethrally inoculated with 10^7 colony

forming units of UPEC (strain UTI89) in 50 uL of PBS. At the indicated time points post inoculation, mice were re-anesthetized and sacrificed via cervical dislocation. After sacrifice, organs were aseptically harvested and UPEC were enumerated. IBCs were enumerated as previously described.[11,12]

Direct bladder inoculation with UPEC: The minimally invasive surgical UTI model was performed as previously described. A midline, ventral incision was made overlying the bladder in anesthetized six to eight-week-old male mice. The bladder was exposed through the incision and directly inoculated with 50 μl of PBS containing 10^7 CFU UPEC using a 30-gauge, 0.5-inch needle. After inoculation, the bladder was replaced and the abdomen was closed with simple, interrupted sutures. At the indicated time points post infection, mice were re-anesthetized, sacrificed, organs were harvested, and UPEC were enumerated.

Murine urothelial bladder isolation: Bladders were dissected from euthanized mice and placed in ice-cold phosphate buffered saline (PBS). To expose the urothelium, bladders were everted and incubated in 2.5 mg/mL Dispase II (Sigma-Aldrich) at 37°C. Following a sixty-minute incubation, the urothelium was removed with forceps under a dissecting microscope and pelleted by centrifugation at 300x*g* for five minutes. A single cell suspension was prepared by incubating the urothelial cells in 0.15% trypsin-EDTA at 37°C. After five minutes, the reaction was neutralized with an equal volume of DMEM/10% FBS and pelleted again by centrifugation. Cells were resuspended in Urolife A media (Lifeline Cell Technology, Frederick MD) at $4x10^5$ cells/mL and grown to confluency in 24 well plates seeded with 0.5 mL of cell suspension/well.

Urothelial antimicrobial neutralization assay: The antimicrobial activity of RNase 7 in isolated culture media from cultured murine urothelial cells was evaluated as described.[3] Briefly, three-day old culture media from confluent cells was inoculated with 10^3 CFU UPEC. When indicated, 0.2 μg of a polyclonal anti-RNase 7 antibody (Sigma-Aldrich) or an antibody for an irrelevant peptide (GAPDH, Cell Signaling) were added to each test isolate forty-five minutes before UPEC inoculation. Ninety minutes after UPEC incubation at 37 °C, serial dilutions of the reaction mixtures were plated on LB agar and the number of colony forming units were determined the following day.

Supplementary Tables and Table Legends:

Supplementary Table 1. Patient clinical demographics and laboratory studies. Patient demographics and clinical data on healthy female controls and girls and adolescents with a history of at least one UTI. Shown are the median values and the range (when applicable).

Demographics of control and UTI cohort (all females)			
	Control (*n*=29)	**Recurrent UTI** (*n*=29)	***P*-value**
Age (years)	9.8 (2.1-19.2)	6.8 (1.2-19.8)	0.043
Method of urine Collection	Clean Catch: 29	Clean Catch: 15 Catheterization: 14	N/A

Characteristics of recurrent UTI cohort		
Characteristic	**Findings**	***P*-value**
Initial UTI	Febrile: 10 Non-febrile: 19	N/A
Microbial cause of initial UTI	*E. coli*: 28 *S. saprophyticus*: 1	N/A
Time period between urine specimen collection and last UTI (days)	Median 86, range 22-281	N/A
Time period between urine specimen collection and last antibiotic dose (days)	Median 67, range 10-202	N/A
History of UTI antibiotic prophylaxis	No history of antibiotic prophylaxis: 25 History of antibiotic prophylaxis: 4[·]	N/A
Dipstick urinalysis result (*n*=29)	Negative: 22 Trace leukocyte esterase: 4 Moderate leukocyte esterase: 1 Small blood: 1 Large blood, trace leukocyte esterase: 1	N/A
VCUG results (*n*=17)	No VUR: 8 + VUR: 9 VUR grade I: 5 VUR grade II: 4	N/A
Renal/bladder ultrasound results (*n*=23)	Normal: 13 Pelviectasis/Mild hydronephrosis: 3 Kidney scarring: 2 Simple kidney cyst: 1 Bladder uroepithelial thickening: 4	N/A
Urine RNase 7/UCr (µg/mg)	Free void collection: median: 0.54, range 0.029-1.45 Catheterization collection: median: 0.77, range 0.14-1.91	0.314

[·]UTI antibiotic prophylaxis was discontinued in all patients (*n*=4) before collection of the urine specimen used in this analysis (median days 37, range 15-67).

Supplementary Table 2. UPEC susceptibility to antibiotics.
Antibiotic susceptibility testing was performed on clinical UPEC isolates using the Vitek 2 testing system.

	UPEC Strain 4	**UPEC Strain 51**	**UPEC Strain 58**
Ampicillin	Resistant	Resistant	Resistant
Amoxicillin/Clavulanic Acid	Resistant	Susceptible	Intermediate
Piperacillin/Tazobactam	Resistant	Susceptible	Susceptible
Cefalotin	Resistant	Resistant	Resistant
Cefazolin	Resistant	Resistant	Resistant
Cefuroxime	Resistant	Resistant	Resistant
Cefoxitin	Resistant	Resistant	Resistant
Cefpodoxime	Resistant	Resistant	Resistant
Ceftazidime	Resistant	Resistant	Resistant
Ceftriaxone	Resistant	Resistant	Resistant
Cefepime	Intermediate	Resistant	Susceptible
Gentamicin	Susceptible	Resistant	Resistant
Tobramycin	Resistant	Intermediate	Intermediate
Ciprofloxacin	Resistant	Resistant	Resistant
Levofloxacin	Resistant	Resistant	Resistant
Tetracycline	Resistant	Susceptible	Resistant
Nitrofurantoin	Intermediate	Resistant	Susceptible
Trimethoprim/Sulfamethoxazole	Susceptible	Resistant	Susceptible

Supplementary Table 3. Serum cytokine profiles in non-infected and UPEC infected mice. Serum cytokine profiles in non-infected and infected RNase 7 transgenic mice (+) and littermate controls (-). Mean cytokine concentrations and SEM are shown. *P*-values evaluate differences between genotypes (Kruskal-Wallis). IL-9 data is not represented due to analyte interference.

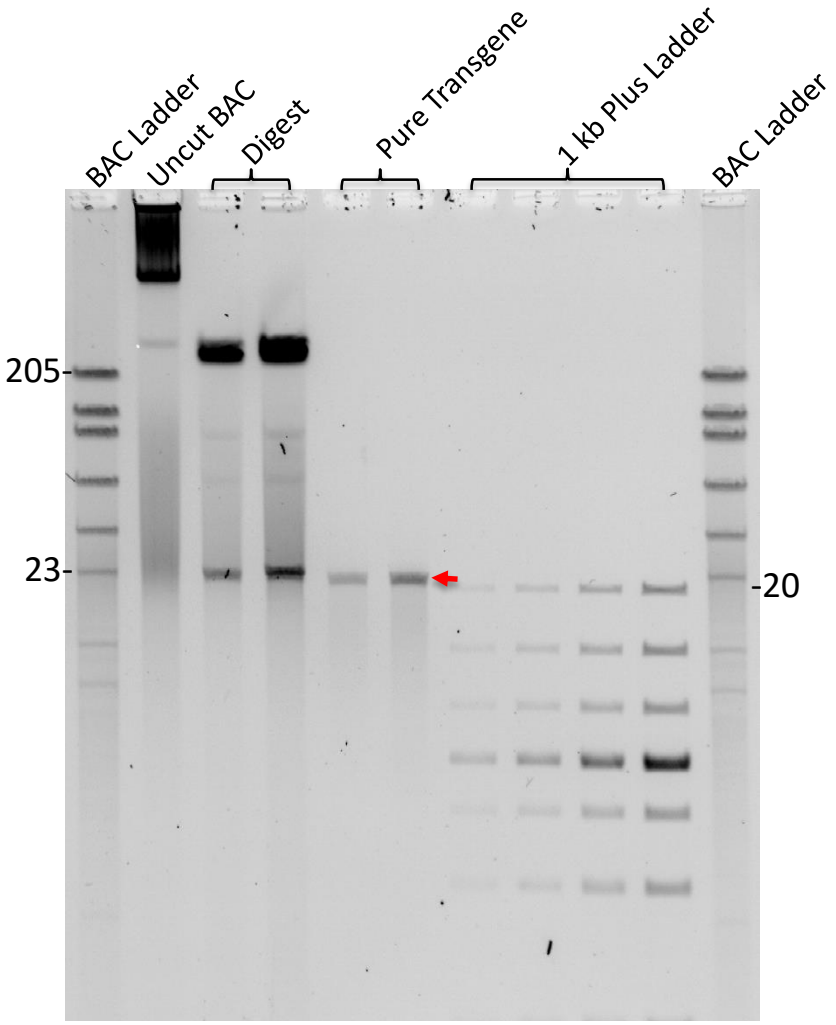
	RNase 7 (-) (*n*=5)	**RNase 7 (+)** (*n*=5)		**RNase 7 (-)** (*n*=5)	**RNase 7 (+)** (*n*=5)	
	Baseline			**24 HPI**		
Cytokine (pg/mL)	**Mean ± SEM**	**Mean** ± SEM	***P*-value**	**Mean ± SEM**	**Mean** ± SEM	***P*-value**
IL-1a	5.59 ± 0.44	5.11 ± 0.32	0.396	4.38 ± 0.36	4.98 ± 0.59	0.421
IL-1b	275.6 ± 17.58	242.1 ± 22.67	0.258	218.4 ± 25.86	241 ± 33.28	0.606
IL-2	23.64 ± 2.68	20.99 ± 3.55	0.559	18.33 ± 3.27	20.73 ± 4.24	0.667
IL-3	21.4 ± 0.89	25.03 ± 3.13	0.493	18.04 ± 1.36	18.96 ± 1.41	0.654
IL-4	6.26 ± 0.23	7.59 ± 0.76	0.315	5.4 ± 0.34	5.67 ± 0.39	0.621
IL-5	18.74 ± 1.51	17.13 ± 1.82	0.506	14.74 ± 1.54	17.4 ± 2.84	0.434
IL-6	19.11 ± 2.42	14.91 ± 1.56	0.218	14.23 ± 0.81	13.63 ± 1.72	0.759
IL-10	68.88 ± 6.26	64.91 ± 6.61	0.699	53.81 ± 5.24	52.74 ± 5.57	0.892
IL-12p40	62.87 ± 5.96	102.2 ± 21.51	0.095	51.43 ± 7.67	64.73 ± 11.83	0.373
IL-12p70	125.8 ± 5.29	159.8 ± 19.88	0.279	106.3 ± 8.53	111.8 ± 8.88	0.664
IL-13	279.9 ± 39.86	206.7 ± 39.32	0.207	194.4 ± 41.66	256.3 ± 65.4	0.448
IL-17	8.17 ± 0.43	12.73 ± 3.22	0.393	8.16 ± 1.78	7.62 ± 1.36	0.837
Eotaxin	859 ± 34.03	819.9 ± 79.59	0.912	752.4 ± 43.78	757.4 ± 61.7	0.949
G-GSF	43.68 ± 2.3	53 ± 6.36	0.185	38.33 ± 1.74	37.84 ± 3.38	0.902
GM-CSF	13.86 ± 0.73	14.81 ± 2.38	0.706	11.44 ± 0.98	12.24 ± 1.49	0.666
INF-G	48.61 ± 5.86	42.08 ± 6.34	0.459	43.53 ± 10.87	38.12 ± 6.73	0.683
KC	28.62 ± 10.81	19.43 ±3.78	0.631	16.4 ± 2.59	13.69 ± 1.26	0.374
MCP-1	287.2 ± 40.51	215 ± 25.96	0.184	212.4 ± 31.62	225.8 ± 34.35	0.78
MIP-1a	1.78 ± 0.24	2.21 ± 0.41	0.669	1.23 ± 0.23	1.36 ± 0.21	0.692
MIP-1b	28.22 ± 2.72	25.17 ± 3.76	0.353	22.51 ± 3.28	23.12 ± 4.22	0.912
RANTES	4.59 ± 0.18	5.57 ± 0.69	0.186	3.81 ± 0.29	4.09 ± 0.29	0.511
TNF-a	274.2 ± 24.07	263.1 ± 33.81	0.448	217.7 ± 25.64	219.5 ± 31.98	0.966

Supplementary Table 4. Bladder cytokine profiles in non-infected and UPEC infected mice. Bladder cytokine profiles in non-infected and infected RNase 7 transgenic mice (+) and littermate controls (-). Mean cytokine concentrations and SEM are shown. *P*-values evaluate differences between genotypes (Kruskal-Wallis). IL-4 and IL-5 data is not represented as concentrations were below the limits of detection at all time points.

	RNase 7 (-) (*n*=5)	**RNase 7 (+)** (*n*=5)		**RNase 7 (-)** (*n*=5)	**RNase 7 (+)** (*n*=5)		**RNase 7 (-)** (*n*=5)	**RNase 7 (+)** (*n*=5)	
	Baseline			**24 HPI**			**48 HPI**		
Cytokine (pg/mL)	**Mean ± SEM**	**Mean ± SEM**	***P*-value**	**Mean ± SEM**	**Mean ± SEM**	***P*-value**	**Mean ± SEM**	**Mean ± SEM**	***P*-value**
IL-1a	124.3±15.5	132.2±29.84	>0.999	170.9±12.85	194.4±26.87	0.971	170.7±12.5	160.4±16.06	>0.999
IL-1b	912.1±195.9	870.6±193.1	0.871	1201±104.1	1521±262.6	0.846	1186±167.62	1101±175.4	>0.999
IL-2	131.3±17.17	157.5±34.64	0.962	189.6±22.23	234.7±27.4	0.811	165.1±17.92	182.8±17.85	0.996
IL-3	19.62±2.05	15.46±1.26	0.37	18.8±1.42	15.15±1.47	0.62	18.9±1.92	15.1±0.52	0.581
IL-6	18.01±3.06	18.86±3.89	>0.999	42.7±4.05	46.85±3.39	0.998	55.33±8.69	49.85±11.56	0.994
IL-9	816.8±101.8	836.6±115.2	>0.999	1133±88.24	1233±218.8	>0.999	1133±88.24	1121±87.13	>0.999
IL-10	40.02±1.64	34.64±2.38	0.881	43.83±1.93	48.5±5.57	0.955	41.55±5.97	43.53±4.19	0.999
IL-12p40	34.58±13.64	33.5±12.54	0.754	106.9±11.36	115.5±103.7	0.997	167±21.37	146.9±10.98	0.878
IL-12p70	120.2±3.54	121.5±8.22	>0.999	138.3±15.97	202.3±48.46	0.461	113.8±30.37	79.55±18.97	0.917
IL-13	1055±244.7	1207±316.1	0.995	1616±146	1859±250.2	0.977	1407±127.5	1239±97.04	0.996
IL-17	31.94±0.82	34.62±4.18	>0.999	56.23±4.84	75.35±15.86	0.536	79.65±19.71	99.65±32.13	0.947
Eotaxin	2229±225.3	1705±183.7	0.422	2330±43.03	1847±346.6	0.624	1871±149.9	1964±166.4	0.996
G-GSF	54.96±15.51	33.32±0.82	0.963	87.75±10.04	144.7±59.28	0.782	161.8±45.1	82.3±18.85	0.479
GM-CSF	71.42±13.69	48.24±10.74	0.151	62.98±15.79	43.75±15.2	0.904	57.5±17.5	31.2±13.7	0.976
INF-G	87.5±7.02	83.46±5.32	0.998	97.05±9.89	121.9±10.53	0.307	91.53±5.78	99.8±8.89	0.978
KC	26.14±4.413	20.22±1.41	>0.999	68.23±20.03	72.83±11.74	>0.999	137.4±35.52	129.6±34.4	0.999
MCP-1	113.8±25.93	71.28±13.83	0.982	261.1±48.41	256.9±39.19	>0.999	377.4±84.53	319±61.44	0.957
MIP-1a	29.3±1.49	27±1.84	0.998	53.75±9.12	65.08±6.93	0.667	45.58±5.17	56.1±4.71	0.729
MIP-1b	196.5±60.01	138.9±35.59	0.961	288.9±52.95	261.6±48.26	0.999	231.6±45.98	269.9±74.01	0.996
RANTES	73.4±6.89	75.56±13.75	>0.999	180.8±34.46	235.7±32.6	0.457	146.8±10	155±13.4	0.999
TNF-a	591.9±90.29	610.2±105.6	>0.999	968.4±76.31	932.7±163.7	>0.999	925.3±83.62	851.5±129.9	0.997

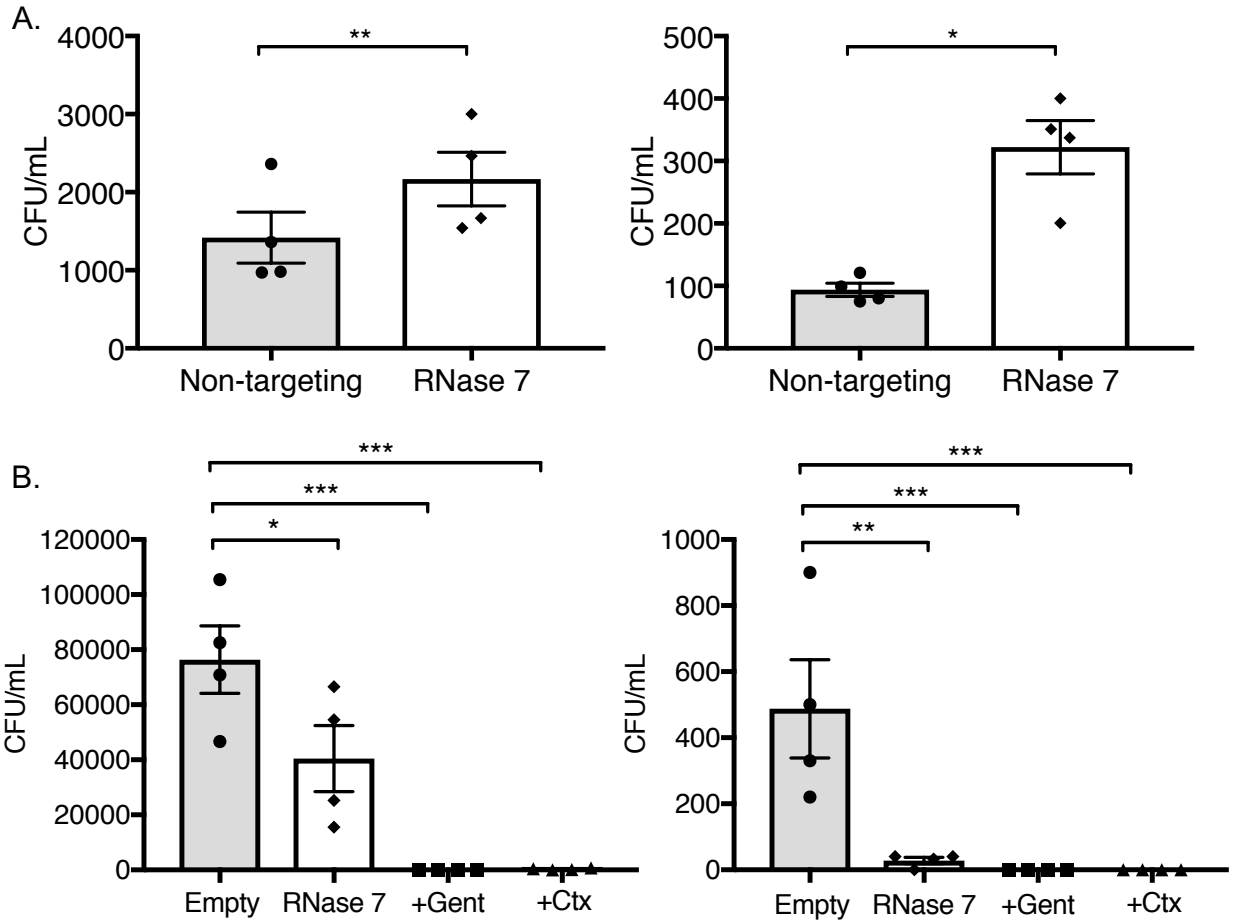
Supplementary Figures and Figure Legends:

Supplementary Figure 1.



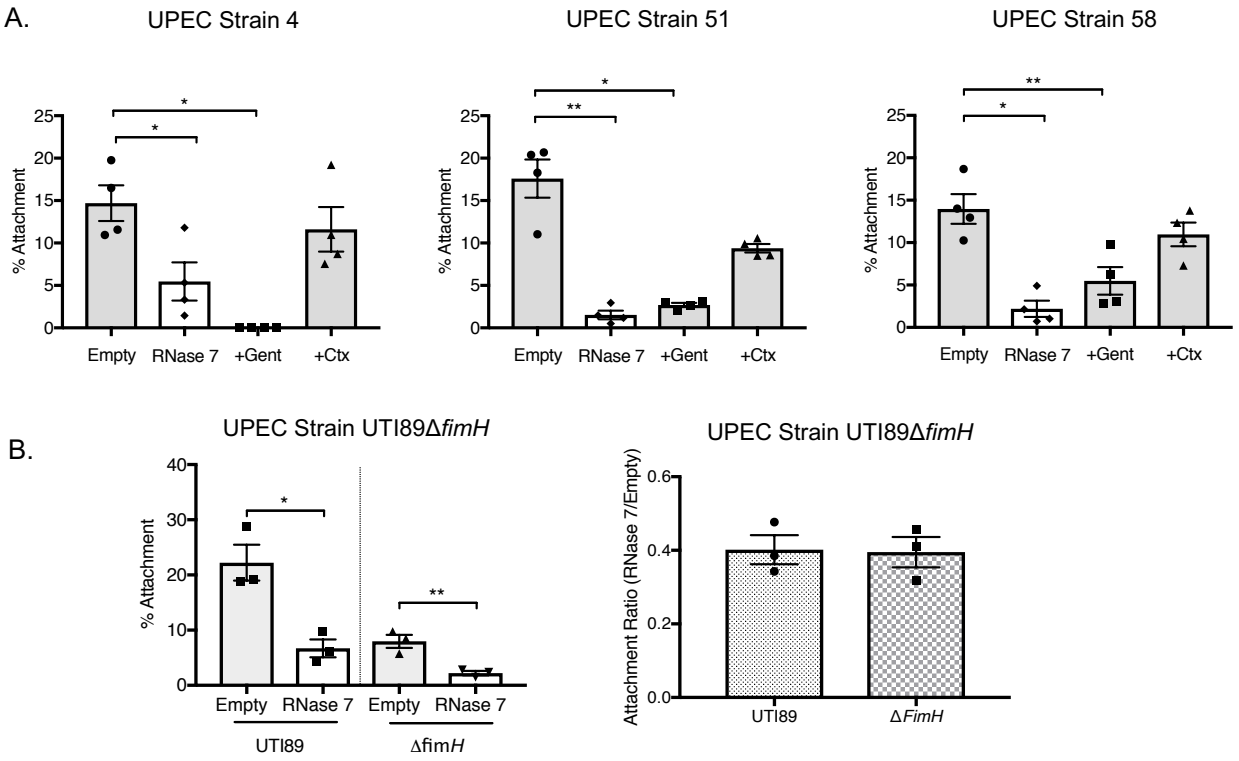
***RNASE7* transgene purification**. Pulsed field gel electrophoresis of the *RNASE7* transgene. Positions of 205 kb and 23 kb bands in the BAC ladder (left) and position of the 20kb band in the Plus ladder (right) are indicated. The red arrow marks the position of the purified transgene fragment.

Supplementary Figure 2.



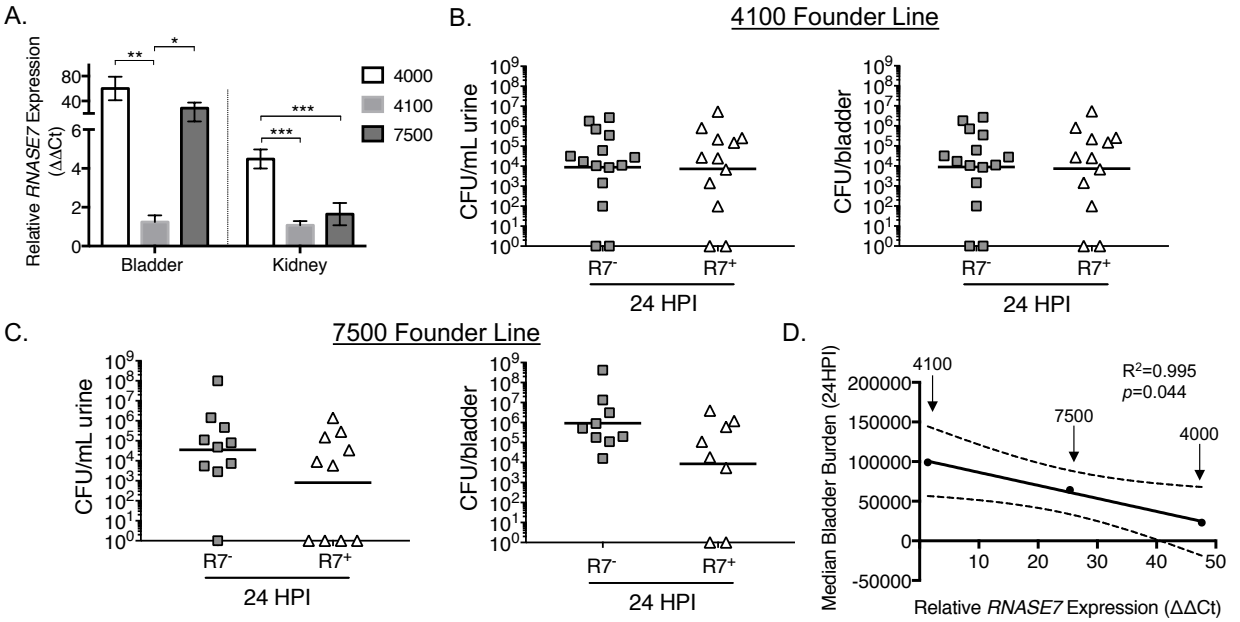
Silencing RNase 7 increases UPEC susceptibility while RNase 7 overexpression decreases UPEC susceptibility. (A) Human 5637 urothelial cells were transiently transfected with a *RNASE7* or a non-targeting control siRNA pool. UPEC attachment (left) and invasion (right) assays were performed as outlined in the methods. Shown are the CFU/mL of UPEC (UTI89) adhering to the cellular surface or invading the cells. Graphs show the mean and SEM from 4 independent experiments performed in triplicate (n=4). These results supplement the normalized data (to total CFU) shown in **Figure 1D**. Asterisks denote significant P-values for the pairwise comparisons (student's t-test). (B) Human UROtsa cells were stably infected with retroviral constructs expressing full-length RNase 7 or empty vector. UPEC attachment (left) and invasion (right) assays were performed in RNase 7 overexpressing cells and control cells (empty). As positive controls, the gentamicin (gent) or ceftriaxone (ctx) were added to the culture media of the control cells. Shown are the CFU/mL UPEC (UTI89) adhering to the cellular surface or invading the UROtsa cells. Graphs show the mean and SEM from 4 independent experiments performed in quadruplicate (n=4). These findings supplement the normalized data (to total CFU) shown in **Figure 2F**. Asterisks identify significant P-values, for the indicated pairwise comparison, as determined by one-way ANOVA with Tukey's modification. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Supplementary Figure 3.



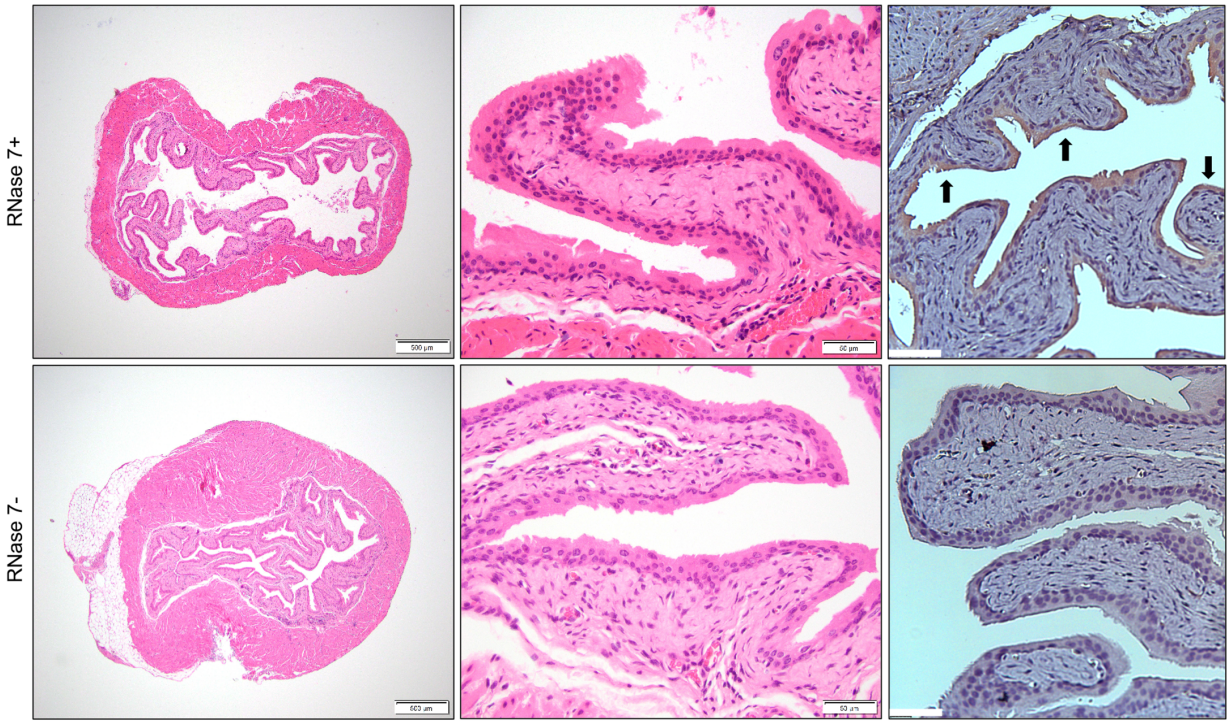
RNase 7 overexpression prevents MDR-UPEC attachment *in vitro*.
Human UROtsa cells were stably infected with retroviral constructs expressing full-length RNase 7 or empty vector. (**A**) Cells were challenged with MDR-UPEC isolates described in the supplementary methods. MDR-UPEC attachment assays were performed in RNase 7 overexpressing cells and control cells (empty). As controls, the gentamicin (gent) or ceftriaxone (ctx) were added to the culture media of the control cells. Shown are the percentage of different UPEC strains adhering to the cellular surface. Graphs show the mean and SEM from 4 independent experiments performed in quadruplicate (n=4). Asterisks identify significant P-values, for the indicated pairwise comparison, as determined by one-way ANOVA with Tukey's modification. (**B**) Cells were also challenged with UTI89 or UTI89Δ*fimH*. Shown are the percentage of UPEC adhering to the cellular surface (left). To account for this attenuated attachment of UTI89Δ*fimH*, the ratio of UPEC attachment (UTI89 and UTI89Δ*fimH*) in control cells and RNase 7 overexpressing cells *is shown*. Asterisks denote significant P-values for the pairwise comparisons (student's t-test). * $P < 0.05$, ** $P < 0.01$.

Supplementary Figure 4.



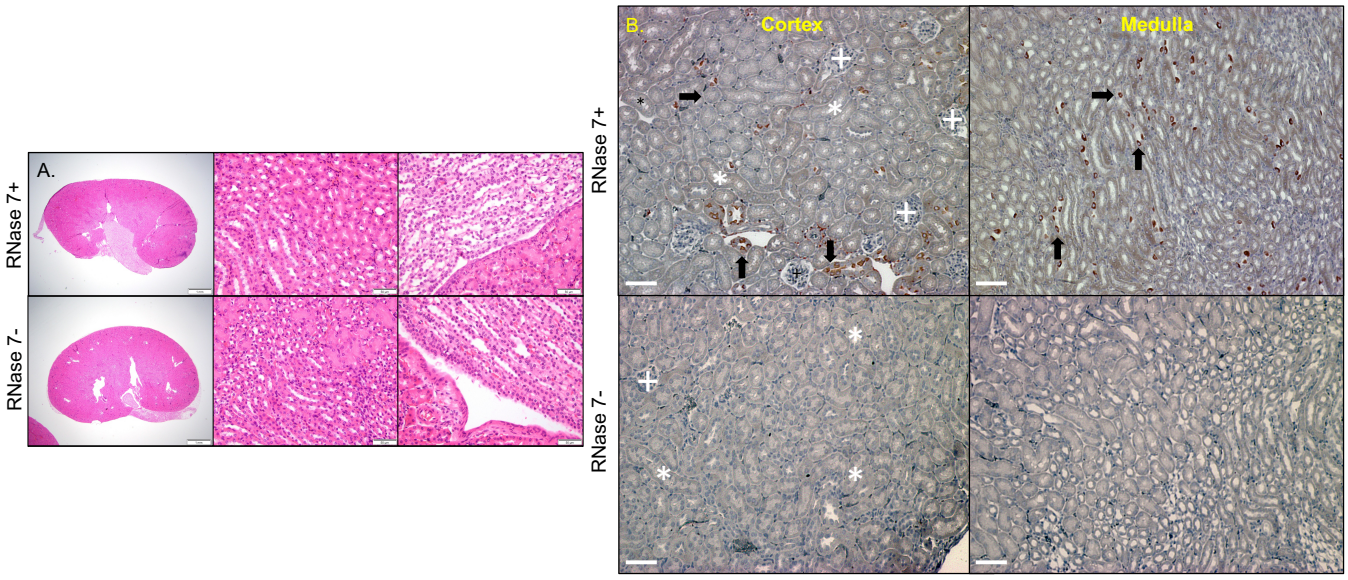
***RNASE7* mRNA expression in founder transgenic mouse lines.**
(**A**) Relative *RNASE7* transcript expression in bladder and kidney tissues harvested from hemizygous RNase 7 transgenic mouse founder lines (n=6 mice/founder line). Asterisks identify significant P-values, for the indicated pairwise comparison (Kruskal-Wallis). * $P < 0.05$, ** $P < 0.01$, ** $P < 0.001$. This data supplements the findings in **Figure 3**. (**B/C**) Female RNase 7 transgenic mice and littermate controls from founder lines (B) 4100 and (C) 7500 were subjected to experimental UTI. At 24 HPI, urine was collected, bladders were harvested, and UPEC colonies were enumerated. Each point denotes burden in a separate mouse. The horizontal line indicates the geometric mean of each group. (**D**) Pearson correlation analysis demonstrates that median UPEC bladder burden at 24HPI (calculated from panels B/C and Figure 4E) inversely correlates to relative bladder *RNASE7* expression (as shown in panel A). The 95% confidence intervals are represented by the dashed lines. The arrows above identify median bladder bacterial burden for each founder line.

Supplementary Figure 5.



Murine bladder histology and RNase 7 urothelial localization.
Representative low and high-power micrographs of paraffin-embedded, fixed bladder tissues from RNase 7 transgenic mice (top panels) and littermate controls (bottom panels) stained with hematoxylin & eosin. Immunohistochemistry (right panels) localizes RNase 7 to the urothelium (brown, arrows). Magnification 20X. These images supplement the findings shown in **Figure 3**.

Supplementary Figure 6.



Murine kidney histology and RNase 7 localization.
(**A**) Representative low and high-power micrographs of paraffin-embedded, fixed kidney tissues from RNase 7 transgenic mice (top panels) and littermate controls (bottom panels) stained with hematoxylin & eosin. Micrographs show intact kidney (left panels), corticomedullary junction (center panels) and renal pelvis/papilla (right panels). (**B**) Immunohistochemistry shows cell-specific RNase 7 expression in cortical (left) and medullary (right) collecting tubules in RNase 7 transgenic mice (top panels, arrows). (+) denote glomeruli in the renal cortex and (*) identify proximal tubules. Magnification 20X. Scale bars denote 50 microns. RNase 7 immunoreactivity was not identified in littermate controls (bottom panels). These images supplement the images shown in **Figure 3**.

Supplemental References:

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