

Supplementary Table 1. The biographic information of seven healthy dogs.

Breed	Sex	Age (years)	Body weight (kg)
Beagle	Male	4.8	11.3
Beagle	Male	1.6	10.9
Beagle	Male	6.1	11.5
Beagle	Male	6.4	11.6
Beagle	Male	6.1	10.9
Beagle	Male	1.3	11.4
Beagle	Male	1.2	10.1

Supplementary Table 2. Sequences of oligonucleotide primers.

Gene	Primer	Sequence (5'-3')	GenBank accession number	Size (base pair)
<i>NLRP3</i> ^{a)}	Forward	ATGGCTGTAGCCTCACCTCACAC	XM_843284.5	135
	Reverse	TTAGCACTTCGCAGAGCAGCA		
<i>NLRP6</i> ^{b)}	Forward	AGCCGGGTCTGGTCATCATC	XM_540513.5	89
	Reverse	ACCTTCAGGGCTTTATAGGGCATC		
<i>NLRP12</i> ^{c)}	Forward	GAGATGAACTGCACCCATGTCAA	XM_003432638.4	116
	Reverse	TGGCTCTAGGCAAAGCTCCAA		
<i>GAPDH</i> ^{d)}	Forward	CATTGCCCTCAATGACCACT	NM_001003142.2	105
	Reverse	TCCTTGGAGGCCATGTAGAC		
<i>TBP</i> ^{e)}	Forward	CTATTTCTTGGTGTGCATGAGG	XM_849432.4	96
	Reverse	CCTCGGCATTCAGTCTTTTC		
<i>SDHA</i> ^{f)}	Forward	GCCTTGGATCTCTTGATGGA	XM_535807.5	92
	Reverse	TTCTTGGCTCTTATGCGATG		
<i>HMBS</i> ^{g)}	Forward	TCACCATCGGAGCCATCT	XM_546491	112
	Reverse	GTTCCCACCACGCTCTTCT		

GAPDH, *TBP*, and *SDHA* were used as reference genes for the duodenal mucosa; *GAPDH*, *TBP*, and *HMBS* were used as reference genes for the colonic mucosa.

^{a)}Nucleotide-binding oligomerization domain-like receptor family pyrin domain-containing 3, ^{b)}Nucleotide-binding oligomerization domain-like receptor family pyrin domain-containing 6, ^{c)}Nucleotide-binding oligomerization domain-like receptor family pyrin domain-containing 12, ^{d)}Glyceraldehyde 3-phosphate dehydrogenase, ^{e)}TATA-binding protein, ^{f)}Succinate dehydrogenase complex, subunit A, ^{g)}Hydroxymethylbilane synthase.

Supplementary Table 3. Clinical and histopathological characteristics of 35 dogs with chronic enteropathy.

Group ^{a)} (<i>n</i>)	Age (years)	Sex ^{b)} (<i>n</i>)	Body weight (kg)	Breeds (<i>n</i>)	CCECAI ^{c)}	Histopathological diagnosis in the duodenum (<i>n</i>)	WSAVA ^{d)} score in the duodenum	Histopathological diagnosis in the colon (<i>n</i>)	WSAVA score in the colon	Clinical signs (<i>n</i>)
ARE (4)	6.8 (4.0-11.6)	M (1), F (1), Fs (2)	12.0 (5.2-33.6)	Beagle (1), Border Collie (1), Flat-Coated Retriever (1), Miniature Dachshund (1)	7 (1-11)	Lymphoplasmacytic duodenitis (4)	10 (4-12)	Lymphoplasmacytic colitis (4)	6.5 (2-8)	Vomiting (4), Large bowel diarrhea (2), Small and large bowel diarrhea (1)
FRE (11)	8.0 (2.1-14.0)	M (2), Mn (3), F (2), Fs (4)	4.1 (1.8-12.4)	Maltese (2), Miniature Dachshund (2), Toy Poodle (2), Miniature Schnauzer (1), Papillon (1), Pomeranian (1), Shetland Sheepdog (1), Shiba (1)	4 (2-16)	Lymphoplasmacytic duodenitis (10), Lymphoplasmacytic and eosinophilic duodenitis (1)	8 (4-11)	Lymphoplasmacytic colitis (9)	5 (1-8)	Vomiting (6), Large bowel diarrhea (5), Small and large bowel diarrhea (4)
IRE (18)	10.0 (1.8-14.1)	M (2), Mn (10), F (2), Fs (4)	6.4 (3.3-24.0)	Pembroke Welsh Corgi (2), Shiba (2), American Pit Bull Terrier (1), Bichon Frise (1), Border Collie (1), Boston Terrier (1), Brussels Griffon (1), Cavalier King Charles Spaniel (1), Cross-breed (1), French Bulldog (1), Jack Russell Terrier (1), Maltese (1), Miniature Dachshund (1), Pug (1), Toy Poodle (1), Wire Fox Terrier (1)	7.5 (3-14)	Lymphoplasmacytic duodenitis (13), Lymphoplasmacytic and eosinophilic duodenitis (3), Lymphoplasmacytic and neutrophilic duodenitis (1), Lymphoplasmacytic , neutrophilic, and eosinophilic duodenitis (1)	10 (3-15)	Lymphoplasmacytic colitis (17), Lymphoplasmacytic and eosinophilic colitis (1)	5 (1-9)	Vomiting (6), Small bowel diarrhea (6), Large bowel diarrhea (3), Small and large bowel diarrhea (9)
NRE (2)	10.3 (7.5-13.0)	Mn (1), F (1)	10.5 (8.4-12.6)	Pembroke Welsh Corgi (1), Shiba (1)	12.5 (11-14)	Lymphoplasmacytic duodenitis (2)	9.5 (8-11)	Lymphoplasmacytic colitis (2)	3 (2-4)	Vomiting (1), Small bowel diarrhea (1), Small and large bowel diarrhea (1)

Age, body weight, CCECAI, and WSAVA score are shown as median (range).

^{a)}ARE: Antibiotic-responsive enteropathy; FRE: Food-responsive enteropathy; IRE: Immunosuppressant-responsive enteropathy; NRE: Non-responsive enteropathy, ^{b)}M: Male, intact; Mn: Male, neutered; F: Female, intact; Fs: Female, spayed, ^{c)}Canine chronic enteropathy clinical activity index, ^{d)}World small animal veterinary association.

Supplementary Table 4. Hematological and blood biochemical analyses of 35 dogs with chronic enteropathy.

Variable	Median (range)	Reference interval	<i>n</i>
White blood cell ($\times 10^2/\mu\text{l}$)	96 (45-295)	50.5-167.6	35/35
Packed cell volume (%)	47.1 (27.6-58.9)	37.3-61.7	35/35
Platelet ($\times 10^4/\mu\text{l}$)	42.1 (10.7-86.4)	14.8-48.4	35/35
Glucose (mg/dl)	107 (78-148)	75-128	35/35
Blood urea nitrogen (mg/dl)	16.6 (6.7-45.7)	9.2-29.2	35/35
Creatinine (mg/dl)	0.7 (0.4-2.0)	0.4-1.4	35/35
Aspartate aminotransferase (U/l)	36 (22-92)	17-44	33/35
Alanine aminotransferase (U/l)	46 (19-509)	17-78	35/35
Alkaline phosphatase (U/l)	152 (45-954)	47-254	35/35
Total bilirubin (mg/dl)	0.2 (0.1-0.4)	0.1-0.5	34/35
Total cholesterol (mg/dl)	156.5 (49-326)	111-312	34/35
Total protein (g/dl)	5.4 (3.0-8.1)	5.0-7.2	35/35
Albumin (g/dl)	2.6 (1.0-4.0)	2.6-4.0	35/35
Lipase ^{a)} (U/l)	83.5 (11-1634)	<160	26/35
Trypsin-like immunoreactivity (ng/ml)	27.0 (7.5-50.0)	>5.2	29/35
C-reactive protein (mg/dl)	0.4 (0.0-20.0)	<1.0	34/35
Calcium (mg/dl)	10.0 (6.2-16.0)	9.3-12.1	28/35
Phosphorus (mg/dl)	3.7 (1.7-4.9)	1.9-5.0	27/35
Sodium (mmol/l)	148 (140-155)	141-152	35/35
Potassium (mmol/l)	4.1 (3.4-5.5)	3.8-5.0	35/35
Chloride (mmol/l)	112 (96-123)	102-117	35/35

^{a)}FUJI DRI-CHEM lipase

Supplementary Table 5. The correlations between mRNA expression levels of *NLRP3* and *NLRP12* in the colonic mucosa of dogs with chronic enteropathy or food-responsive enteropathy.

	CE ^{a)}	FRE ^{b)}
	<i>NLRP3</i> ^{c)}	<i>NLRP3</i>
<i>NLRP12</i> ^{d)}	$r_s=0.3636, P=0.0375$	$r=0.3272, P=0.3901$

The correlation between mRNA expression levels of *NLRP3* and *NLRP12* in the colonic mucosa of dogs with CE was analyzed by the Spearman's rank correlation coefficient (r_s), while that was calculated by the Pearson product-moment correlation coefficient (r) in dogs with FRE.

^{a)}Chronic enteropathy, ^{b)}Food-responsive enteropathy, ^{c)}Nucleotide-binding oligomerization domain-like receptor family pyrin domain-containing 3, ^{d)}Nucleotide-binding oligomerization domain-like receptor family pyrin domain-containing 12.

Supplementary Table 6. The number of dogs that developed large bowel diarrhea in dogs with chronic enteropathy.

	Large bowel diarrhea	
	+	-
ARE	3	1
FRE	9	2
IRE/NRE	13	7

The numbers in the table indicate the number of dogs. The Fisher's exact test did not detect a significant association between the number of dogs that developed large bowel diarrhea and ARE, FRE, or IRE/NRE ($P=0.7492$).

^{a)}ARE: Antibiotic-responsive enteropathy; FRE: Food-responsive enteropathy; IRE: Immunosuppressant-responsive enteropathy; NRE: Non-responsive enteropathy.

Supplementary Table 7. The correlations between mRNA expression levels of inflammasome sensor subunits and clinical or histopathological severity score in the colonic mucosa of dogs with chronic enteropathy or food-responsive enteropathy

	CE ^{a)}		FRE ^{b)}	
	<i>NLRP3</i> ^{c)}	<i>NLRP12</i> ^{d)}	<i>NLRP3</i>	<i>NLRP12</i>
CCECAI ^{e)}	$r_s = -0.12, P = 0.51$	$r_s = -0.14, P = 0.45$	$r_s = 0.41, P = 0.27$	$r_s = 0.36, P = 0.34$
WSAVA ^{f)} score	$r_s = 0.13, P = 0.46$	$r_s = 0.15, P = 0.40$	$r_s = 0.57, P = 0.24$	$r_s = 0.13, P = 0.74$

The correlations were analyzed by the Spearman's rank correlation coefficient (r_s).

^{a)}Chronic enteropathy, ^{b)}Food-responsive enteropathy, ^{c)}Nucleotide-binding oligomerization domain-like receptor family pyrin domain-containing 3,

^{d)}Nucleotide-binding oligomerization domain-like receptor family pyrin domain-containing 12, ^{e)}Canine chronic enteropathy clinical activity index,

^{f)}World small animal veterinary association.