

Supplementary Materials: Local Colonic Administration of a Serine Protease Inhibitor Improves Post-Inflammatory Visceral Hypersensitivity in Rats

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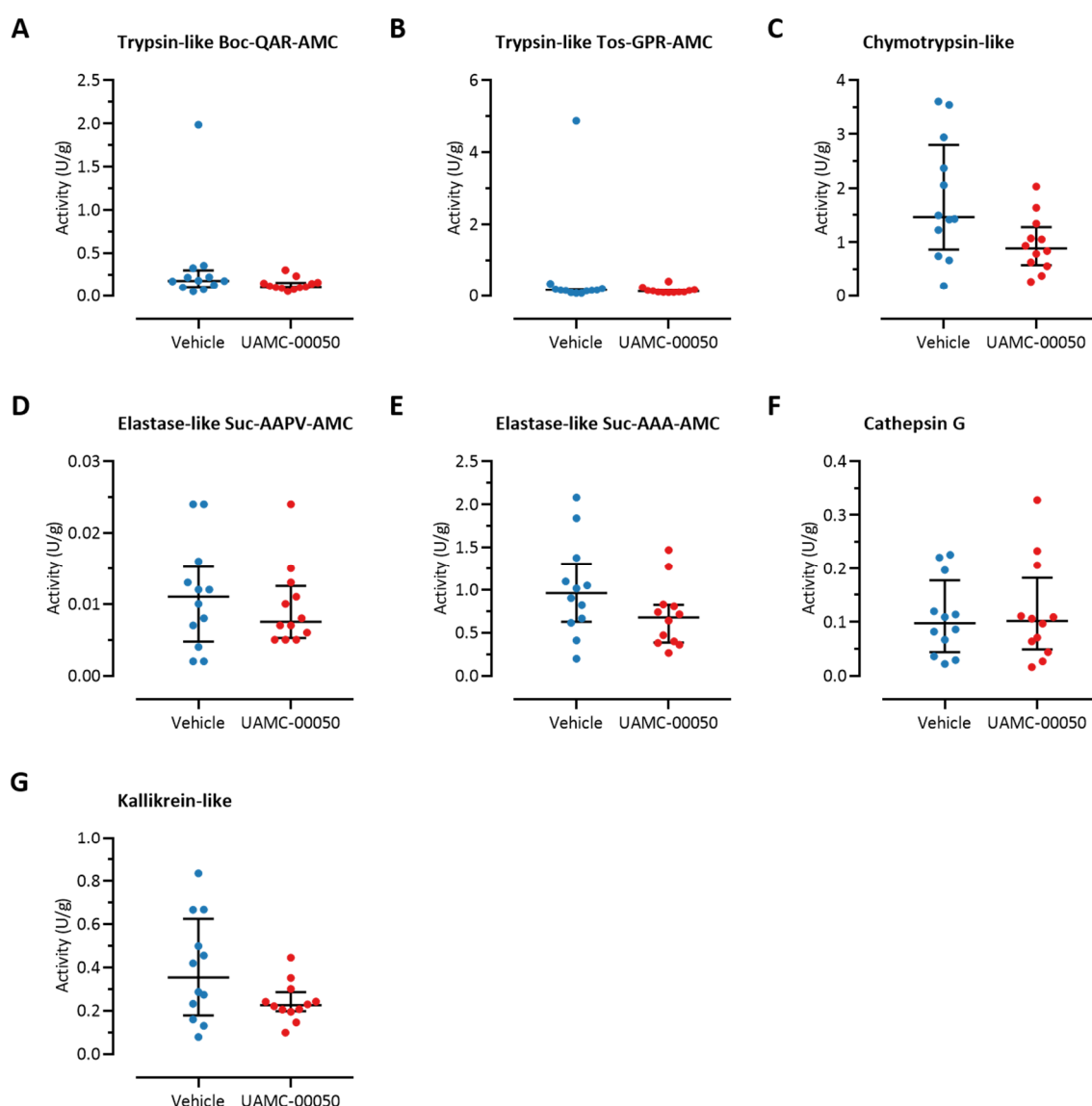


Figure S1. Proteolytic activities in colonic tissue of control rats treated with UAMC-00050 (5 mg/kg) or vehicle (5% DMSO). (a) Trypsin-like activity using Boc-Gln-Ala-Arg-AMC. (b) Trypsin-like activity using Tos-Gly-Pro-Arg-AMC. (c) Chymotrypsin-like activity. (d) Elastase-like activity using Suc-Ala-Ala-Pro-Val-AMC. (e) Elastase-like activity using Suc-Ala-Ala-Ala-AMC. (f) Cathepsin G activity. (g) Kallikrein activity. Proteolytic activities were analysed using two-way ANOVA with factors ‘treatment’ and ‘group’, followed by Mann-Whitney U tests with Bonferroni correction for multiplicity; $n = 12$ per group. Analysis was performed on the full dataset (involving the 4 combinations of control/post-colitis and vehicle/UAMC-00050), but visualization is split across Figure 2, Figure 5 and Supplementary Figure 1 to allow for easier interpretation of the data. Data are presented including median and IQR.

Table S1. Scoring system for inflammation – colonoscopy.

Item	Aspect	Score
Ulceration	Normal mucosa	0
	Hyperemia	1
	Ulceration(s) occupying < 25% of the lumen circumference	2
	Ulceration(s) occupying 25 – 50% of the lumen circumference	3
	Ulceration(s) occupying > 50% but not the full circumference	4
	Ulceration(s) occupying the full circumference	5
Stenosis	Absent	0
	Present	1
Edema	Absent	0
	Present	1
Bleeding	Absent	0
	Present	1
Extent of damage	Range 0 – 10 cm	0 – 10
Total damage score		0 – 19

Table S2. Scoring system for inflammation – macroscopy.

Macroscopic Finding	Score
Normal mucosa	0
Localized hyperemia	1
Ulceration(s) without hyperemia or bowel wall thickening	2
Ulceration(s) with hyperemia or bowel wall thickening at 1 site	3
Ulceration(s) with hyperemia or bowel wall thickening at 2 or more sites	4
Major sites of damage extending up to 1 cm along the length of the colon	5
Major sites of damage extending up > 1 cm along the length of the colon	6 – 10
Total damage score	0 – 10

Table S3. Scoring system for inflammation – microscopy.

Histopathological finding	Normal	Minimal	Mild	Maximal
Inflammatory infiltrate	0	1	2	3
Number of infiltrated layers	0	1	2	3
Mucosal tissue damage	0	1	2	3
Mucosal edema	absent = 0; present = 1			
Total damage score	0 – 10			

Table S4. Pharmacokinetic parameters.

Parameter	Unit	Value
A	ng/mL	500.7
Alpha	1/min	0.119
B	ng/mL	17.9
Beta	1/min	0.010
k10	1/min	0.087
k12	1/min	0.028
k21	1/min	0.014
t1/2Alpha	min	5.800
t1/2Beta	min	66.5
C0	ng/ml	518.7
V	(mg)/(ng/mL)	0.006
CL	(mg)/(ng/mL)/min	0.000507175
V2	(mg)/(ng/mL)	0.011

CL2	(mg)/(ng/mL)/min	0.000162136
AUC 0-t	ng/mL*min	5422
AUC 0-inf	ng/mL*min	5915
AUMC	ng/mL*min ²	200,489
MRT	min	33.9
Vss	mg/(ng/mL)	0.017
