

Supplementary figures

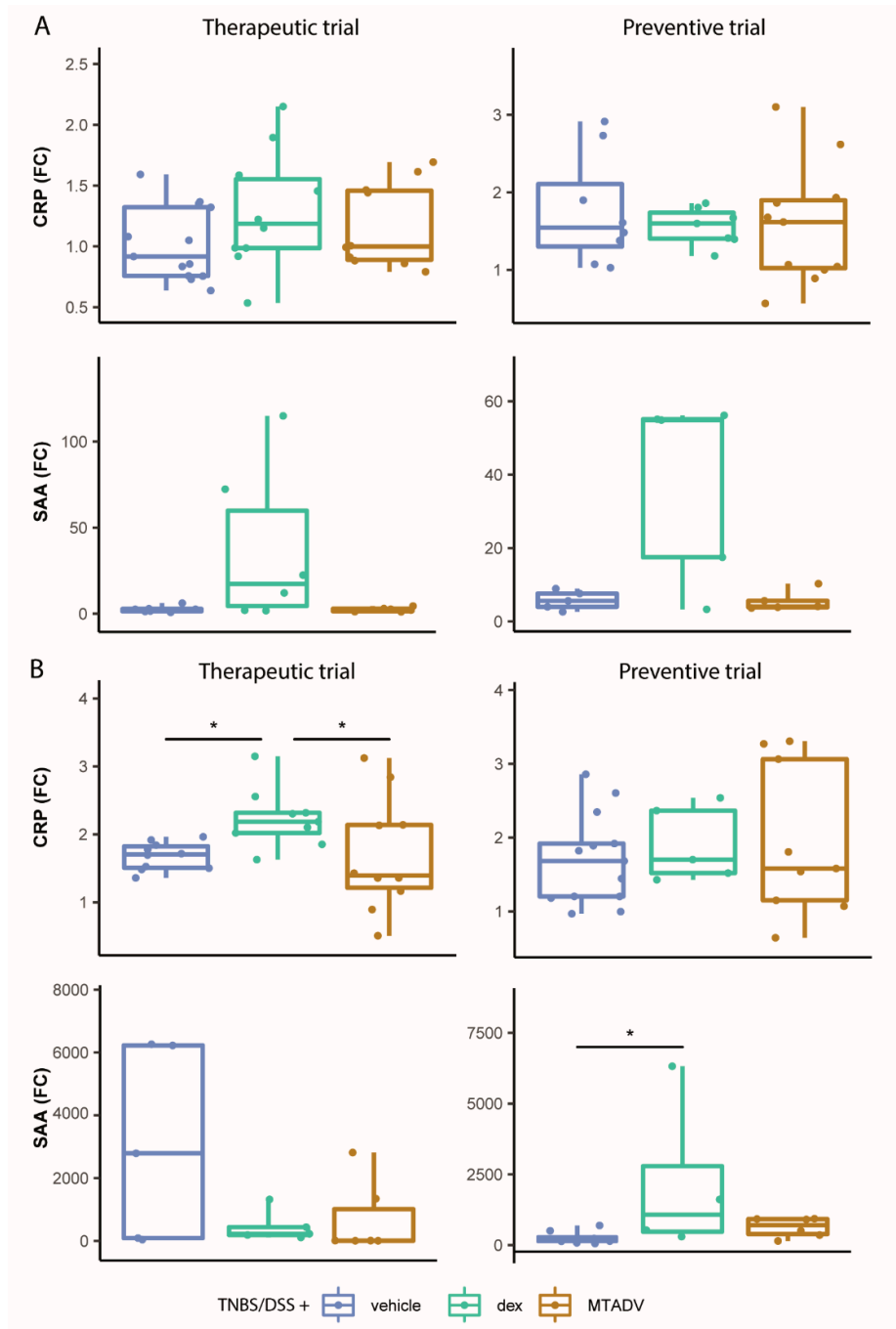


Figure S1. Concentration of plasmatic APP in each treatment group. APP protein concentration is expressed as ng/ml for CRP and ug/ml for SAA for both therapeutic and preventive trials in the TNBS (A) and DSS (B) models. Data are represented as points summarized in boxplots indicating IQR and bars indicating maximum and minimum. The median point is depicted as a bar inside the box. Treatment groups are differentiated using colours. Asterisks mark significance between the groups indicated by lines (Kruskal-Wallis test with a post-hoc Dunn's test). Significance levels are: *p-value \leq 0.05; **p-value \leq 0.01; ***p-value \leq 0.001. APP, acute-phase protein; CRP, C-reactive protein; dex, dexamethasone; DSS, dextran sulphate sodium; FC, fold change; IQR, interquartile range; SAA, Serum Amyloid Antigen; MTADV, 5-MER peptide methionine-threonine-alanine-aspartic acid-valine; TNBS, trinitrobenzenesulfonic acid.

Supplementary tables

Table S1. BLI raw data correlation to mRNA from inflammatory and oxidative stress markers in all the animal groups stratified by sex.

		<i>Il10</i>	<i>Tgfb1</i>	<i>Il6</i>	<i>Vegfa</i>	<i>Tjp1</i>	<i>Nos2</i>	<i>Tnfa</i>	<i>Hif1a</i>	<i>Il1b1</i>
Both sexes	pvalue	0.70	0.04	0.06	0.01	0.02	0.01	0.032	0.87	0.09
	rho	-0.04	-0.19	0.18	-0.24	-0.22	0.25	0.20	0.02	0.16
F	pvalue	0.03	0.26	0.01	0.96	0.36	0.25	0.072	0.32	0.03
	rho	0.29	0.15	0.33	0.00	-0.12	0.15	0.24	0.13	0.29
M	pvalue	0.63	0.00	0.81	0.00	0.02	0.01	0.22	0.57	0.63
	rho	0.07	-0.43	0.03	-0.46	-0.3	0.34	0.17	-0.08	0.07

Spearman correlation analyses. Red and blue colors indicate significant ($p \leq 0.05$) negative and positive correlations, respectively. BLI; Bioluminescence intensity; DSS, dextran sulfate sodium; F, female; M, male; TNBS, trinitrobenzenesulfonic acid.

Table S2. BLI raw data correlation to mRNA anti-inflammatory/pro-inflammatory markers of all the animal together and stratified by sex

		<i>Il10/Il6</i>	<i>Tgfb1/Il6</i>	<i>Il10/Tnfa</i>	<i>Tgfb1/Tnfa</i>	<i>Il10/Il1b1</i>	<i>Tgfb1/Il1b1</i>
Both sexes	pvalue	0.00	0.02	0.01	0.00	0.00	0.02
	rho	-0.31	-0.22	-0.28	-0.25	-0.32	-0.22
F	pvalue	0.00	0.02	0.03	0.03	0.00	0.03
	rho	-0.40	-0.30	-0.32	-0.29	-0.44	-0.29
M	pvalue	0.15	0.36	0.09	0.00	0.10	0.25
	rho	-0.22	-0.13	-0.26	-0.37	-0.25	-0.16

Spearman correlation analyses. Red and blue colors indicate significant ($p \leq 0.05$) negative and positive correlations. BLI, Bioluminescence intensity; DSS, dextran sulfate sodium; F, female; M, male; TNBS, trinitrobenzenesulfonic acid.

Table S3. BLI correlation to mRNA anti-inflammatory/pro-inflammatory markers of all the animals stratified by model and sex

				<i>Il10/Il6</i>	<i>Tgfb1/Il6</i>	<i>Il10/Tnfa</i>	<i>Tgfb1/Tnfa</i>	<i>Il10/Il1b1</i>	<i>Tgfb1/Il1b1</i>
Both sexes	TNBS	Therapeutic	pvalue	0.62	0.68	0.53	0.41	0.36	0.45
			rho	-0.12	-0.08	-0.15	-0.15	-0.23	-0.14
		Preventive	pvalue	0.62	0.68	0.53	0.41	0.36	0.45
			rho	-0.12	-0.08	-0.15	-0.15	-0.23	-0.14
	DSS	Therapeutic	pvalue	0.00	0.01	0.06	0.04	0.01	0.03
			rho	-0.48	-0.48	-0.36	-0.40	-0.47	-0.41
		Preventive	pvalue	0.45	0.04	0.39	0.46	0.83	0.81
			rho	0.17	0.39	-0.19	-0.15	-0.05	0.05
F	TNBS	Therapeutic	pvalue	0.08	0.16	0.61	0.70	0.02	0.02
			rho	-0.59	-0.37	-0.19	-0.11	-0.77	-0.61
		Preventive	pvalue	0.15	0.23	0.33	0.87	0.11	0.5
			rho	0.47	0.33	0.33	-0.05	0.52	0.19
	DSS	Therapeutic	pvalue	0.33	0.43	0.70	0.52	0.24	0.49
			rho	-0.27	-0.22	0.11	0.18	-0.33	-0.19
		Preventive	pvalue	0.14	0.09	0.43	0.24	0.69	0.44
			rho	0.48	0.5	-0.26	-0.37	-0.14	-0.24
M	TNBS	Therapeutic	pvalue	0.13	0.43	1.00	0.32	0.44	0.37
			rho	0.55	0.17	-0.00	-0.25	0.3	0.24
		Preventive	pvalue	0.91	0.89	0.86	0.52	0.61	0.90
			rho	-0.05	-0.06	-0.07	-0.22	-0.19	-0.05
	DSS	Therapeutic	pvalue	0.22	0.52	0.03	0.04	0.72	0.39
			rho	-0.37	-0.20	-0.60	-0.58	0.12	0.27
		Preventive	pvalue	0.44	0.05	0.78	0.78	0.6	0.21
			rho	0.24	0.52	-0.09	-0.08	0.17	0.34

Spearman correlation analyses. Red and blue colors indicate significant ($p \leq 0.05$) negative and positive correlations. BLI, Bioluminescence; DSS, dextran sulfate sodium; F, female; M, male; RD, Raw data; TNBS, trinitrobenzenesulfonic acid.

Table S4. Macroscopic evaluation measurements (median \pm SD) stratified by model, trial and sex compared by treatment and between sexes in each treatment group.

			median ± SD (UMW)							p-value (Dunn's test)		
			Gene	Sex	controls	p-value	dex	p-value	MTADV	p-value	ctl vs dex	ctl vs MTADV
TNBS	Therapeutic	Spleen weight (g)	F	0.13 ± 0.06	ns	0.04 ± 0.01	ns	0.1 ± 0.02	ns	0.007	ns	0.025
			M	0.09 ± 0.02		0.07 ± 0.02		0.09 ± 0.01		0.042	ns	0.050
		Colon weight/length (g/cm)	F	0.03 ± 0.01	ns	0.03 ± 0	ns	0.04 ± 0.01	ns	ns	ns	0.050
			M	0.04 ± 0.01		0.03 ± 0.01		0.03 ± 0.01		ns	ns	ns
		Hyperaemia	F	0.83 ± 0.98	ns	0.4 ± 0.55	ns	0.8 ± 0.84	ns	ns	ns	ns
			M	0.71 ± 0.76		0.4 ± 0.55		0.8 ± 0.84		ns	ns	ns
		Strictures number	F	1.67 ± 0.82	ns	1.2 ± 0.84	ns	1.8 ± 0.84	ns	ns	ns	ns
			M	2 ± 0.82		1.4 ± 0.89		2.2 ± 1.48		ns	ns	ns
		Wallace score	F	3 ± 0.89	ns	1.8 ± 1.3	ns	3.6 ± 0.55	ns	ns	ns	0.015
			M	2.71 ± 0.49		1.8 ± 1.1		2.4 ± 1.34		ns	ns	ns
		Adherences	F	2.33 ± 0.82	ns	0.6 ± 0.55	ns	2.4 ± 0.89	0.049	0.011	ns	0.011
			M	1.57 ± 0.79		0.6 ± 0.55		1 ± 0.71		0.031	ns	ns
	Preventive	Spleen weight (g)	F	0.06 ± 0.02	ns	0.06 ± 0.02	ns	0.05 ± 0.02	ns	ns	ns	ns
			M	0.06 ± 0.02		0.06 ± 0.01		0.08 ± 0.01		ns	ns	0.050
		Colon weight/length (g/cm)	F	0.03 ± 0	0.029	0.03 ± 0	ns	0.03 ± 0	0.009	0.015	ns	0.050
			M	0.04 ± 0		0.03 ± 0		0.04 ± 0		0.029	ns	0.017
		Hyperaemia	F	1.75 ± 1.26	ns	1.4 ± 0.55	ns	1.57 ± 0.53	ns	ns	ns	ns
			M	1.75 ± 0.96		1.25 ± 0.5		1.4 ± 0.89		ns	ns	ns
		Strictures number	F	2 ± 0	ns	0.6 ± 0.89	ns	1.43 ± 0.79	ns	0.013	ns	ns
			M	2.5 ± 1.29		1.5 ± 0.58		0.6 ± 0.55		ns	0.012	ns
		Wallace score	F	3 ± 1.5	ns	5 ± 1	ns	3 ± 1	ns	ns	ns	ns
			M	3.5 ± 1		5 ± 2		3 ± 2		ns	ns	ns
		Adherences	F	1.5 ± 0.71	ns	2.2 ± 1.3	ns	1.33 ± 1.03	ns	ns	ns	ns
			M	1.5 ± 0.58		2.33 ± 1.53		1.33 ± 0.58		ns	ns	ns
DSS	Therapeutic	Spleen weight (g)	F	0.1 ± 0.03	ns	0.04 ± 0	ns	0.08 ± 0.01	ns	0.004	ns	0.016
			M	0.08 ± 0.02		0.05 ± 0.02		0.11 ± 0.05		ns	ns	0.003
		Colon weight/length (g/cm)	F	0.1 ± 0.03	0.008	0.04 ± 0	ns	0.08 ± 0.01	0.008	ns	ns	ns
			M	0.04 ± 0		0.03 ± 0.01		0.04 ± 0.01		0.031	ns	0.021
		Hyperaemia	F	1.4 ± 0.55	ns	1.4 ± 0.55	ns	1.6 ± 0.55	ns	ns	ns	ns
			M	1.8 ± 0.84		1 ± 0		1.6 ± 0.55		0.050	ns	ns
		Strictures number	F	1.6 ± 1.52	ns	2 ± 1	ns	2.4 ± 1.14	ns	ns	ns	ns
			M	1.2 ± 0.45		1 ± 1		1 ± 1		ns	ns	ns
		Wallace score	F	5.2 ± 2.05	ns	3.6 ± 1.34	ns	3 ± 0	ns	ns	0.032	ns
			M	4.4 ± 3.13		3 ± 0		3 ± 0		ns	ns	ns
		Adherences	F	1 ± 0	ns	0.4 ± 0.55	0.041	2.2 ± 0.84	ns	ns	ns	0.002
			M	2.2 ± 1.1		1.4 ± 0.55		2.4 ± 0.55		ns	ns	ns
	Preventive	Spleen weight (g)	F	0.1 ± 0.06	ns	0.11 ± 0.01	ns	0.11 ± 0.03	ns	ns	ns	ns
			M	0.13 ± 0.05		0.13 ± 0.04		0.12 ± 0.04		ns	ns	ns
		Colon weight/length (g/cm)	F	0.03 ± 0.01	ns	0.03 ± 0	ns	0.03 ± 0	ns	ns	ns	ns
			M	0.03 ± 0.01		0.03 ± 0		0.03 ± 0		ns	ns	ns
		Hyperaemia	F	1.17 ± 0.41	ns	1.33 ± 0.58	ns	1.8 ± 0.84	ns	ns	ns	ns
			M	1.57 ± 0.98		0.67 ± 0.58		1.2 ± 0.45		ns	ns	ns
		Strictures number	F	0 ± 0	ns	0 ± 0	ns	0.4 ± 0.89	ns	ns	ns	ns
			M	0.43 ± 0.79		1 ± 0		0 ± 0		ns	ns	0.010
		Wallace score	F	8 ± 1.79	0.016	5.67 ± 3.21	ns	5.6 ± 1.52	ns	ns	0.050	ns
			M	3.71 ± 2.5		5.67 ± 2.52		5.2 ± 1.79		ns	ns	ns
		Adherences	F	1.67 ± 1.03	ns	2 ± 0	ns	1.6 ± 0.89	ns	ns	ns	ns
			M	1.86 ± 0.38		2.33 ± 0.58		0.8 ± 0.45		ns	0.010	0.004

Data are given as median \pm sd and the result of the statistical test between groups is given as p-value. DSS, dextran sulfate sodium; F, female; M, male; MTADV, 5-MER peptide methionine-threonine-alanine-aspartic acid-valine; ns, non-significant; SD, standard deviation; TNBS, trinitrobenzenesulfonic acid.

Table S5. mRNA expression (FC) of inflammatory and oxidative stress markers stratified by both trial and sex in the TNBS models compared by treatment and between sexes in each treatment group.

			median (IQR; UMW)						p-value (Dunn's test)			
			Gene	Sex	controls	p-value	dex	p-value	MTADV	p-value	ctl vs dex	ctl vs MTADV
TNBS	Therapeutic	Hif1a	F	1.1 (1-1.3)	ns	1.2 (1.1-1.4)	ns	1.6 (1.4-2.5)	ns	ns	ns	ns
			M	1.3 (1-1.4)		1.2 (1-1.4)		1.4 (1.3-1.4)		ns	ns	ns
		Il10	F	0.8 (0.6-0.9)	ns	0.4 (0.4-0.7)	ns	1 (0.7-1.1)	ns	ns	ns	ns
			M	0.4 (0.4-0.5)		0.6 (0.6-0.7)		0.8 (0.5-1.2)		ns	ns	ns
		Il6	F	1.4 (1-1.5)	ns	0.7 (0.6-0.8)	ns	36.5 (1.7-45)	ns	ns	ns	0.003
			M	0.7 (0.6-1)		0.8 (0.6-0.9)		1.6 (1.2-1.9)		ns	0.050	0.040
		Nos2	F	0.8 (0.6-1.3)	0.012	0.5 (0.4-0.6)	ns	1.2 (0.5-1.5)	ns	ns	ns	ns
			M	0.3 (0.3-0.4)		0.4 (0.4-0.4)		0.8 (0.6-0.9)		ns	0.027	ns
		Tgfb1	F	1.4 (1.3-2)	ns	1.3 (1.2-1.4)	ns	2.7 (2.3-2.8)	ns	ns	ns	0.009
			M	1.4 (1.1-1.5)		1.3 (1.1-1.4)		2.3 (2.2-2.4)		ns	0.008	0.006
		Tnfa	F	0.9 (0.8-1.2)	0.017	0.7 (0.6-0.8)	ns	1 (0.9-1)	ns	ns	ns	0.046
			M	0.6 (0.5-0.6)		0.5 (0.4-0.8)		0.8 (0.7-1.1)		ns	0.040	ns
		Vegfa	F	1.4 (1.2-1.6)	ns	1.4 (1.3-1.6)	ns	1.5 (1.5-1.6)	ns	ns	ns	ns
			M	1.3 (1.1-1.4)		1.5 (1.1-1.8)		1.5 (1.4-1.5)		ns	ns	ns
		Tpj1	F	1.3 (1.1-1.5)	ns	1.5 (1.5-1.8)	ns	1.4 (1.3-1.7)	ns	ns	ns	ns
			M	1.3 (1.3-1.7)		1.7 (1-1.7)		1.5 (1.5-1.7)		ns	ns	ns
	Il1b1	F	1.4 (0.8-1.6)	ns	1 (0.6-1.2)	ns	4.2 (1.4-24.3)	ns	ns	ns	0.019	
		M	0.4 (0.4-0.6)		0.4 (0.3-1.1)		2.1 (0.9-2.2)		ns	0.038	0.028	
	Preventive	Hif1a	F	1.1 (1.1-1.3)	ns	1.7 (1.4-1.8)	ns	2.7 (2.1-2.9)	ns	ns	0.001	0.018
			M	1.6 (1.5-1.8)		2.1 (1.5-2.2)		2.3 (2.1-3.3)		ns	ns	ns
		Il10	F	0.8 (0.8-0.8)	ns	0.4 (0.3-0.5)	ns	0.8 (0.7-0.9)	ns	ns	ns	0.018
			M	0.6 (0.5-0.8)		0.8 (0.6-1)		1 (0.9-1.2)		ns	ns	ns
		Il6	F	1.7 (1.6-1.9)	ns	9.6 (4.7-21.7)	ns	21.8 (5.8-81.6)	ns	ns	0.050	ns
			M	9.6 (0.8-46.4)		84.6 (54.3-93.8)		52.9 (1.9-128)		ns	ns	ns
		Nos2	F	0.7 (0.5-0.9)	0.002	1.4 (1.2-1.6)	ns	0.8 (0.8-2)	0.039	0.030	ns	ns
			M	2 (1.5-2.5)		2.3 (1.3-2.5)		3.3 (2.1-3.5)		ns	ns	ns
		Tgfb1	F	1.5 (1.4-1.5)	ns	1.9 (1.8-1.9)	ns	2.6 (1.7-2.8)	ns	ns	0.041	ns
			M	1.3 (1.1-1.6)		1.8 (1.6-2.2)		1.7 (1.6-3.9)		ns	ns	ns
		Tnfa	F	0.8 (0.7-0.9)	ns	1.3 (1.3-1.4)	ns	1.3 (1.2-1.9)	ns	ns	ns	ns
			M	1.1 (1-1.4)		1.8 (1.2-2.4)		1.6 (1.6-2)		ns	ns	ns
		Vegfa	F	1.2 (1.1-1.2)	ns	1.7 (1.2-1.7)	ns	1.9 (1.5-2.1)	ns	ns	0.050	ns
			M	1.4 (1.1-1.7)		1.7 (1.5-1.8)		1.5 (1.2-2.2)		ns	ns	ns
		Tpj1	F	1.4 (1.3-1.5)	ns	1.1 (1.1-1.1)	ns	1.6 (1.3-1.8)	ns	ns	ns	0.024
			M	1.3 (1-1.5)		1.4 (1.3-1.6)		1.6 (1.5-1.7)		ns	ns	ns
		Il1b1	F	1 (0.7-1.6)	ns	4.9 (3.3-28.2)	ns	4.9 (2.8-12.6)	ns	0.016	0.024	ns
			M	7 (1.3-32)		7.5 (6.8-33.9)		2.8 (2.6-30.7)		ns	ns	ns

Data are given as median (IQR) and the result of the statistical test between groups is given as p-value. F, female; FC, Fold-change; IQR, interquartile range; M, male; MTADV, 5-MER peptide methionine-threonine-alanine-aspartic acid-valine; ns, non-significant, TNBS, trinitrobenzenesulfonic acid, UMW; U Mann Whitney.

Table S6. mRNA expression (FC) of inflammatory and oxidative stress markers stratified by both trial and sex in the DSS models compared by treatment and between sexes in each treatment group.

				median (IQR; UMW)					p-value (Dunn's test)			
				controls	p-value	dex	p-value	MTADV	p-value	ctl vs dex	ctl vs MTADV	dex vs MTADV
DSS	Therapeutic	Hif1a	F	2.6 (2.1-3)	ns	1.8 (1.3-2.3)	ns	1.1 (0.8-1.2)	ns	ns	0.006	ns
			M	1.6 (1.6-2.9)		2.2 (1.7-2.3)		1.9 (1.7-2.3)		ns	ns	ns
		Il10	F	1.3 (1.2-1.3)	ns	1.5 (1.2-1.9)	ns	1.3 (1.1-1.4)	ns	ns	ns	ns
			M	1.5 (1-3.5)		1.3 (1.2-1.4)		0.8 (0.8-0.8)		ns	0.040	ns
		Il6	F	2.8 (2.6-4.8)	0.009	9.4 (4.6-13.1)	ns	0.9 (0.8-1.8)	0.001	ns	ns	0.009
			M	69.9 (30.3-83)		29.5 (25.8-41.4)		30.4 (25.1-33.7)		ns	ns	ns
		Nos2	F	1.4 (0.9-2)	0.009	0.5 (0.5-0.9)	ns	2.6 (2.1-2.6)	ns	ns	ns	0.004
			M	4.5 (3.4-6.5)		1.7 (1.4-1.7)		8.2 (5.3-12.2)		0.048	ns	0.007
		Tgfb1	F	1.6 (1.5-1.6)	ns	1.4 (1.4-1.5)	ns	1.2 (1.2-1.6)	ns	ns	ns	ns
			M	1.3 (0.8-1.5)		1.3 (1.2-1.9)		1.3 (0.7-1.3)		ns	ns	ns
		Tnfa	F	1.7 (1.6-2.7)	ns	0.9 (0.7-1.1)	ns	1.5 (1.4-1.5)	0.013	0.002	ns	0.024
			M	2.2 (2-2.7)		1.5 (0.9-1.6)		3.1 (2.9-3.6)		ns	ns	0.004
		Vegfa	F	1.1 (1.1-1.2)	0.017	2 (1.7-2)	ns	0.8 (0.8-1.1)	ns	0.034	ns	0.003
			M	0.8 (0.7-0.9)		1.1 (1-1.2)		0.9 (0.8-0.9)		0.011	ns	0.034
		Tpj1	F	1.6 (1.5-1.7)	0.017	1.7 (1.6-1.7)	ns	0.8 (0.7-1)	ns	ns	0.016	0.004
			M	0.9 (0.9-1)		1.4 (1.3-1.5)		0.7 (0.7-0.7)		ns	ns	0.001
		Il1b1	F	3.3 (2.4-4.5)	0.029	3.2 (2.7-4.4)	0.031	1.8 (1.5-2.5)	0.004	ns	ns	ns
			M	26.1 (16.7-37.4)		21.5 (10.1-39)		14.1 (8.5-14.8)		ns	ns	ns
	Preventive	Hif1a	F	1.1 (1.1-1.2)	ns	1.4 (1.2-1.7)	0.024	1.3 (1.2-1.6)	0.049	ns	ns	ns
			M	1.6 (1.4-1.7)		2.9 (2.9-3.5)		2.4 (1.9-2.5)		0.003	0.029	ns
		Il10	F	0.8 (0.7-0.9)	ns	1.4 (1.3-1.5)	ns	0.8 (0.8-1)	ns	ns	ns	ns
			M	1.1 (0.5-1.8)		NA (NA-NA)		0.8 (0.7-1.1)		NA	ns	NA
		Il6	F	16.2 (12.4-18.1)	ns	33.9 (33-45.2)	0.035	21.3 (16.6-40.3)	0.034	ns	ns	ns
			M	59 (21.8-79.5)		701 (445.9-2012.7)		148.5 (116-167.9)		0.002	ns	ns
		Nos2	F	2.6 (2.2-2.7)	0.009	3.7 (2.7-3.8)	ns	3.2 (2.9-5)	ns	ns	ns	ns
			M	3.3 (2.5-4.7)		1.4 (1.4-1.8)		4.4 (4-5.2)		ns	ns	0.030
		Tgfb1	F	1.3 (1.2-1.3)	ns	1.4 (1.2-1.5)	0.013	1.7 (1.6-1.8)	ns	ns	0.033	ns
			M	1.4 (1.2-1.8)		2.5 (2.2-2.6)		2.2 (1.9-2.4)		0.013	0.044	ns
		Tnfa	F	2.4 (1.8-2.5)	ns	2.6 (2.4-2.7)	ns	2.1 (2-2.3)	0.015	ns	ns	ns
			M	2.5 (1.9-3.1)		4.1 (3.2-4.1)		3.5 (3.4-5.2)		ns	0.031	ns
		Vegfa	F	0.9 (0.8-0.9)	ns	0.7 (0.7-0.8)	0.003	0.9 (0.9-1)	ns	ns	ns	0.02
			M	0.7 (0.7-0.8)		1.8 (1.4-1.9)		0.9 (0.8-0.9)		0.003	ns	ns
		Tpj1	F	0.9 (0.9-1)	ns	0.5 (0.5-0.5)	ns	0.6 (0.6-0.6)	ns	0.002	ns	ns
			M	0.6 (0.6-0.9)		0.6 (0.6-0.7)		0.8 (0.7-0.8)		ns	ns	ns
		Il1b1	F	6 (4.7-7.6)	ns	7.7 (7.4-11.8)	ns	12.8 (10.9-15.7)	ns	ns	ns	ns
			M	16.3 (9.4-29.7)		34.3 (26.5-38.7)		27 (26.7-34.3)		ns	ns	ns

Data are given as median (IQR) and the result of the statistical test between groups is given as p-value. DSS, dextran sulfate sodium; F, female; IQR, interquartile range; M, male; MTADV, 5-MER peptide methionine-threonine-alanine-aspartic acid-valine; ns, non-significant, UMW; U Mann Whitney.

Table S7. FCs of CRP and SAA stratified by sex in preventive and therapeutic approaches compared between treatments and between sex in each treatment group.

			APP	Sex	median (IQR; UMW)					p-value (Dunn's test)		
					controls	p-value	dex	p-value	MTADV	p-value	ctl vs dex	ctl vs MTADV
TNBS	Therapeutic	CRP	F	1.0 (0.8-1.3)	ns	1.5 (1.2-1.6)	ns	1.0 (0.9-1.5)	ns	ns	ns	ns
			M	0.9 (0.8-1.2)		1.0 (0.9-1.2)		1.0 (0.9-1.4)		ns	ns	ns
		SAA	F	1.6 (1.2-2.2)	ns	22.4 (17.3-47.4)	ns	2.1 (1.6-2.4)	ns	0.037	ns	ns
			M	2.6 (2.6-6.2)		2.0 (1.9-58.4)		3.0 (2.1-3.7)		ns	ns	ns
	Preventive	CRP	F	1.2 (1.1-1.4)	ns	1.6 (1.4-1.7)	ns	1.0 (0.9-1.7)	ns	ns	ns	ns
			M	2.3 (1.8-2.8)		1.8 (1.6-1.8)		1.7 (1.6-2.6)		ns	ns	ns
		SAA	F	4.0 (3.3-4.8)	ns	17.5 (10.4-36.3)	ns	7.2 (4-18.1)	ns	ns	ns	ns
			M	8.9 (8.3-2988.3)		56.2 (55.5-472.1)		4.7 (4.3-5.2)		ns	ns	0.044
DSS	Therapeutic	CRP	F	1.7 (1.5-1.8)	ns	2.1 (1.9-2.3)	ns	1.2 (0.9-1.4)	0.001	ns	0.048	0.001
			M	1.7 (1.5-1.9)		2.6 (2.2-3.1)		2.1 (2.1-2.8)		0.009	ns	ns
		SAA	F	68.7 (56.8-80.6)	0.033	189.5 (151.0-315.8)	ns	9.6 (7.6-11.9)	0.016	ns	ns	0.009
			M	6224.3 (4508.1-6242.9)		1322.8 (775.5-3163.9)		2080.7 (1713.5-2447.8)		ns	ns	ns
	Preventive	CRP	F	1.2 (1-1.2)	ns	1.5 (1.5-1.6)	ns	1.4 (1.1-2.0)	ns	ns	ns	ns
			M	1.9 (1.8-2.3)		2.5 (2.4-2.5)		1.8 (1.5-3.1)		ns	ns	ns
		SAA	F	134.5 (79.1-140.6)	ns	955.0 (626.5-1283.5)	ns	924.3 (922.0-926.5)	ns	ns	ns	ns
			M	367.3 (224.2-853.4)		3424.5 (1977.1-4871.9)		427.7 (300.7-603.5)		ns	ns	ns

Data are given as median (interquartile range) and the result of the statistical test between groups is given as p-value. DSS, dextran sulfate sodium; F, female; FC, fold change; IQR, interquartile range; M, male; MTADV, 5-MER peptide methionine-threonine-alanine-aspartic acid-valine; ns, non-significant, TNBS, trinitrobenzenesulfonic acid.

Table S8. Correlation between inflammatory and oxidative stress mRNA expression in both therapeutic and preventive approaches in the TNBS model in females.

	<i>Hif1a</i>	<i>Il10</i>	<i>Il6</i>	<i>Nos2</i>	<i>Tgfb1</i>	<i>Tnfa</i>	<i>Vegfa</i>	<i>Tjp1</i>	<i>Il1b1</i>	Therapeutic
<i>Hif1a</i>		0.21	0.42	-0.19	0.64	-0.00	0.77	0.51	0.17	
<i>Il10</i>	0.51		-0.21	0.60	0.26	0.7	-0.30	-0.04	0.75	
<i>Il6</i>	0.64	-0.11		0.26	0.42	0.39	0.43	-0.04	0.59	
<i>Nos2</i>	0.34	0.29	0.33		-0.16	0.61	-0.27	-0.41	0.55	
<i>Tgfb1</i>	0.62	0.25	0.73	0.38		0.11	0.31	0.17	0.23	
<i>Tnfa</i>	0.50	0.04	0.73	0.41	0.49		-0.28	-0.47	0.78	
<i>Vegfa</i>	0.68	0.01	0.83	0.24	0.56	0.62		0.36	-0.16	
<i>Tjp1</i>	0.46	0.57	0.10	-0.31	0.36	-0.18	0.29		-0.20	
<i>Il1b1</i>	0.64	-0.19	0.86	0.66	0.74	0.66	0.71	-0.11		
Preventive										Therapeutic

Spearman linear regression analyses. Red and blue colors indicate significant ($p \leq 0.05$) negative and positive correlations respectively. The grey diagonal division separates therapeutic (top), from preventive (bottom) correlations. TNBS, trinitrobenzenesulfonic acid.

Table S9. Correlation between inflammatory and oxidative stress mRNA expression in both therapeutic and preventive approaches in the TNBS model in males.

	<i>Hif1a</i>	<i>Il10</i>	<i>Il6</i>	<i>Nos2</i>	<i>Tgfb1</i>	<i>Tnfa</i>	<i>Vegfa</i>	<i>Tjp1</i>	<i>Il1b1</i>	Therapeutic
<i>Hif1a</i>		0.14	0.36	0.23	0.44	0.09	0.42	0.58	0.01	
<i>Il10</i>	0.49		0.23	0.48	0.32	0.56	0.01	-0.27	0.85	
<i>Il6</i>	0.81	0.52		0.26	0.92	0.64	0.65	0.81	0.38	
<i>Nos2</i>	0.23	0.39	0.12		0.33	0.48	0.33	-0.02	0.24	
<i>Tgfb1</i>	0.88	0.37	0.87	0.41		0.52	0.34	0.62	0.40	
<i>Tnfa</i>	0.63	0.28	0.71	0.67	0.75		-0.27	-0.01	0.77	
<i>Vegfa</i>	0.79	0.36	0.93	0.27	0.89	0.67		0.63	-0.49	
<i>Tjp1</i>	0.19	0.28	0.16	-0.04	0.18	0.02	0.24		-0.19	
<i>Il1b1</i>	0.57	0.15	0.86	0.32	0.73	0.62	0.87	-0.08		
Preventive										Therapeutic

Spearman linear regression analyses. Red and blue colors indicate significant ($p \leq 0.05$) negative and positive correlations respectively. The grey diagonal division separates therapeutic (top), from preventive (bottom) correlations. TNBS, trinitrobenzenesulfonic acid.

Table S10. Correlation between inflammatory and oxidative stress mRNA expression in both therapeutic and preventive approaches in the DSS model in females.

	<i>Hif1a</i>	<i>Il10</i>	<i>Il6</i>	<i>Nos2</i>	<i>Tgfb1</i>	<i>Tnfa</i>	<i>Vegfa</i>	<i>Tjp1</i>	<i>Il1b1</i>	Therapeutic
<i>Hif1a</i>		0.22	0.61	-0.50	0.63	0.07	0.45	0.67	0.64	
<i>Il10</i>	-0.07		0.60	-0.41	0.46	-0.38	0.59	0.16	0.48	
<i>Il6</i>	0.29	0.26		-0.62	0.36	-0.38	0.67	0.61	0.89	
<i>Nos2</i>	0.01	0.03	0.39		-0.19	0.65	-0.60	-0.75	-0.46	
<i>Tgfb1</i>	0.45	-0.23	0.11	-0.25		0.38	0.32	0.35	0.39	
<i>Tnfa</i>	0.06	-0.01	0.19	0.71	-0.06		-0.45	-0.22	-0.23	
<i>Vegfa</i>	-0.03	-0.35	-0.75	-0.18	0.50	-0.18		0.67	0.43	
<i>Tjp1</i>	-0.08	-0.50	-0.60	-0.45	-0.25	-0.14	0.43		0.40	
<i>Il1b1</i>	0.30	-0.09	0.50	0.68	0.20	0.47	-0.15	-0.27		
	Preventive									

Spearman linear regression analyses. Red and blue colors indicate significant ($p \leq 0.05$) negative and positive correlations respectively. The grey diagonal division separates therapeutic (top), from preventive (bottom) correlations. DSS, dextran sulfate sodium.

Table S11. Correlation between inflammatory and oxidative stress mRNA expression in both therapeutic and preventive approaches in the DSS model in males.

	<i>Hif1a</i>	<i>Il10</i>	<i>Il6</i>	<i>Nos2</i>	<i>Tgfb1</i>	<i>Tnfa</i>	<i>Vegfa</i>	<i>Tjp1</i>	<i>Il1b1</i>	Therapeutic
<i>Hif1a</i>		0.29	0.09	-0.23	0.05	-0.17	0.15	0.35	0.33	
<i>Il10</i>	-0.19		0.25	-0.10	0.46	-0.13	0.36	0.41	0.56	
<i>Il6</i>	0.70	0.47		0.22	0.23	0.17	-0.29	-0.23	0.67	
<i>Nos2</i>	-0.26	-0.48	-0.46		-0.13	0.96	-0.41	-0.69	0.18	
<i>Tgfb1</i>	0.68	0.43	0.84	-0.38		-0.06	0.55	0.37	0.64	
<i>Tnfa</i>	0.53	-0.13	0.40	0.32	0.45		-0.29	-0.67	0.18	
<i>Vegfa</i>	0.65	0.06	0.78	-0.29	0.78	0.66		0.7	0.17	
<i>Tjp1</i>	0.23	-0.71	-0.25	0.47	-0.04	0.18	0.00		0.15	
<i>Il1b1</i>	0.45	0.59	0.57	-0.36	0.66	0.49	0.46	-0.33		
	Preventive									

Spearman linear regression analyses. Red and blue colors indicate significant ($p \leq 0.05$) negative and positive correlations respectively. The grey diagonal division separates therapeutic (top), from preventive (bottom) correlations. DSS, dextran sulfate sodium.

Table S12. Correlation between plasmatic protein levels of CRP and SAA, and mRNA expression of inflammation markers separated by animal model and design.

				<i>Il10</i>	<i>Tgfb1</i>	<i>Il6</i>	<i>Vegfa</i>	<i>Tjp1</i>	<i>Nos2</i>	<i>Tnfa</i>	<i>Hif1a</i>	<i>Il1b1</i>
CRP	TNBS	Therapeutic	p-value	0.34	0.71	0.10	0.57	0.64	0.40	0.68	0.10	0.37
			rho	0.22	0.07	-0.31	-0.10	-0.08	0.15	0.07	0.29	0.17
		Preventive	p-value	0.15	0.81	0.29	0.24	0.81	0.07	0.96	0.35	0.12
			rho	0.32	-0.05	0.22	0.23	-0.05	0.36	0.01	0.18	0.31
	DSS	Therapeutic	p-value	0.50	0.91	6E-3	0.20	0.17	0.93	0.77	0.02	2E-3
			rho	0.13	-0.02	0.49	0.24	0.26	-0.02	0.05	0.43	0.55
		Preventive	p-value	0.81	0.14	0.04	0.21	0.37	0.64	0.69	3E-3	0.04
			rho	-0.05	0.30	0.41	-0.26	-0.18	0.10	0.08	0.56	0.41
SAA	TNBS	Therapeutic	p-value	0.60	0.62	0.10	0.04	0.32	0.13	0.17	0.42	0.74
			rho	0.16	-0.12	-0.43	-0.47	-0.23	-0.35	0.32	-0.19	0.09
		Preventive	p-value	0.80	0.43	3E-3	0.04	0.67	0.31	0.32	0.40	8E-4
			rho	-0.07	0.20	0.67	0.48	0.11	0.25	0.25	0.21	0.73
	DSS	Therapeutic	p-value	0.72	0.77	0.00	0.69	0.74	0.06	0.06	0.04	0.00
			rho	-0.10	-0.08	0.87	-0.10	0.09	0.47	0.46	0.50	0.91
		Preventive	p-value	0.70	0.32	0.06	0.49	0.09	0.60	0.46	0.31	0.19
			rho	0.11	0.25	0.45	0.17	-0.41	0.13	0.19	0.25	0.32

Spearman linear regression analyses. Red and blue colors indicate significant ($p \leq 0.05$) negative and positive correlations respectively. CRP, C-reactive protein; DSS, dextran sulfate sodium; SAA, Serum amyloid antigen; TNBS, trinitrobenzenesulfonic acid.

Table S13. Correlation between plasmatic CRP and SAA, and mRNA expression of inflammation markers separated by model, trial and sex.

					<i>Il10</i>	<i>Tgfb1</i>	<i>Il6</i>	<i>Vegfa</i>	<i>Tjp1</i>	<i>Nos2</i>	<i>Tnfa</i>	<i>Hif1a</i>	<i>Il1b1</i>
CRP	F	TNBS	Therapeutic	p-value	0.71	0.7	0.27	1.00	0.96	0.56	0.46	0.53	0.64
				rho	0.14	0.11	-0.29	0.00	0.01	-0.16	0.20	0.17	0.14
			Preventive	p-value	0.52	0.37	0.80	0.91	0.31	0.17	0.43	0.71	0.40
				rho	-0.22	-0.25	-0.07	0.03	-0.28	0.38	-0.22	-0.10	0.24
		DSS	Therapeutic	p-value	0.35	0.37	0.01	1E-3	0.00	8E-5	0.06	8E-3	0.07
				rho	0.26	0.25	0.63	0.78	0.87	-0.84	-0.50	0.66	0.48
			Preventive	p-value	0.47	0.18	0.03	0.53	0.26	0.14	0.08	0.1	0.11
				rho	0.24	0.41	0.64	-0.20	-0.36	0.45	0.52	0.5	0.49
	M	TNBS	Therapeutic	p-value	0.79	0.98	0.28	0.72	0.63	0.37	0.59	0.08	0.65
				rho	0.1	0.01	-0.34	-0.09	-0.13	0.23	-0.14	0.43	0.12
			Preventive	p-value	0.12	0.77	0.31	0.25	0.54	0.64	0.99	0.20	0.32
				rho	0.50	0.10	0.34	0.36	0.20	-0.15	-0.01	0.40	0.31
		DSS	Therapeutic	p-value	0.52	0.43	0.66	0.02	0.16	0.79	0.85	0.49	0.55
				rho	0.18	0.22	-0.13	0.61	0.38	-0.08	0.05	0.19	0.17
			Preventive	p-value	0.59	0.41	0.89	0.18	0.39	0.55	0.21	0.67	0.77
				rho	-0.17	-0.24	0.04	-0.38	-0.25	-0.17	-0.36	0.13	-0.09
SAA	F	TNBS	Therapeutic	p-value	0.50	0.27	0.02	0.25	0.49	0.25	0.88	0.49	0.84
				rho	0.32	-0.42	-0.77	-0.43	-0.27	-0.43	0.07	-0.27	0.10
			Preventive	p-value	0.70	0.08	0.02	0.04	0.71	0.02	0.01	0.22	0.01
				rho	-0.17	0.59	0.76	0.66	-0.14	0.76	0.78	0.43	0.77
		DSS	Therapeutic	p-value	0.18	0.31	3E-3	0.03	0.01	0.02	0.15	0.12	3E-3
				rho	0.50	0.38	0.88	0.73	0.82	-0.78	-0.53	0.56	0.88
			Preventive	p-value	0.50	0.50	0.04	0.75	0.10	0.06	0.36	0.98	0.02
				rho	0.32	0.29	0.76	-0.14	-0.64	0.71	0.38	-0.02	0.83
	M	TNBS	Therapeutic	p-value	0.80	0.63	0.66	0.04	0.69	0.20	0.17	0.71	0.54
				rho	0.14	0.16	-0.21	-0.64	-0.14	-0.42	0.45	-0.13	0.22
			Preventive	p-value	0.84	1.00	0.15	0.24	0.30	0.05	0.39	0.98	0.11
				rho	-0.11	0.00	0.57	0.48	0.43	-0.74	-0.36	-0.02	0.62
		DSS	Therapeutic	p-value	0.75	0.30	0.15	0.33	0.88	0.46	0.54	0.62	0.14
				rho	0.14	0.43	0.57	-0.40	-0.07	0.31	0.26	0.21	0.64
			Preventive	p-value	0.70	0.84	0.22	0.41	0.84	0.43	1.00	0.22	0.79
				rho	-0.17	0.08	0.43	0.30	-0.08	-0.28	0.01	0.43	-0.10

Spearman linear regression analyses. Red and blue colors indicate significant ($p \leq 0.05$) negative and positive correlations respectively. CRP, C-reactive protein; DSS, dextran sulfate sodium; SAA, Serum amyloid antigen; TNBS, trinitrobenzenesulfonic acid.

Table S14: Macroscopic colon examination score (Wallace).

Score	Macroscopic colon examination (Wallace)
0	no damage
1	hyperaemia without ulcers
2	hyperaemia and wall thickening without ulcers
3	one ulceration site without wall thickening
4	two or more ulceration sites
5	0.5 cm extension of inflammation or major damage
6	1 cm extension of inflammation or severe damage
the score was then increased by 1 up to a maximal score of 10	
10*	*every 0.5 cm of damage
	*stricture presence
	*presence of mild or severe adhesion respectively