Supporting Information for "**The TLR9 agonist MGN1703 triggers a potent type I interferon response in the sigmoid colon**" by Krarup, Abdel-Mohsen, Schleimann, *et al.*

Table S1 **(continued on multiple pages). Significantly regulated genes from RNASeq analysis of intestinal mononuclear cells.**

#	Name	p value*	p value adjusted for false discovery rate^	log2-fold- change (treatment/baseline)
1	IFI27	1.15E-08	7.97E-05	-2.430314241
2	OAS1	9.31E-09	7.97E-05	-2.287057906
3	IFITM1	3.21E-08	8.92E-05	-2.041336871
4	IFI6	3.00E-08	8.92E-05	-3.719797937
5	HERC6	2.86E-08	8.92E-05	-2.127016974
6	IRF9	4.81E-08	8.96E-05	-1.15975609
7	XAF1	5.16E-08	8.96E-05	-3.138333563
8	OAS2	4.48E-08	8.96E-05	-2.20610977
9	MX1	1.12E-07	1.73E-04	-3.023753645
10	EIF2AK2	1.65E-07	2.30E-04	-1.580238143
11	IFI44L	2.60E-07	3.02E-04	-4.766144209
12	PARP9	3.51E-07	3.75E-04	-2.036965696
13	ISG15	8.46E-07	8.40E-04	-3.032851779
14	PRR15	9.17E-07	8.50E-04	-1.075908931
15	IFI44	1.28E-06	9.39E-04	-2.807789174
16	CAMK2N1	1.25E-06	9.39E-04	-1.632563818
17	OAS3	1.50E-06	9.51E-04	-2.538528456
18	IL17RE	1.47E-06	9.51E-04	-1.468018636
19	IFI35	2.69E-06	1.56E-03	-1.282126812
20	LY6E	3.13E-06	1.67E-03	-1.912375056
21	USP18	3.02E-06	1.67E-03	-2.401140199
22	ACTN4	3.59E-06	1.85E-03	-1.124444868
23	IFIT1	5.46E-06	2.30E-03	-3.219484671
24	DDX58	7.34E-06	2.76E-03	-1.383124633
25	CHPF	8.20E-06	2.86E-03	1.134025899
26	RSAD2	1.04E-05	3.45E-03	-2.843705122
27	AGRN	1.40E-05	4.37E-03	-1.234860759
28	HELZ2	1.66E-05	4.80E-03	-1.672723117
29	TSPAN1	1.96E-05	4.93E-03	-1.276393792
30	STAT1	1.87E-05	4.93E-03	-1.27057515
31	UBE2L6	2.01E-05	4.93E-03	-1.059722782
32	DTX3L	2.39E-05	5.22E-03	-1.270663518
33	FXYD3	2.67E-05	5.37E-03	-1.044109986
34	PRSS3	2.74E-05	5.45E-03	-1.197766746
35	NHSL1	2.97E-05	5.66E-03	-1.058114364
36	TPST2	3.28E-05	5.67E-03	1.046302586
37	WDR54	3.24E-05	5.67E-03	1.086859449
38	CMPK2	3.30E-05	5.67E-03	-2.510841825
39	LAMP3	3.24E-05	5.67E-03	-1.581895604
40	BHLHA15	3.44E-05	5.67E-03	1.267991751
41	MARVELD3	3.51E-05	5.67E-03	-1.101657822
42	SAMD9L	3.89E-05	6.10E-03	-1.304646251
43	SPINK5	4.20E-05	6.34E-03	-1.25582451
44	TMEM54	4.80E-05	6.81E-03	-1.094761959

Supporting Information for "**The TLR9 agonist MGN1703 triggers a potent type I interferon response in the sigmoid colon**" by Krarup, Abdel-Mohsen, Schleimann, *et al.*

Table S1 **(continued on multiple pages)**. **Significantly regulated genes from RNASeq analysis of intestinal mononuclear cells.**

#	Name	p value*	p value adjusted for false discovery rate^	log2-fold- change (treatment/baseline)
45	QPCT	5.32E-05	7.05E-03	1.078605003
46	SEMA4G	5.22E-05	7.05E-03	-1.185756496
47	NXPE2	5.67E-05	7.37E-03	-1.118165053
48	TRIM22	5.86E-05	7.51E-03	-1.273075211
49	BTNL3	5.98E-05	7.56E-03	-1.562435368
50	DDX60	6.82E-05	8.12E-03	-2.106045391
51	MEI1	6.63E-05	8.12E-03	1.248405594
52	NOS1AP	6.82E-05	8.12E-03	-1.016866875
53	PCLO	7.20E-05	8.28E-03	-1.250735256
54	KIAA1211L	7.57E-05	8.52E-03	-1.013592713
55	ANGPTL6	8.21E-05	8.93E-03	-1.143923952
56	HNF1B	8.62E-05	9.29E-03	-1.020475057
57	PRR15L	9.30E-05	9.31E-03	-1.135064056
58	HOXB9	8.70E-05	9.31E-03	-1.251806522
59	DDX60L	8.90E-05	9.31E-03	-1.183983707
60	DHX58	8.87E-05	9.31E-03	-1.68500251
61	NEURL1B	9.27E-05	9.31E-03	-1.065921385
62	IFIT3	9.72E-05	9.39E-03	-2.734323502
63	MX2	1.01E-04	9.58E-03	-1.840242803
64	FCER1A	1.03E-04	9.59E-03	1.18004276
65	SPIRE2	1.26E-04	1.08E-02	-1.040696415
66	CASC9	1.32E-04	1.10E-02	-1.364409674
67	GPA33	1.42E-04	1.15E-02	-1.07675672
68	EPSTI1	1.48E-04	1.16E-02	-1.857638044
69	PCK1	1.52E-04	1.18E-02	-1.426715071
70	RAPGEF1	1.57E-04	1.19E-02	1.263903842
71	SMIM22	1.67E-04	1.23E-02	-1.16558075
72	IRF7	1.73E-04	1.23E-02	-1.536975754
73	MOV10	1.75E-04	1.23E-02	-1.036391307
74	TMC5	1.76E-04	1.23E-02	-1.29657681
75	SLC4A4	1.70E-04	1.23E-02	-1.095921595
76	MT1E	1.84E-04	1.27E-02	-1.022426106
77	PLSCR1	1.89E-04	1.27E-02	-1.373579611
78	MTRNR2L3	1.92E-04	1.27E-02	-1.320865303
79	ZG16B	1.83E-04	1.27E-02	-1.048190454
80	TLR9	1.94E-04	1.27E-02	1.066609961
81	BTC	1.88E-04	1.27E-02	-1.368298281
82	PARP12	2.07E-04	1.30E-02	-1.687774812
83	WNT10A	2.13E-04	1.33E-02	1.282118433
84	PRAP1	2.13E-04	1.33E-02	-1.603020181
85	MTRNR2L6	2.27E-04	1.37E-02	-1.25971512
86	CLDN8	2.28E-04	1.37E-02	-1.259474265
87	CADM1	2.31E-04	1.38E-02	1.029791617
88	ODF3B	2.36E-04	1.40E-02	-1.304580079

Supporting Information for "**The TLR9 agonist MGN1703 triggers a potent type I interferon response in the sigmoid colon**" by Krarup, Abdel-Mohsen, Schleimann, *et al.*

Table S1 (continued on multiple pages). Significantly regulated genes from RNASeq analysis of intestinal mononuclear cells.

#	Name	p value*	p value adjusted for false discovery rate^	log2-fold- change (treatment/baseline)
89	CDHR5	2.41E-04	1.41E-02	-1.255228856
90	CEACAM7	2.44E-04	1.41E-02	-1.854918983
91	ETV7	2.52E-04	1.43E-02	-1.327311504
92	KLF5	2.63E-04	1.47E-02	-1.324400405
93	NUPR1	2.81E-04	1.50E-02	-1.031354712
94	MUC20	2.82E-04	1.50E-02	-1.255470337
95	GSDMB	2.72E-04	1.50E-02	-1.403602159
96	SLC26A3	2.84E-04	1.50E-02	-1.347006378
97	DERL3	2.92E-04	1.53E-02	1.066391248
98	MB21D2	2.94E-04	1.53E-02	1.264216064
99	ASAP2	2.93E-04	1.53E-02	-1.113008362
100	FUT6	3.01E-04	1.54E-02	-1.400066329
101	CDKN2B-AS1	3.06E-04	1.54E-02	-1.435344765
102	MTRNR2L2	3.19E-04	1.57E-02	-1.304780204
103	TMPRSS4	3.18E-04	1.57E-02	-1.018236677
104	PELI1	3.26E-04	1.57E-02	1.169426422
105	HSD11B2	3.29E-04	1.57E-02	-1.206979759
106	PLEKHG6	3.23E-04	1.57E-02	-1.547503135
107	CDC42EP5	3.39E-04	1.59E-02	-1.257922771
108	SAMD5	3.90E-04	1.67E-02	-1.04391697
109	TBC1D9	3.91E-04	1.67E-02	1.013708447
110	KRT20	4.04E-04	1.67E-02	-1.076903401
111	MEP1A	4.07E-04	1.67E-02	-1.148264089
112	PHGR1	4.24E-04	1.71E-02	-1.132063673
113	DAPP1	4.30E-04	1.72E-02	1.275165088
114	FABP1	4.54E-04	1.78E-02	-1.11331536
115	IL1RL1	4.56E-04	1.78E-02	1.073360132
116	LGALS9	4.55E-04	1.78E-02	-1.060547729
117	RRAD	4.67E-04	1.80E-02	1.108924524
118	BCL2L11	4.78E-04	1.83E-02	1.123958845
119	TLN2	4.88E-04	1.85E-02	-1.031408557
120	TSHR	4.93E-04	1.86E-02	1.690813172
121	MGAT4B	4.98E-04	1.87E-02	-1.013495827
122	CEACAM3	4.99E-04	1.87E-02	-1.590164553
123	ZNF804A	5.32E-04	1.95E-02	1.186313196
124	MAGIX	5.45E-04	1.97E-02	-1.062842732
125	SAMD9	5.58E-04	1.98E-02	-1.123457276
126	CCR10	5.66E-04	1.99E-02	1.06333957
127	HSPA13	5.71E-04	2.01E-02	1.019547736
128	CCL28	5.79E-04	2.01E-02	-1.072557867
129	EDN3	6.13E-04	2.07E-02	-1.235813252
130	BCL2L14	6.29E-04	2.09E-02	-1.205681527
131	SCARNA9L	6.29E-04	2.09E-02	-3.522611362
132	MT1G	6.52E-04	2.13E-02	-1.195707835

Table S1 **(continued on multiple pages). Significantly regulated genes from RNASeq analysis of intestinal mononuclear cells.**

#	Name	p value*	p value adjusted for false discovery rate^	log2-fold- change (treatment/baseline)
133	VSIG2	6.63E-04	2.15E-02	-1.077996113
134	CES3	6.79E-04	2.16E-02	-1.136735223
135	MTRNR2L1	6.98E-04	2.21E-02	-1.26894469
136	CA4	7.14E-04	2.22E-02	-1.465851352
137	MTRNR2L8	7.25E-04	2.23E-02	-1.229280059
138	BEST4	7.31E-04	2.23E-02	-1.289010182
139	PTPRK	7.52E-04	2.28E-02	-1.046698018
140	C19orf33	7.61E-04	2.29E-02	-1.333357016
141	GALNT12	7.99E-04	2.33E-02	-1.34980749
142	GPR125	8.22E-04	2.38E-02	-1.202847521
143	EIF2AK3	8.45E-04	2.39E-02	1.050736914
144	NBEAL1	8.37E-04	2.39E-02	-1.078415727
145	CEACAM1	8.50E-04	2.39E-02	-1.07265358
146	PLA2G10	8.36E-04	2.39E-02	-1.277099496
147	MOXD1	8.30E-04	2.39E-02	1.159965015
148	OTOP2	8.43E-04	2.39E-02	-1.113053841
149	SLC8A3	8.44E-04	2.39E-02	1.026961707
150	HDC	8.71E-04	2.41E-02	1.115724188
151	XDH	8.68E-04	2.41E-02	-1.073049815
152	CAPN8	8.89E-04	2.44E-02	-1.31025888
153	TRPM6	8.90E-04	2.44E-02	-1.528944957
154	PDGFA	9.05E-04	2.46E-02	-1.226149504
155	PTPRH	9.20E-04	2.48E-02	-1.054044336
156	PARVB	9.29E-04	2.49E-02	1.022474101
157	BCAS1	9.38E-04	2.50E-02	-1.016886919
158	LYPD8	9.63E-04	2.53E-02	-1.533570942
159	SMOX	9.74E-04	2.55E-02	1.063304552
160	MOB3B	9.79E-04	2.55E-02	-2.656346794
161	MTRNR2L9	9.87E-04	2.56E-02	-1.209462548
162	SLC25A34	1.01E-03	2.57E-02	-1.091704235
163	FERMT1	1.05E-03	2.60E-02	-1.00291516
164	CCDC64B	1.08E-03	2.64E-02	-1.216928173
165	CD177	1.09E-03	2.67E-02	-1.184461824
166	B3GALT5	1.10E-03	2.68E-02	-1.478014827
167	MTRNR2L10	1.13E-03	2.70E-02	-1.250576369
168	SLC51B	1.14E-03	2.70E-02	-1.073617478
169	CD207	1.15E-03	2.70E-02	1.795526582
170	IFIT5	1.17E-03	2.74E-02	-1.327705562
171	BTNL8	1.24E-03	2.78E-02	-1.340071801
172	LLGL2	1.32E-03	2.91E-02	-1.052332269
173	FAM49A	1.33E-03	2.91E-02	1.245991767
174	HIST1H4D	1.33E-03	2.91E-02	-1.529024564
175	CA1	1.35E-03	2.94E-02	-1.191487408
176	FBXL8	1.36E-03	2.95E-02	-1.011746401

Table S1 (**continued on multiple pages**). **Significantly regulated genes from RNASeq analysis of intestinal mononuclear cells.**

#	Name	p value*	p value adjusted for false discovery rate^	log2-fold- change (treatment/baseline)
177	HSF4	1.36E-03	2.95E-02	-1.011746401
178	TRAF1	1.37E-03	2.95E-02	1.018467097
179	A1CF	1.36E-03	2.95E-02	-1.002130271
180	B3GNT8	1.38E-03	2.97E-02	-1.018782633
181	RHBDL2	1.40E-03	2.99E-02	-1.212034111
182	BCL2L15	1.42E-03	3.01E-02	-1.14907254
183	LRRC19	1.45E-03	3.06E-02	-1.196523323
184	HHLA2	1.48E-03	3.07E-02	-1.132864453
185	IGLL5	1.53E-03	3.10E-02	1.065539924
186	PNOC	1.53E-03	3.10E-02	1.290032701
187	LGR4	1.57E-03	3.14E-02	-1.053612925
188	MUC12	1.60E-03	3.18E-02	-1.103552296
189	GAL3ST2	1.62E-03	3.18E-02	-1.213909898
190	SOWAHA	1.62E-03	3.18E-02	-1.042315194
191	SERPINE1	1.65E-03	3.22E-02	1.186790681
192	CHST2	1.66E-03	3.22E-02	1.062433629
193	CEBPA	1.66E-03	3.22E-02	-1.358814803
194	HNF4A	1.68E-03	3.25E-02	-1.086008563
195	LGALS3BP	1.71E-03	3.28E-02	-1.102679453
196	MS4A12	1.76E-03	3.33E-02	-2.545266366
197	ITPKA	1.77E-03	3.33E-02	-1.587024471
198	PART1	1.77E-03	3.33E-02	-1.120544829
199	MOGAT2	1.86E-03	3.44E-02	-1.235029097
200	NR1I2	1.98E-03	3.56E-02	-1.003646195
201	CYP2B6	1.98E-03	3.56E-02	-1.098258341
202	OASL	2.06E-03	3.66E-02	-1.360298796
203	SLC7A5	2.08E-03	3.67E-02	1.054631313
204	FCRL5	2.07E-03	3.67E-02	1.095499923
205	KIF13A	2.08E-03	3.67E-02	-1.428602831
206	FRMD1	2.15E-03	3.75E-02	-1.220576177
207	CHRM3	2.17E-03	3.75E-02	-1.123362825
208	PKDCC	2.19E-03	3.75E-02	-1.29329248
209	PIGZ	2.23E-03	3.79E-02	-1.429099512
210	GATA6	2.25E-03	3.81E-02	-1.119256506
211	MAB21L3	2.30E-03	3.81E-02	-1.025554629
212	PITPNM3	2.29E-03	3.81E-02	-1.060928377
213	IL23A	2.31E-03	3.82E-02	1.425404537
214	JHDM1D-AS1	2.37E-03	3.88E-02	-1.10061894
215	FAM177B	2.38E-03	3.88E-02	-1.385137339
216	GPM6A	2.47E-03	3.98E-02	1.591826754
217	RMRP	2.50E-03	3.99E-02	-1.06633084
218	ARHGEF10L	2.52E-03	4.02E-02	-1.242340958
219	SULT1B1	2.55E-03	4.04E-02	-1.260138164
220	CEACAM6	2.56E-03	4.05E-02	-1.212491009

Supporting Information for “**The TLR9 agonist MGN1703 triggers a potent type I interferon response in the sigmoid colon**” by Krarup, Abdel-Mohsen, Schleimann, *et al.*

Table S1 **(continued on multiple pages)**. **Significantly regulated genes from RNASeq analysis of intestinal mononuclear cells.**

#	Name	p value*	p value adjusted for false discovery rate^	log2-fold- change (treatment/baseline)
221	B4GALNT3	2.57E-03	4.05E-02	-1.232077064
222	CCDC88A	2.74E-03	4.22E-02	1.001852606
223	ABHD17C	2.84E-03	4.29E-02	-1.198963989
224	CD1C	2.85E-03	4.30E-02	1.500612093
225	KLK15	2.86E-03	4.30E-02	-1.814149089
226	RNU6-28P	2.91E-03	4.32E-02	-7.067681587
227	C21orf88	2.93E-03	4.35E-02	-1.764848948
228	HERC5	3.00E-03	4.41E-02	-1.097912254
229	TP53INP1	3.02E-03	4.41E-02	1.118630388
230	TMEM150B	3.17E-03	4.55E-02	-2.003230683
231	GUCA2A	3.18E-03	4.56E-02	-1.524395819
232	ITGA8	3.28E-03	4.64E-02	1.033983647
233	ZNF69	3.33E-03	4.67E-02	-1.249617121
234	HOOK2	3.40E-03	4.71E-02	-1.529601723
235	OSR2	3.40E-03	4.71E-02	1.243263288
236	RNF186	3.42E-03	4.72E-02	-1.037261361
237	CYP2C18	3.43E-03	4.73E-02	-1.318672309
238	NR5A2	3.51E-03	4.80E-02	-1.106897876
239	MYO1A	3.53E-03	4.80E-02	-1.001161905
240	WDR78	3.60E-03	4.82E-02	-1.208287889
241	GDA	3.64E-03	4.84E-02	-1.259760582
242	HOMER1	3.65E-03	4.85E-02	1.137522678
243	AKR1C3	3.66E-03	4.85E-02	-1.08762426
244	FLT3	3.69E-03	4.87E-02	1.513218014
245	ATP2C2	3.76E-03	4.92E-02	-1.13714097
246	SLC17A4	3.84E-03	4.98E-02	-2.266032814
247	PLEKHA6	3.86E-03	4.98E-02	-1.169073167
248	CD1E	3.86E-03	4.98E-02	2.223412249

* Wilcoxon signed-rank tests were used to determine statistical significance between on-treatment time point and the baseline time point.

^ False discovery rates (FDR) were computed using the Benjamini-Hochberg procedure to adjust for multiple comparisons.

Table S2 (continued on multiple pages). Fecal relative abundance of sequences derived from individual taxa

Taxonomic Rank	*P*-Value[a]	FDR-*P*[b]	BL # Seqs	Treatment # Seqs
Phylum				
Firmicutes	0.21	0.83	10223.75	9056.00
Bacteroidetes	0.60	0.83	2459.13	2925.00
Proteobacteria	0.67	0.83	786.00	1046.75
Actinobacteria	0.83	0.83	745.75	928.13
Class				
Clostridia	0.25	0.80	9217.25	7890.75
Erysipelotrichi	0.29	0.80	658.88	878.50
Coriobacteriia	0.34	0.80	494.00	571.50
Bacteroidia	0.60	0.87	2461.00	2950.75
Bacilli	0.83	0.87	338.88	307.88
Gammaproteobacteria	0.83	0.87	672.38	754.88
Actinobacteria	0.87	0.87	254.88	338.88
Order				
Clostridiales	0.25	0.92	9219.00	7910.38
Erysipelotrichales	0.34	0.92	659.25	877.38
Coriobacteriales	0.43	0.92	503.63	576.38
Bacteroidales	0.60	0.92	2454.38	2924.13
Aeromonadales	0.83	0.92	409.50	696.25
Bifidobacteriales	0.87	0.92	251.75	328.13
Lactobacillales	0.92	0.92	312.63	278.50
Family				
Coriobacteriaceae	0.40	0.96	496.63	598.50
Erysipelotrichaceae	0.40	0.96	661.50	857.00
Bacteroidaceae	0.53	0.96	1148.00	1369.50
Lachnospiraceae	0.53	0.96	2937.13	2448.63
Ruminococcaceae	0.53	0.96	3592.63	3108.50
Bifidobacteriaceae	0.60	0.96	245.50	337.38
Rikenellaceae	0.60	0.96	126.63	220.63
Clostridiaceae	0.64	0.96	210.88	242.63
Succinivibrionaceae	0.74	0.96	405.38	708.25
Lactobacillaceae	0.75	0.96	192.63	145.88
Prevotellaceae	0.87	0.96	691.13	817.25
Veillonellaceae	0.92	0.96	814.50	625.63
[Paraprevotellaceae]	0.96	0.96	135.13	174.88
Genus				
Blautia	0.46	0.92	667.00	553.38
Lactobacillus	0.49	0.92	201.50	145.13
Bacteroides	0.56	0.92	1150.88	1325.75
Bifidobacterium	0.59	0.92	248.75	340.00
Coprococcus	0.67	0.92	438.88	413.88
Ruminococcus	0.67	0.92	601.13	376.25
Catenibacterium	0.74	0.92	238.75	295.13
Dialister	0.75	0.92	471.50	259.50
[Ruminococcus]	0.75	0.92	271.00	223.25

Table S2 (continued on multiple pages). Fecal relative abundance of sequences derived from individual taxa

Taxonomic Rank	*P*-Value[a]	FDR-*P*[b]	BL # Seqs	Treatment # Seqs
Faecalibacterium	0.75	0.92	1147.25	1069.25
Megasphaera	0.82	0.92	153.75	140.13
Prevotella	0.87	0.92	686.13	825.25
Succinivibrio	0.91	0.92	408.00	702.50
Collinsella	0.92	0.92	280.00	255.75
[Eubacterium]	0.92	0.92	212.00	262.25

Seqs = average number of sequences in defined group.
Table is sorted by *P*-Value for each taxonomic rank.
Kruskal-Wallis non-parametric one-way analysis of variance.
[a]*P*-value : $P < 0.05$; [b]False Discovery Rate: FDR-$P < 0.05$

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Table S3. Fecal alpha diversity indices

Comparison	**Taxonomic level**	**Alpha Diversity Index**	***P*-value**^{a}	**Mean±SD (BL)**	**Mean±SD (Treatment)**
BL v Treatment	Phylum	Shannon (log-e)	0.109	0.86 ± 0.26	1.01 ± 0.22
BL v Treatment	Class	Shannon (log-e)	**0.027**^{a}	1.13 ± 0.27	1.34 ± 0.23
BL v Treatment	Order	Shannon (log-e)	**0.033**^{a}	1.14 ± 0.29	1.35 ± 0.23
BL v Treatment	Family	Shannon (log-e)	**0.031**^{a}	2.10 ± 0.27	2.26 ± 0.31
BL v Treatment	Genus	Shannon (log-e)	0.230	2.78 ± 0.24	2.87 ± 0.34
BL v Treatment	Phylum	Simpson (1-λ)	0.148	0.43 ± 0.15	0.51 ± 0.11
BL v Treatment	Class	Simpson (1-λ)	0.085	0.52 ± 0.13	0.61 ± 0.08
BL v Treatment	Order	Simpson (1-λ)	0.087	0.52 ± 0.13	0.61 ± 0.84
BL v Treatment	Family	Simpson (1-λ)	**0.048**^{a}	0.81 ± 0.05	0.84 ± 0.04
BL v Treatment	Genus	Simpson (1-λ)	0.641$^{\wedge}$	0.90 ± 0.02	0.90 ± 0.04
BL v Treatment	Phylum	Evenness (Pielou’s)	0.098	0.37 ± 0.11	0.44 ± 0.08
BL v Treatment	Class	Evenness (Pielou’s)	**0.028**^{a}	0.40 ± 0.09	0.47 ± 0.08
BL v Treatment	Order	Evenness (Pielou’s)	**0.013**^{a}	0.36 ± 0.08	0.42 ± 0.07
BL v Treatment	Family	Evenness (Pielou’s)	0.071	0.56 ± 0.06	0.59 ± 0.075
BL v Treatment	Genus	Evenness (Pielou’s)	0.588	0.65 ± 0.03	0.66 ± 0.08
BL v Treatment	Phylum	Species Richness (Margalef)	0.892$^{\wedge}$	10.38 ± 2.77	10.25 ± 2.19
BL v Treatment	Class	Species Richness (Margalef)	0.832$^{\wedge}$	17.86 ± 5.17	18.50 ± 4.81
BL v Treatment	Order	Species Richness (Margalef)	0.689	25.50 ± 7.58	26.38 ± 7.05
BL v Treatment	Family	Species Richness (Margalef)	0.312	44.75 ± 11.06	48.13 ± 9.23
BL v Treatment	Genus	Species Richness (Margalef)	0.439	73.30 ± 17.30	77.00 ± 10.94

Data assessed across groups for normality (histograms, skewness/kurtosis, & Shapiro-Wilk test).
P-value^{a} = $P < 0.05$: paired *t*-test or (^) non-parametric Wilcoxon signed paired rank *t*-test.
SD = Standard Deviation, BL=baseline before treatment, Treatment=end time point after treatment.

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Table S4. IHC staining reagents.

Target	Antigen Retrieval Buffer	Primary Antibody	Secondary Antibody
CXCL10	Citrate Buffer, Sigma Aldrich Cat. # C9999 or Golden Bridge International Labs Cat. # B05C-100B.	Clone 33036 at 1:100 dilution, R&D Systems cat. # AF-266-NA	Anti-goat conjugated to HRP – GBI Labs cat. #D43-18
IL-21	Diva Decloaker, Biocare Medical Cat. # DV2004MX	Polyclonal at 1:800 dilution, LSBio cat. # LS-B1364	Anti-rabbit conjugated to HRP – GBI Labs cat. #D39-18
ISG-15	Citraconic Anhydride, Sigma Aldrich Cat. # 125318-100G	Polyclonal at 1:250 dilution, Sigma Aldrich cat. # HPA004627	Anti-rabbit conjugated to HRP – GBI Labs cat. #D13-110
MX1	Citraconic Anhydride, Sigma Aldrich Cat. # 125318-100G	Unspecified clone at 1:1000 dilution from Freiburg University	Anti-mouse conjugated to HRP – GBI Labs cat. #D37-18
MPO	Citrate Buffer, Sigma Aldrich Cat. # C9999 or Golden Bridge International Labs Cat. # B05C-100B.	Polyclonal at 1:1000 dilution, Dako cat. # A0398	Anti-rabbit conjugated to HRP – GBI Labs cat. #D13-110

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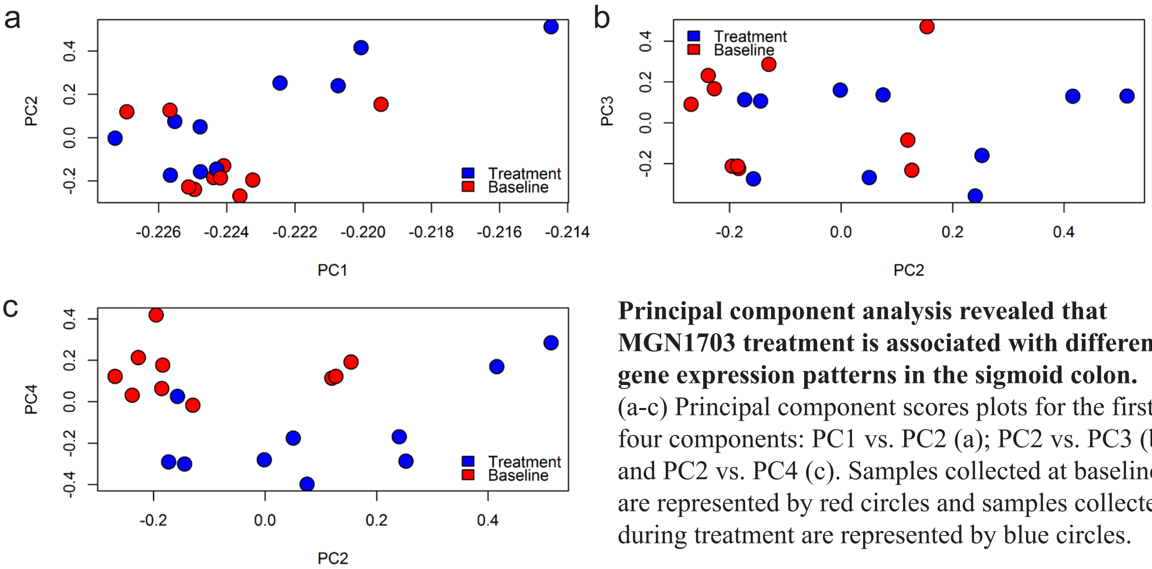
Table S5. Quality Control of quantification strategy - C1 vs. C2*.

Target	Linear regression	t test	Bland-Altman plot
CXCL10	r2 = 0.77	p = 0.39	Bias = -968.3; SD = 1346
IL-21	r2 = 0.95	p = 0.91	Bias = 13.9; SD = 66.88
ISG-15	r2 = 0.73	p = 0.75	Bias = -77.9; SD = 297.1
MX1	r2 = 0.74	p = 0.77	Bias = 219.2; SD = 927.5
MPO	r2 = 0.94	p = 0.93	Bias = -7.3; SD = 55.16

*Count 1 (C1) and Count 2 (C2) values for each marker were plotted in C1/C2 plots and linear regressions were performed. In addition, C1 and C2 values were compared using a t-test, and a Bland-Altman plot was generated using the average of the two counts versus the difference between the two counts.

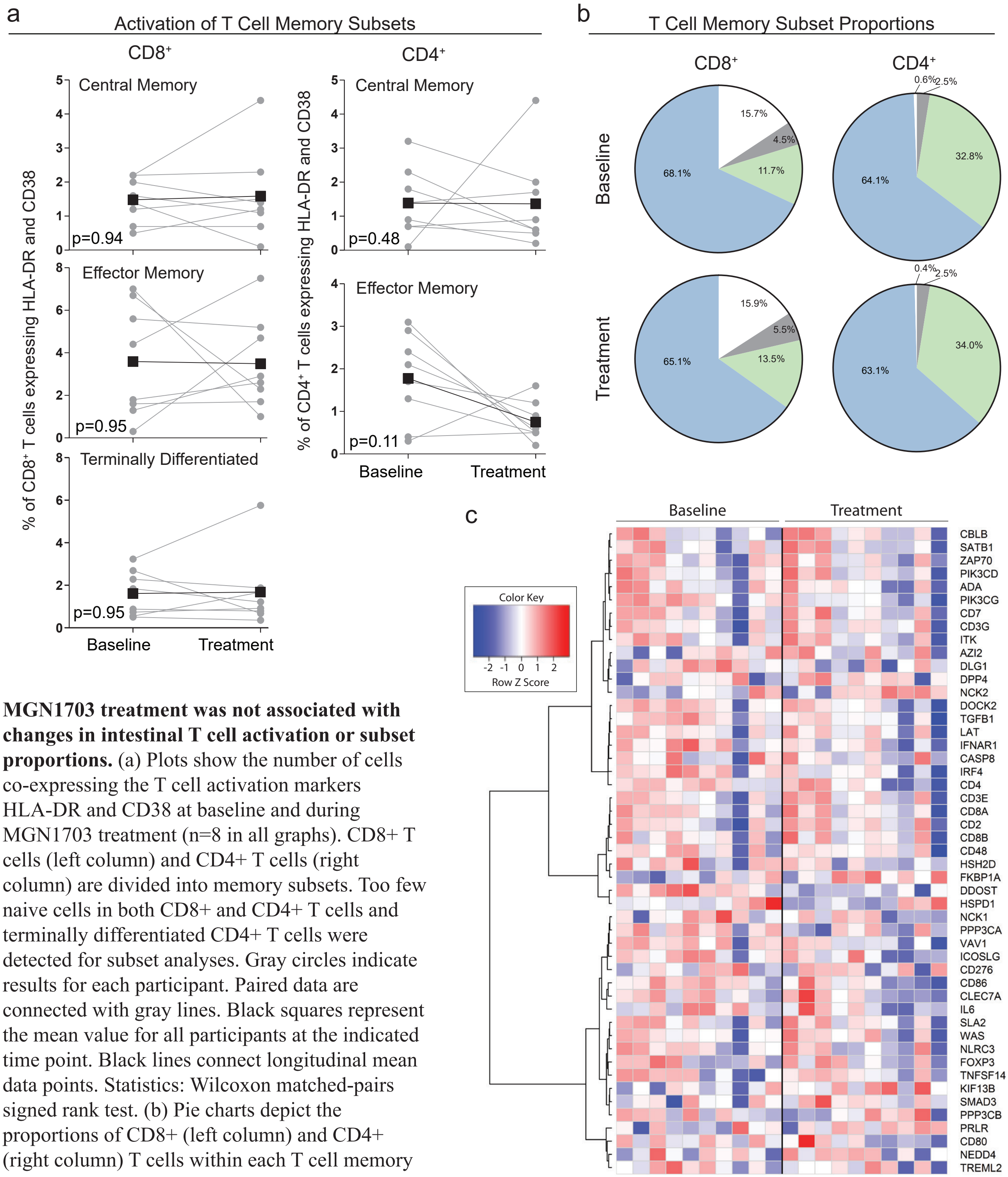
Supporting Information for **“The TLR9 agonist MGN1703 triggers a potent type I interferon response in the sigmoid colon”** by Krarup, Abdel-Mohsen, Schleimann, et al.

SUPPLEMENTAL FIGURE 1



Principal component analysis revealed that MGN1703 treatment is associated with differential gene expression patterns in the sigmoid colon. (a-c) Principal component scores plots for the first four components: PC1 vs. PC2 (a); PC2 vs. PC3 (b) and PC2 vs. PC4 (c). Samples collected at baseline are represented by red circles and samples collected during treatment are represented by blue circles.

SUPPLEMENTAL FIGURE 2



MGN1703 treatment was not associated with changes in intestinal T cell activation or subset proportions. (a) Plots show the number of cells co-expressing the T cell activation markers HLA-DR and CD38 at baseline and during MGN1703 treatment (n=8 in all graphs). CD8+ T cells (left column) and CD4+ T cells (right column) are divided into memory subsets. Too few naive cells in both CD8+ and CD4+ T cells and terminally differentiated CD4+ T cells were detected for subset analyses. Gray circles indicate results for each participant. Paired data are connected with gray lines. Black squares represent the mean value for all participants at the indicated time point. Black lines connect longitudinal mean data points. Statistics: Wilcoxon matched-pairs signed rank test. (b) Pie charts depict the proportions of CD8+ (left column) and CD4+ (right column) T cells within each T cell memory subsets at baseline (top row) and during MGN1703 treatment (bottom row). (c) RNASeq heat map showing the relative regulation of genes associated with T cell activation. Individual participants (n=10) are depicted in the columns and one gene is depicted per row. The dendrogram reveals the relatedness of individual genes.