

Supplementary information

Table S1: Transcription of genes that are commonly or stimulation-specifically activated in Caco-2 cells after exposure to insect-fractions.

Insects	No. of genes	Genes
BCD BPD BchPD MPD	34	HMGCR UGCG LMO7 TM4SF1 JUND ARHGAP18 HSD3B1 DUSP6 PRELID3B ACSL3 CCL20 RSRC2 SQLE SPRED1 PCK1 NUDT4 ENC1 ZFP36L1 SC5D ARL5B BMP2 HMGCS1 EREG FAM107B TIPARP ACSL5 IDI1 AREG SLC20A1 CYP1A1 SLC30A1 INSIG1 BET1 MSMO1
BPD	23	KRCC1 MT1F ENPP4 CDKN1A DENND4C TCIM STAM CLDN4 ADM CD2AP PPP1R15B CHTF8 CD55 MUC13 CCND1 BPNT2 MAPK11P1L TXNIP ERG28 MT-CYB PPTC7 JMJD1C ZFP36L2
BchPD	68	SMIM24 PPP1CC YIPF6 MCM3 AZIN1 PTPRR VMP1 FAM3C IER3 MTA2 CYCS INSIG2 HSPA13 MAP3K7 DDTL GGPS1 ARF6 ANP32E TBCC CXADR TUBAL3 PEX13 RPL21 LYPLA1 SCOC PTBP3 RSL24D1 PPIL4 TMEM135 FOXN2 PRR15L PFDN4 LRRC19 PM20D2 TAF1D CETN3 TMED5 GCH1 CHMP1B XPO1 BLCAP ETNK1 NCOA7 ARFIP1 G0S2 CREBZF NOP2 EIF2A UBE2B GLYCTK RNF128 TMF1 KCTD9 MCL1 PI4K2B PPIG SELENOI TMEM106B GMFB BTG3 TST RPF2 PERP RYBP GPBP1 CHMP2B NEK7 CLK1
MPD	34	EMP1 RRAS2 CDC42SE1 EPB41L4B TSPAN12 AK3 HIGD1A DNAJA2 FAT1 CSTF2 FAM102A SMIM3 MAF TSKU ATF3 GPRC5A AKIRIN2 SNTB1 FGA CPT1A EPAS1 KLF10 RHEB GNG10 AMACR WDFY1 RESF1 TOB1 GOLIM4 OBI1 NCR3LG1 SLC46A1 NADK2 KLF4
BCD	20	BLOC1S5-TXNDC5 SOS1 GTF2A1 BMF MAN1A1 PAXBP1 SLC35A3 SVIP RAB9A ATP8B2 TRIM2 EDC3 C2orf72 ESF1 SLC5A3 DCDC2 MOB4 LYSMD3 GLRX SLC25A24

Table S2: Transcriptional changes (Fold changes compared to ED >1.6) in cell proliferation function-related genes following Caco-2 exposure to insect-derived fractions.

Gene acronym	Gene name	BPD	BchPD	MPD	BCD
EREG	epiregulin	3.13	3.84	2.74	1.97
AREG	amphiregulin	2.76	3.28	2.31	1.77
GDF15	growth differentiation factor 15	2.17	2.70	N.D	N.D
SLC20A1	solute carrier family 20 member 1	2.40	2.56	2.60	1.48
JUND	JunD proto-oncogene, AP-1 transcription factor subunit	2.24	2.49	1.79	1.87
BMP2	bone morphogenetic protein 2	2.16	2.44	2.32	1.45
KLF6	Kruppel like factor 6	2.10	2.36	1.43	1.37
RND3	Rho family GTPase 3	1.55	1.92	1.40	N.D
HMGB2	high mobility group box 2	1.42	1.83	1.41	N.D
JUN	Jun proto-oncogene, AP-1 transcription factor subunit	2.24	1.81	N.D	N.D
TCIM	transcriptional and immune response regulator	2.35	N.D	N.D	N.D
KLF4	Kruppel like factor 4	N.D	N.D	2.04	N.D
FZD5	frizzled class receptor 5	1.54	1.76	1.69	N.D
GMFB	glia maturation factor beta	1.34	1.65	1.31	1.43
ARHGAP18	Rho GTPase activating protein 18	1.57	1.63	1.53	1.59
HBP1	HMG-box transcription factor 1	1.43	1.62	1.33	N.D
MAPK6	mitogen-activated protein kinase 6	1.42	1.60	N.D	1.44
KLF11	Kruppel like factor 11	1.66	2.01	1.71	N.D
CCNL1	cyclin L1	1.60	1.58	1.47	1.40
RHOB	ras homolog family member B	1.89	1.37	1.98	N.D
RHPN2	rhopilin Rho GTPase binding protein 2	1.80	1.63	1.89	N.D

Figure S1: Schematic overview of Caco-2 cells and THP-1 macrophages co-culture model.

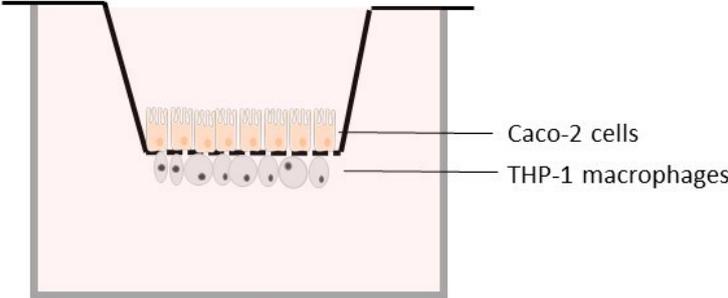


Figure S2: Post-treatment with insect-derived fractions did not significantly ($p < 0.05$) reduce Caco-2 barrier damaging effect of *C. difficile*-derived toxin A.

