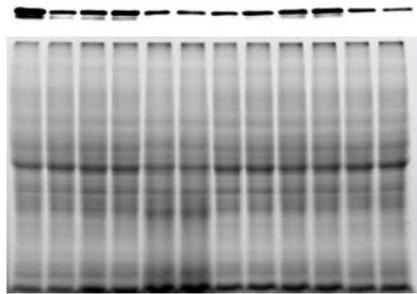


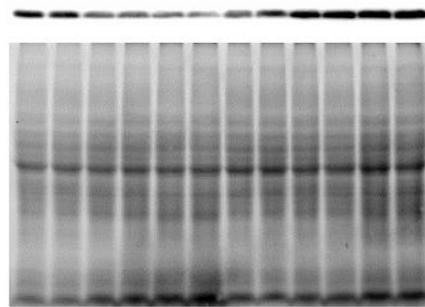
**Figure S1.** HE figures of rat jejunum and colon tissue (ruler scale of 100  $\mu\text{m}$ ). DB could repair jejunum barrier dysfunction by improving microvilli, inhibiting crypt loss, edema and inflammatory cell infiltration (**A**,  $n = 9$ ). Slight inflammatory cell infiltration was observed in colon of SMG rats and DB could improve this injury in colon tissue (**B**,  $n = 9$ ).

**Ileum**

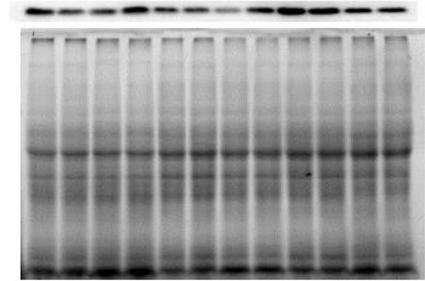
E-Cadherin



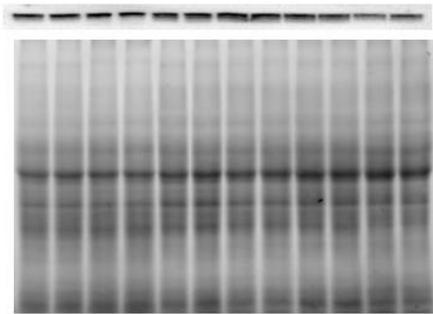
Occludin



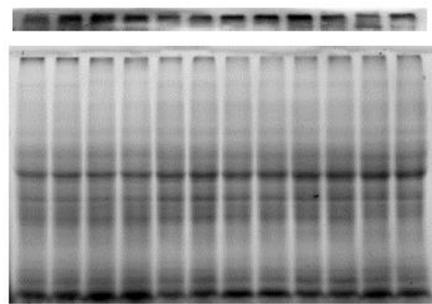
Claudin-1



$\beta$ -Catenin

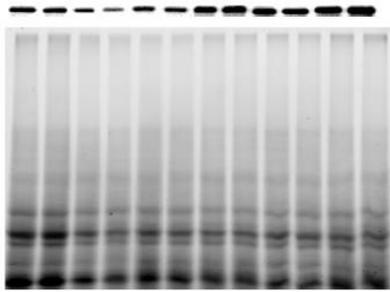


ZO-1

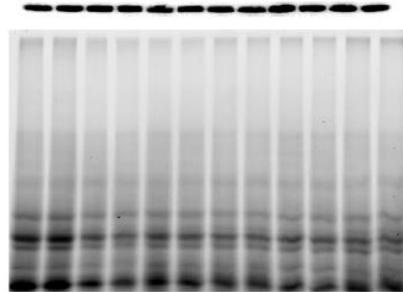


**Colon**

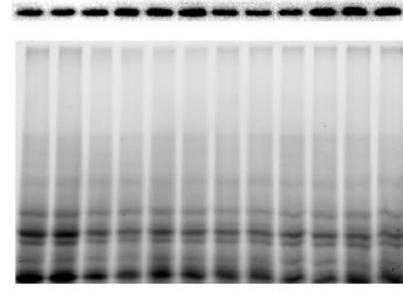
E-Cadherin



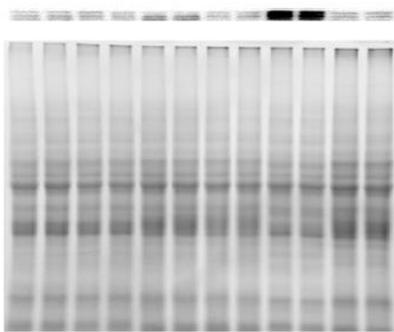
Occludin



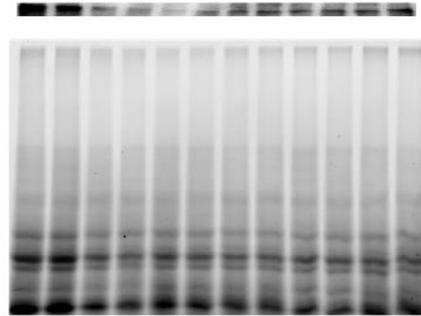
Claudin-1



$\beta$ -Catenin

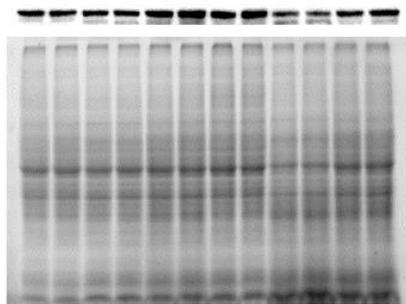


ZO-1

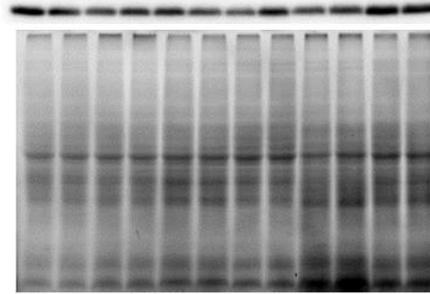


**Jejunum**

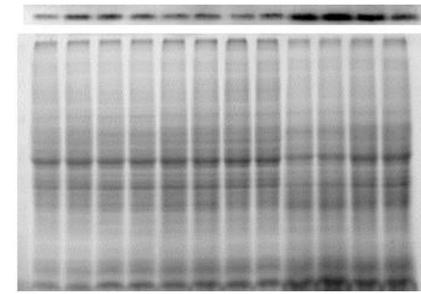
E-Cadherin



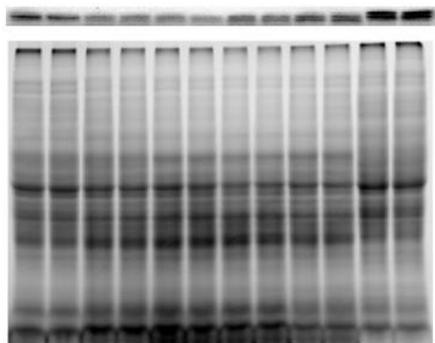
Occludin



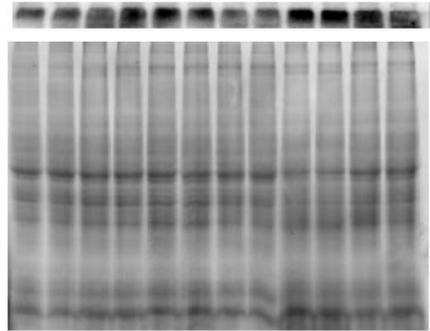
Claudin-1



$\beta$ -Catenin

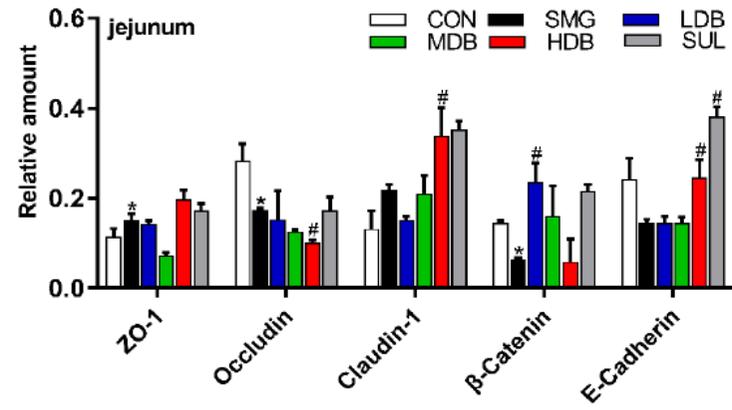
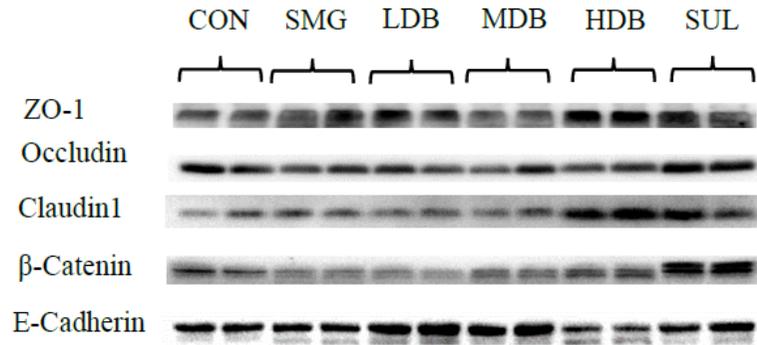


ZO-1

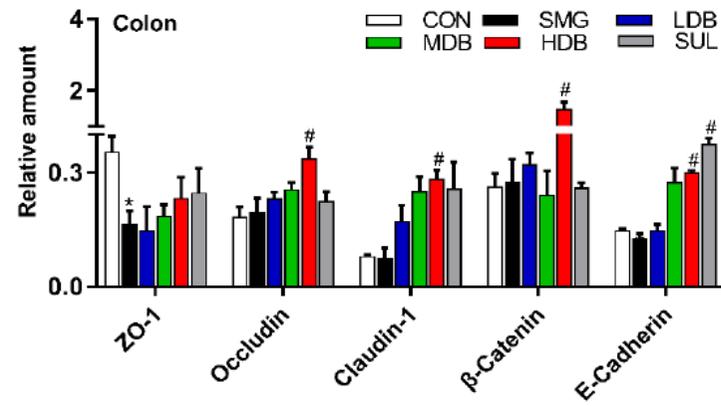
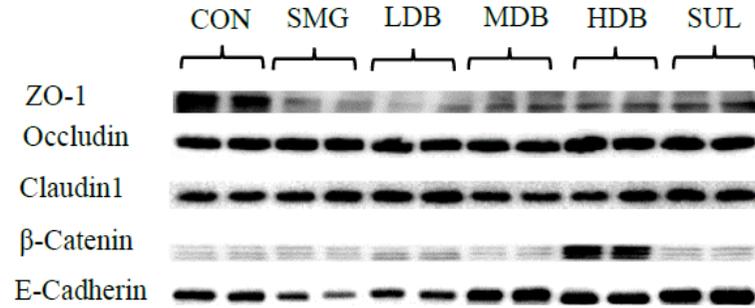


**Figure S2.** Western-blot bands of TJ and AJ proteins in rat ileum, colon and jejunum, and their corresponding total protein gels.

**A**

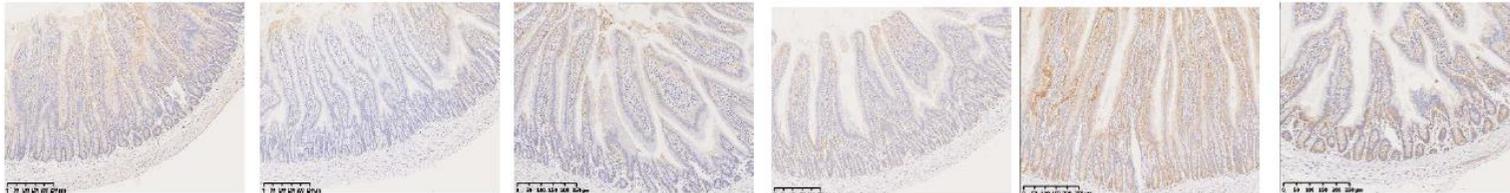


**B**

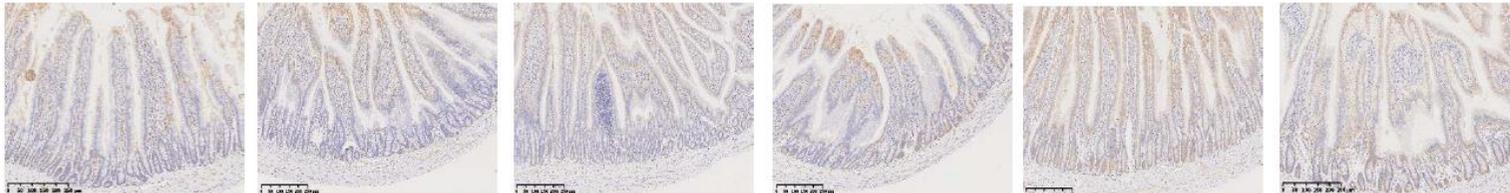


**C Jejunum**

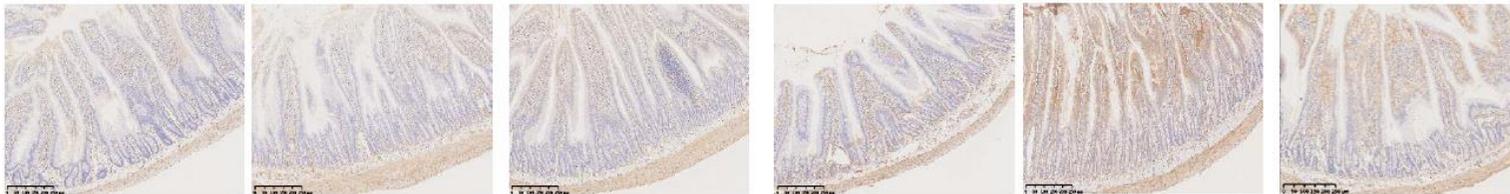
Occludin



Claudin-1



ZO-1



CON

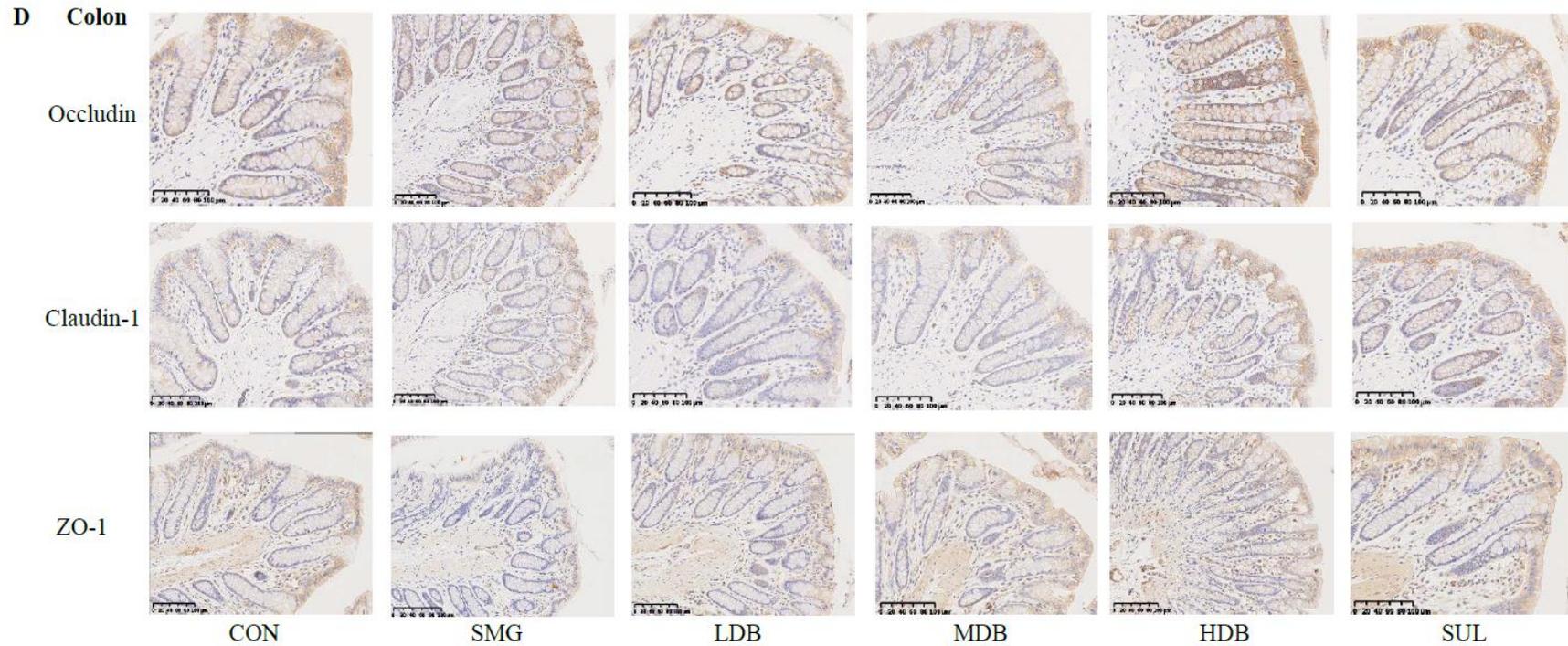
SMG

LDB

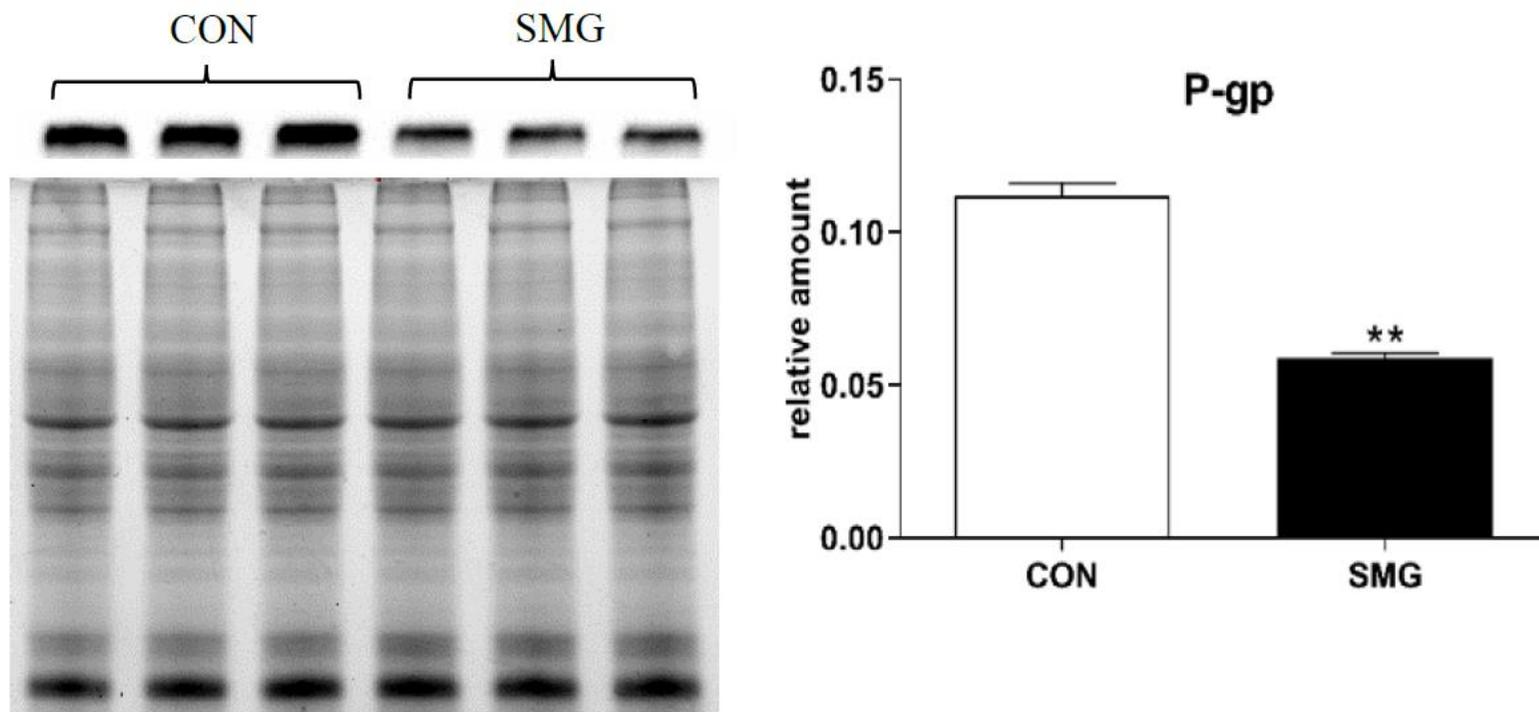
MDB

HDB

SUL

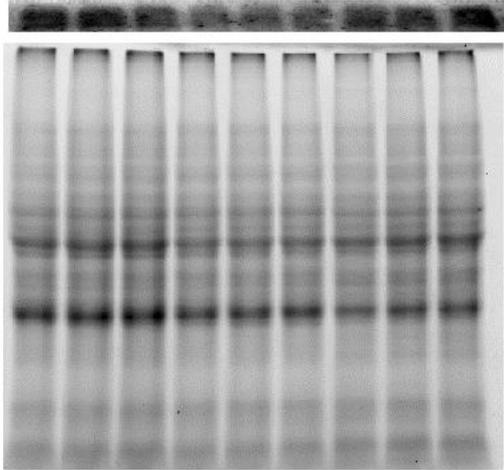


**Figure S3.** DB protected the intestinal epithelial barrier injury by increasing the expression of TJ and AJ proteins in the jejunum (A) and colon (B) tissues of SMG rat ( $n = 9$ ). The expression of occludin, claudin-1 and ZO-1 detected by immunohistochemistry (brown granules represent TJ protein) in SMG rat jejunum (C) and colon (D) tissues (ruler scale of 100  $\mu\text{m}$ ) ( $n = 9$ ). \*  $p < 0.05$  and \*\*  $p < 0.01$ , compared with CON group. #  $p < 0.05$  and ##  $p < 0.01$ , compared with SMG group. Their corresponding total protein gels in rat colon and jejunum were shown in Supplementary Figure S2.

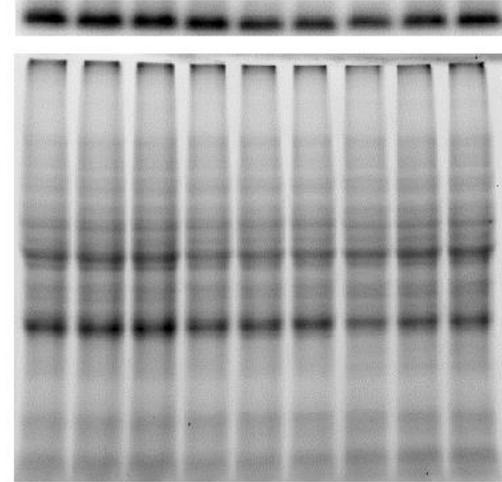


**Figure S4.** The expression of P-glycoprotein (P-gp) by Western-blot method to demonstrate a pattern consistent with MS analysis.

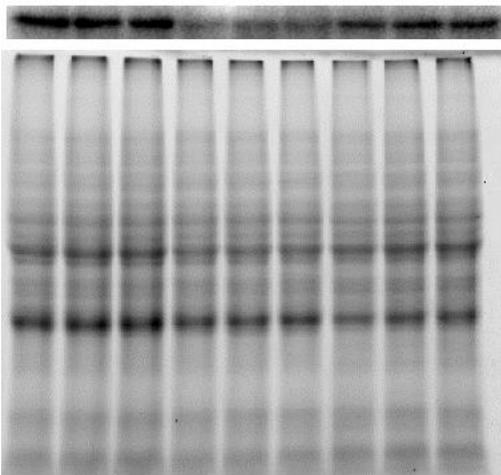
Dock180



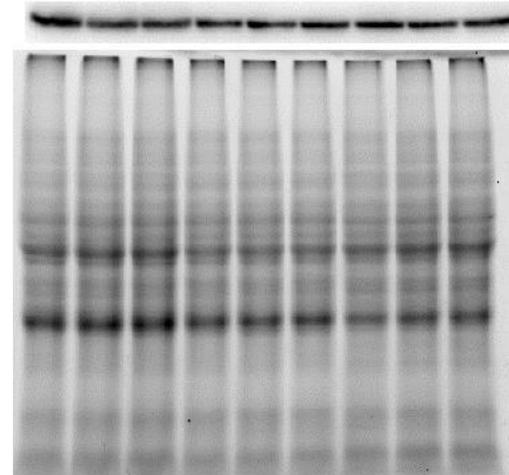
Rac1



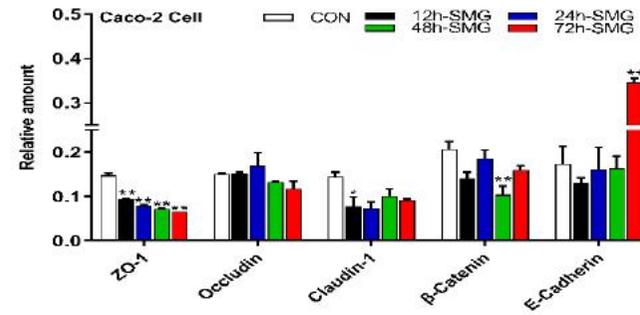
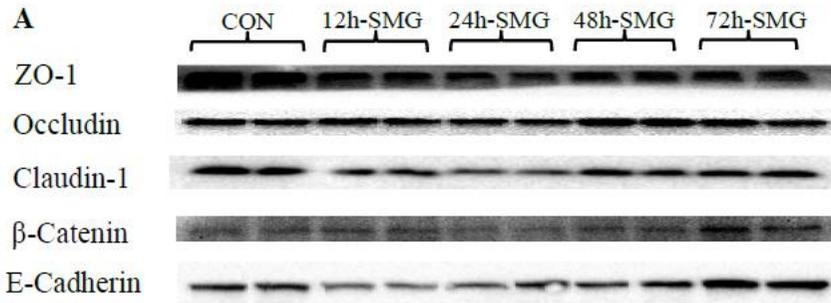
WAVE2



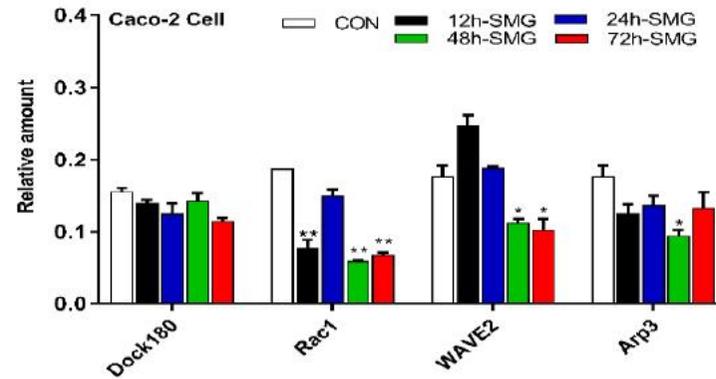
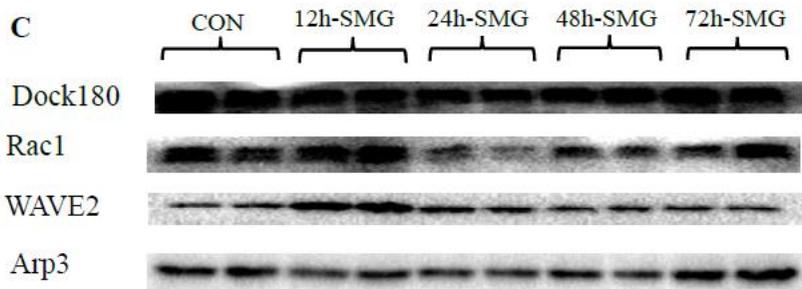
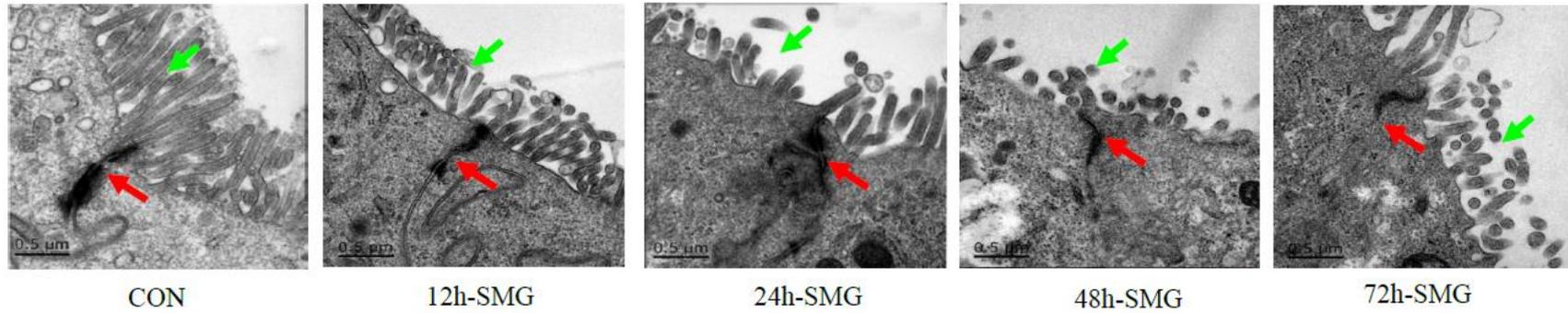
Arp3

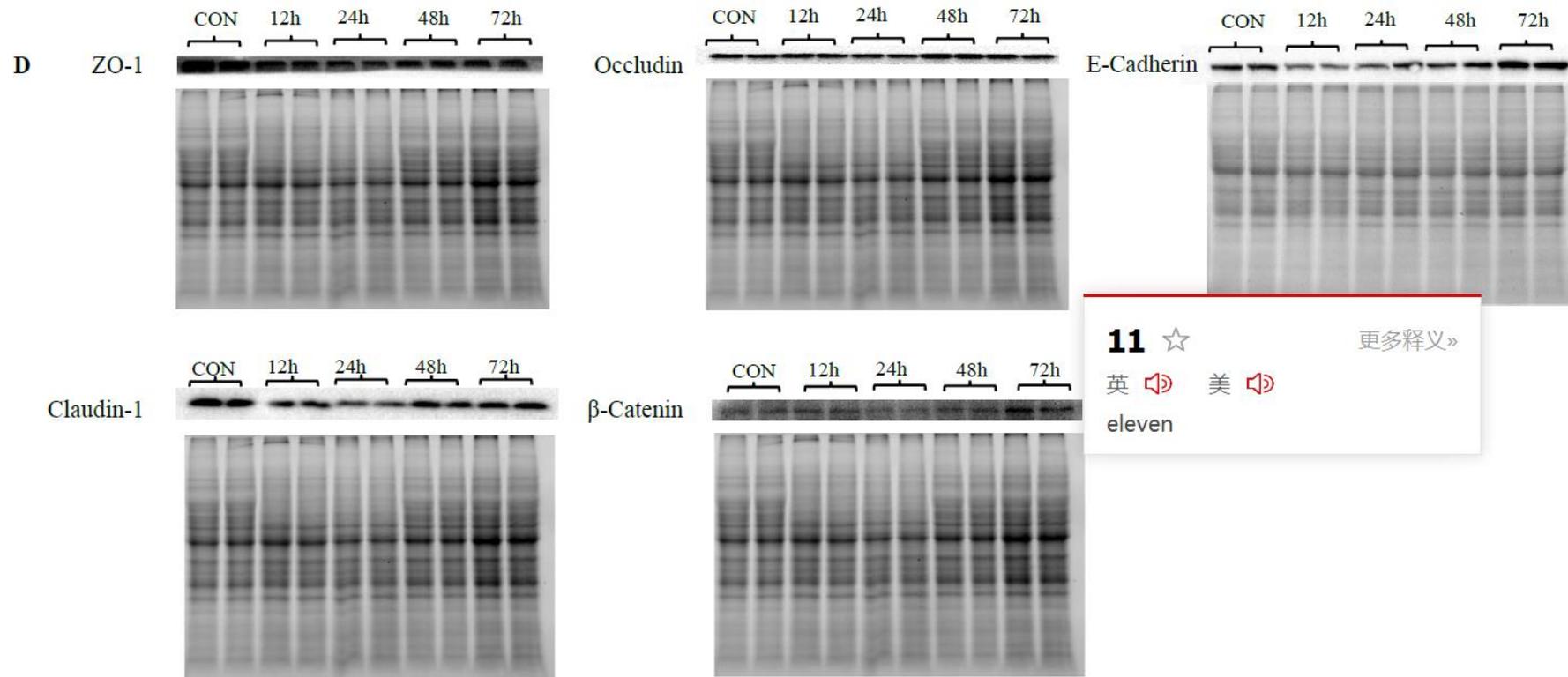


**Figure S5.** Western-blot bands of Dock180, Rac1, WAVE2, Arp3 and its corresponding total protein gels in rat ileum.



**B**





11 ☆

[更多释义»](#)

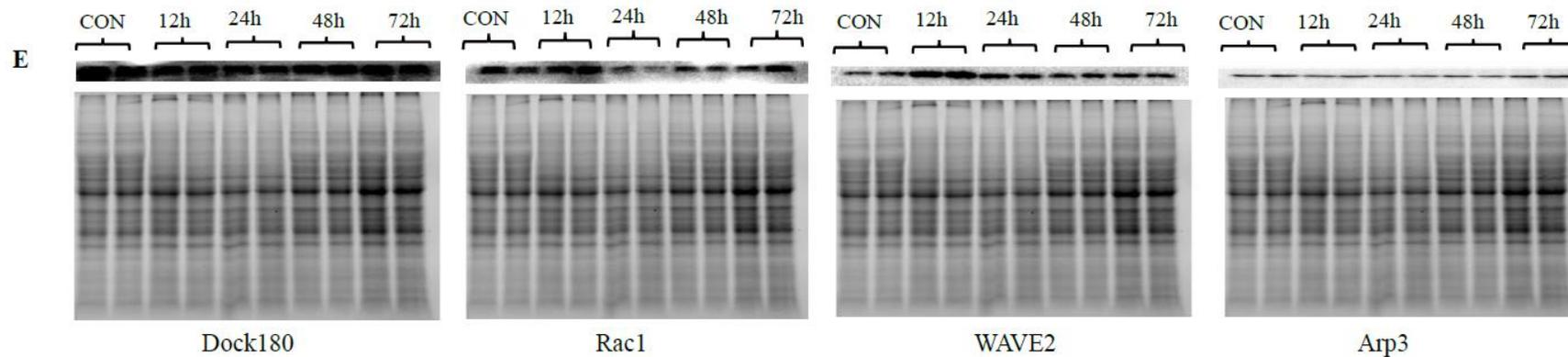
英



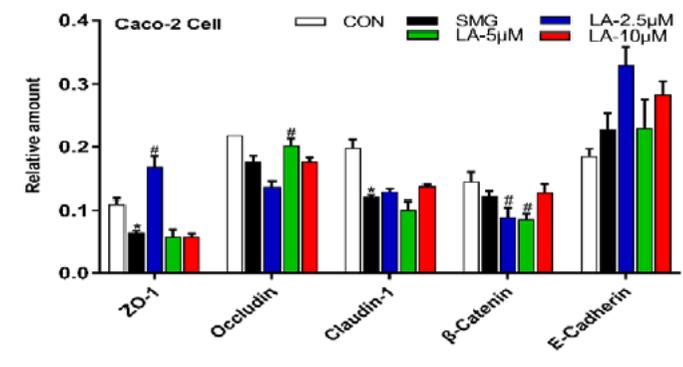
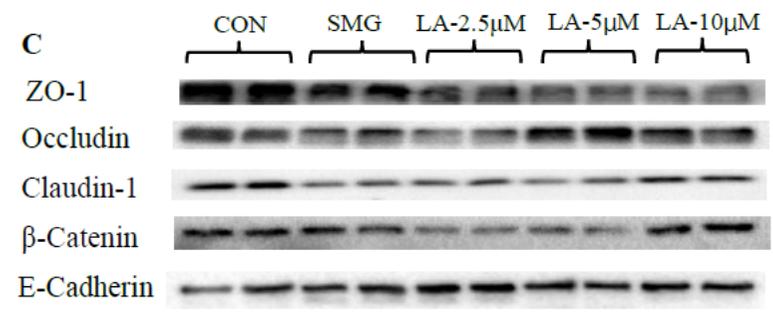
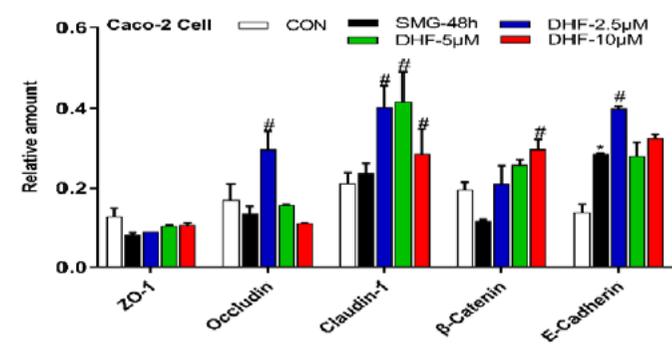
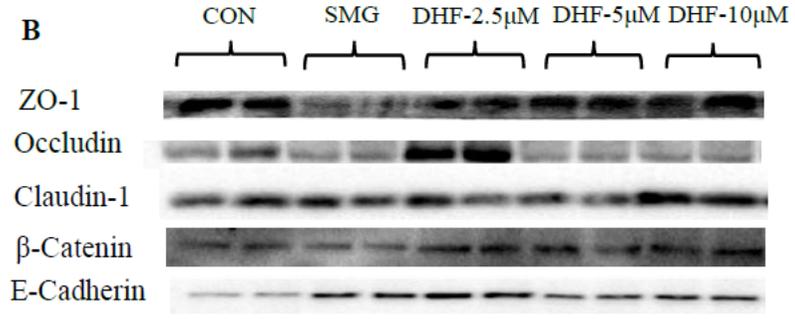
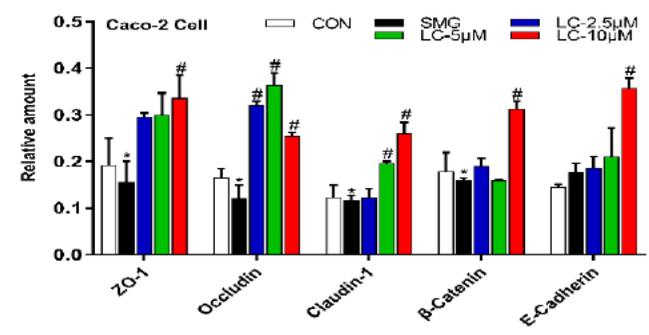
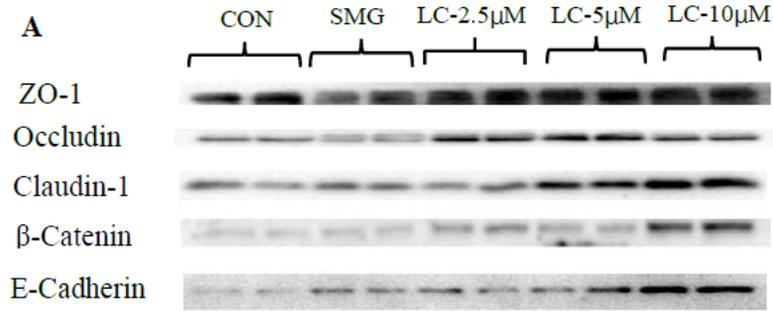
美



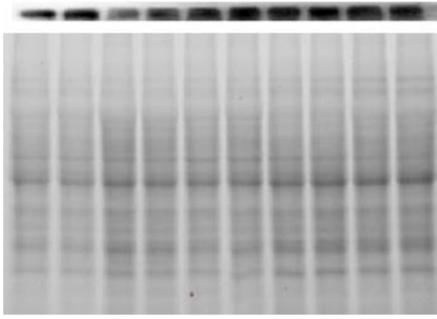
eleven



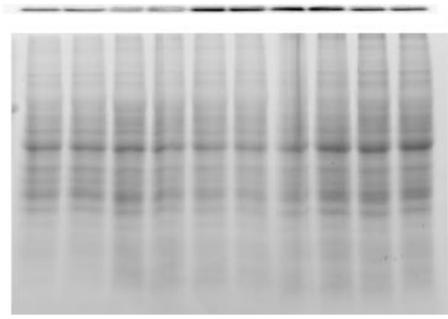
**Figure S6.** Expression of TJ and AJ proteins in Caco-2 cells with different duration of microgravity simulation (A). Several proteins were down-regulated under 48 h-SMG. TEM images of Caco-2 cells with different duration of microgravity simulation (B). The results showed that 48 h-SMG led to most serious damage with broken microvilli and enlarged cellular space. Expression of Rac1-WAVE2-Arp3 pathway proteins in Caco-2 cells with different duration of microgravity simulation (C). All proteins except Dock180 were down-regulated under 48 h-SMG. Note: \*  $p < 0.05$  and \*\*  $p < 0.01$ , compared with CON group. The relative expression levels of proteins were expressed as the ratio of gray value of the target band to that of total proteins in the same sample. The total proteins of AJ, TJ, Rac1-WAVE 2-Arp3 pathway proteins in Caco-2 cells with different duration of microgravity simulation (D-E).



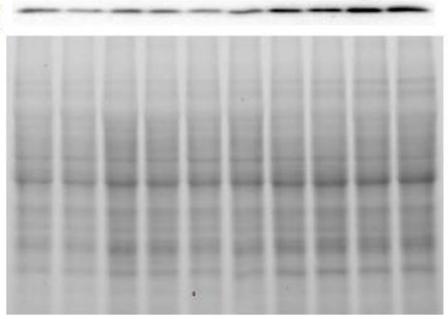
ZO-1



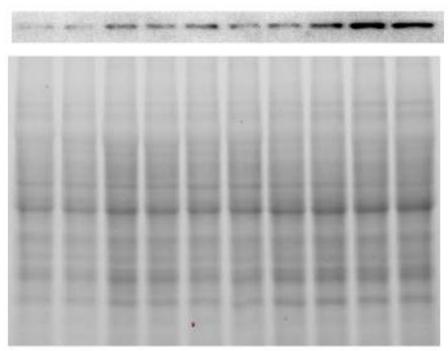
Occludin



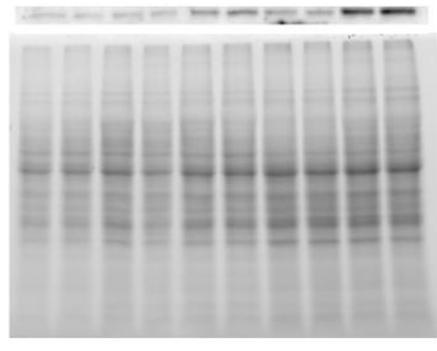
Claudin-1



$\beta$ -Catenin

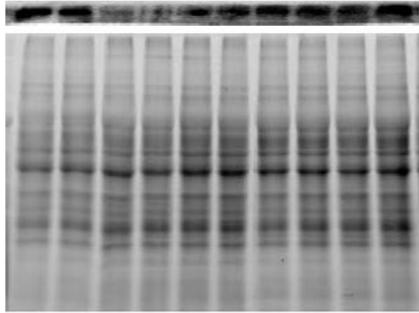


E-cadherin

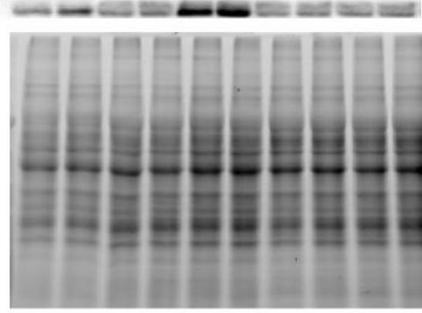


**D-LC**

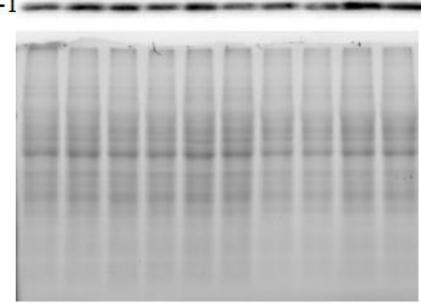
ZO-1



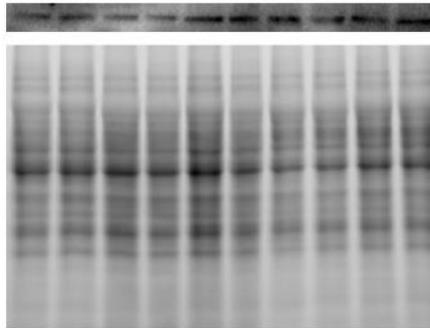
Occludin



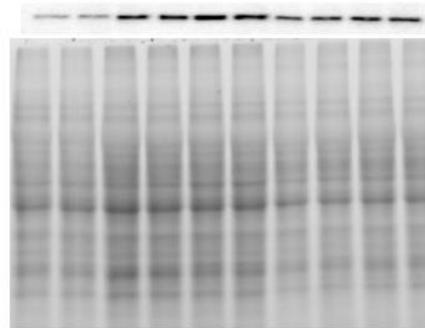
Claudin-1



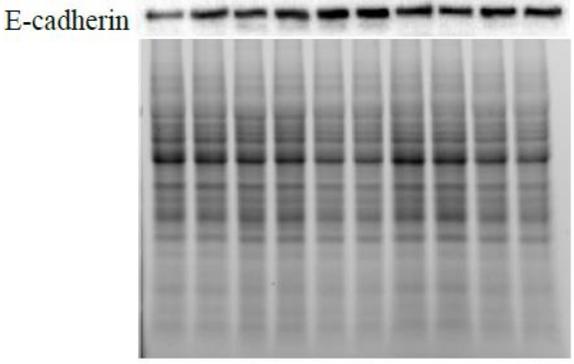
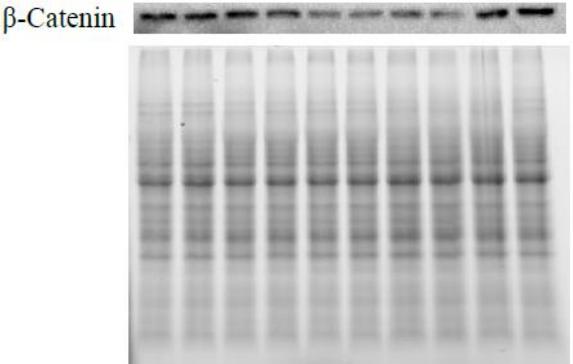
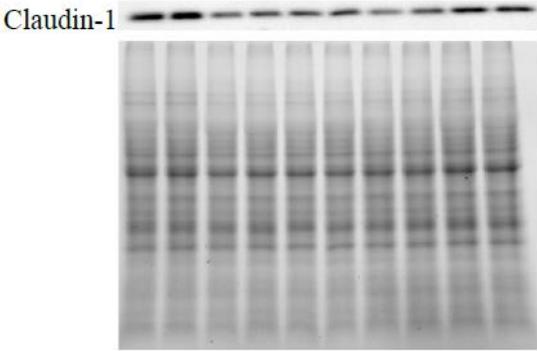
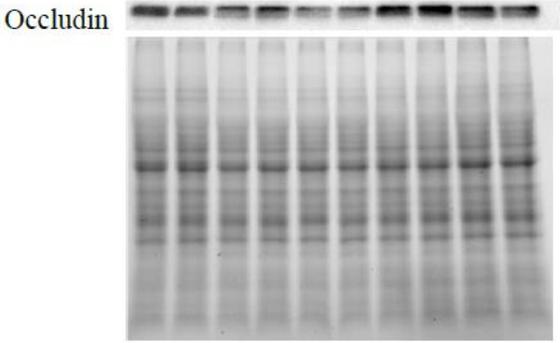
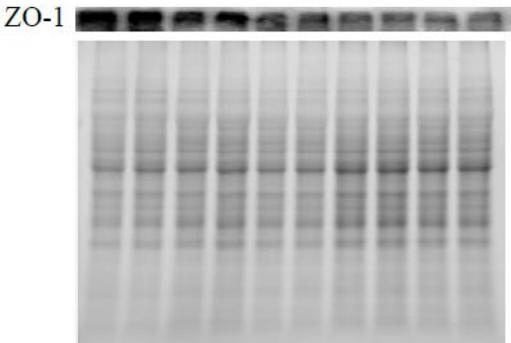
$\beta$ -Catenin



E-cadherin

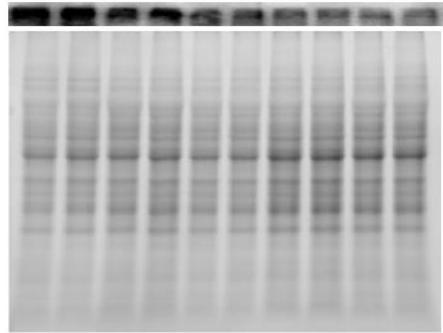


**E-7,4'-DHF**

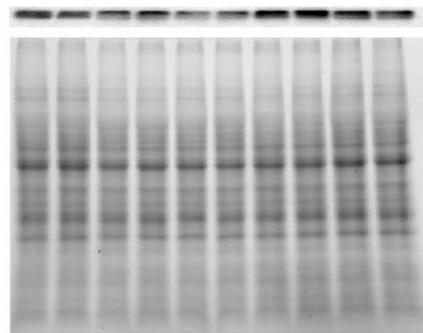


**F-LA**

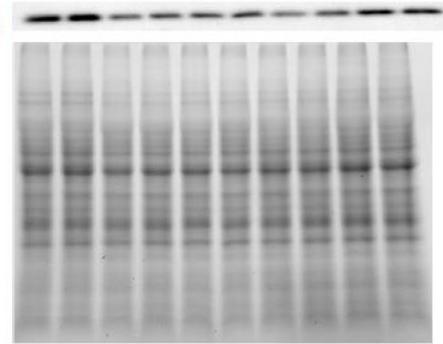
ZO-1



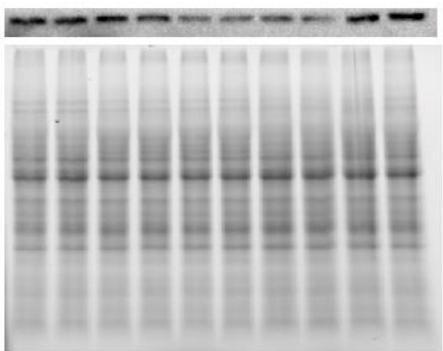
Occludin



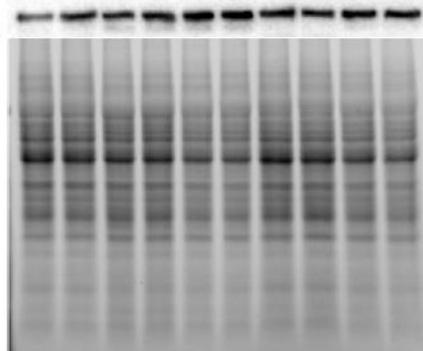
Claudin-1



$\beta$ -Catenin

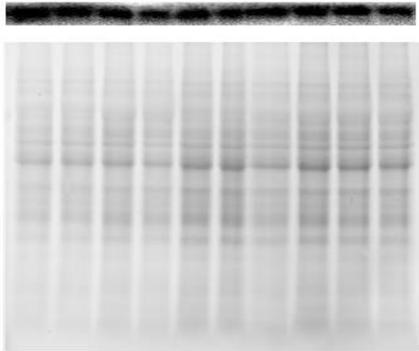


E-cadherin

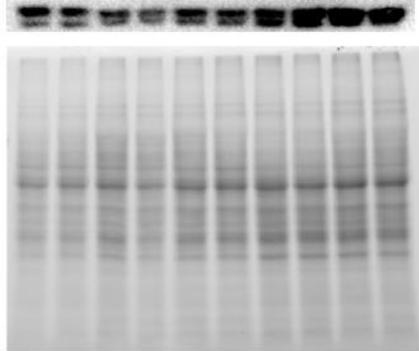


**G-LC**

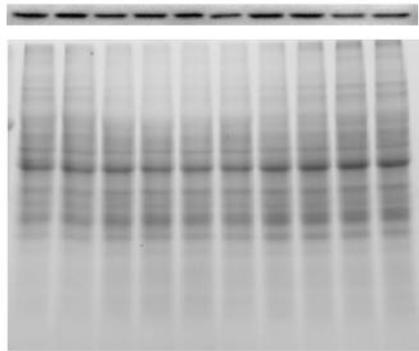
Dock180



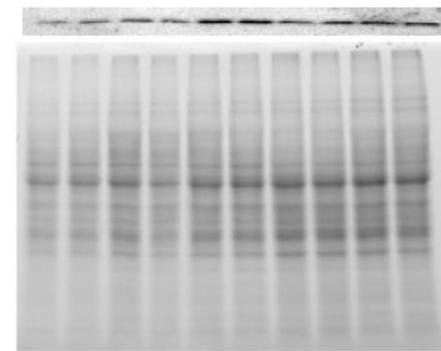
Rac1



WAVE2

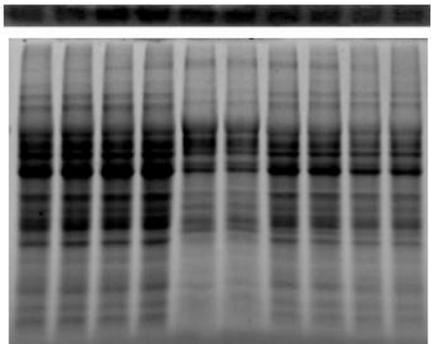


Arp3

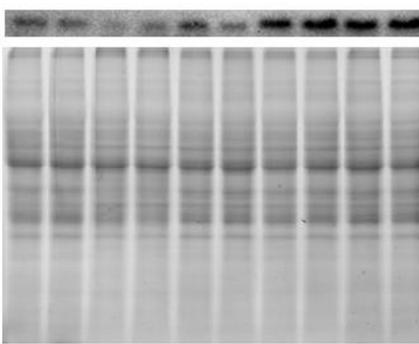


**H-7,4'-DHF**

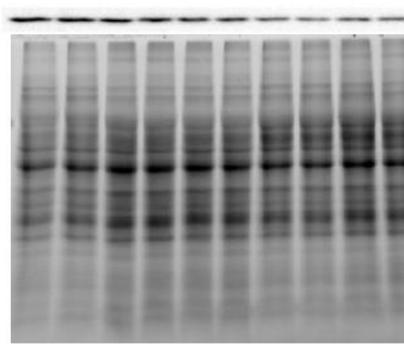
Dock180



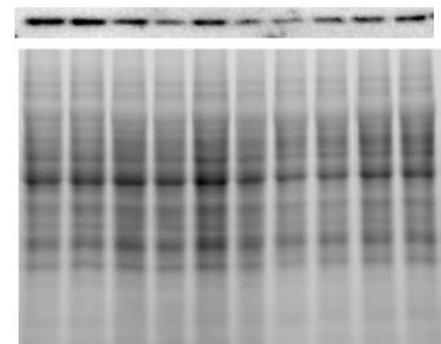
Rac1

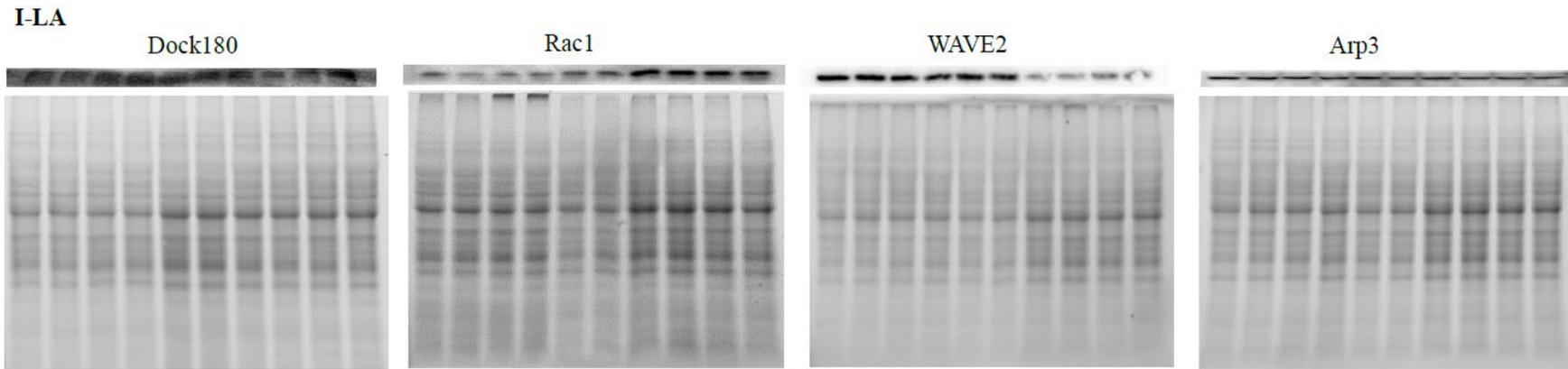


WAVE2



Arp3





**Figure S7.** Expression of AJ and TJ proteins in SMG-treated Caco-2 cells incubated with LC (A), 7,4'-DHF (B) and LA (C). LC and LA increased AJ and TJ proteins better than 7,4'-DHF. The total proteins gel corresponding to every band was listed in D (LC), E (7,4'-DHF), and F (LA), respectively. The Western-blot bands of Rac1-WAVE2-Arp3 pathway proteins in SMG-treated Caco-2 and their corresponding total proteins gel of LC (G), 7,4'-DHF (H) and LA (I).

**Supplementary Table S1 Docking energy (Kcal/mol) of different differentially expressed proteins and chemical structures of loureirin A, loureirin B, loureirin C, 7,4'-DHF, pterostilbene and resveratrol.**

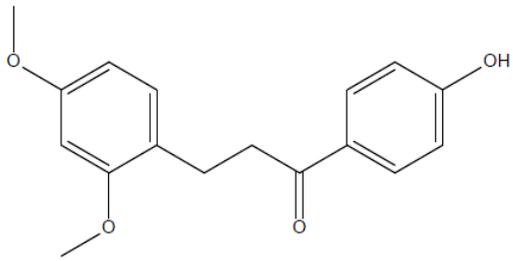
Num	Gene Name	Protein ID	Docking energy (Kcal/mol)					
			Loureirin A	Loureirin B	Loureirin C	7,4'- DHF	Resveratrol	Pterostilbene
1	actin, gamma 1(Actg1)	P63259	-7.24	-6.81	-6.59	-6.54	-6.21	-5.34
2	phosphoinositide-3-kinase regulatory subunit 1(Pik3r1)	F1LNG5	-7.15	-6.2	-6.51	-6.17	-6.03	-5.72
3	integrin subunit beta 1(Itgb1)	A0A0G2JSK5	-5.52	-5.38	-5.46	-6.71	-5.94	-6.68
4	actinin, alpha 1(Actn1)	Q6T487	-6.15	-6.24	-6.12	-6.5	-6.18	-6.8
5	vinculin (Vcl)	R9PXU6	-7.61	-7.24	-7.01	-7.02	-6.84	-6.73
6	rho-associated coiled-coil containing protein kinase 2(Rock2)	F1LQT3	-6.56	-6.58	-7.16	-7.02	-5.99	-5.5
7	protein phosphatase 1, regulatory subunit 12A(Ppp1r12a)	A0A0G2JWJ0	-6.59	-5.69	-5.88	-7.52	-6.87	-6.89
8	myosin light chain kinase(Mylk)	A0A0G2K0Q7	-7.61	-6.08	-6.5	-9.31	-8.52	-8.34
9	integrin alpha 2(Itga2)	A0A0G2K470	-5.92	-5.9	-6.01	-6.95	-6.59	-6.07
10	rho-associated coiled-coil containing protein kinase 1(Rock1)	D3ZN37	-6.24	-5.76	-5.86	-6.97	-6.17	-6.15
11	dedicator of cyto-kinesis 1(Dock1)	D3ZZW1	-6.08	-5.64	-7.27	-6.27	-6.46	-6.61
12	mitogen activated protein kinase kinase 1(Map2k1)	Q01986	-7.07	-6.9	-8.67	-7.29	-7.6	-7.62
13	v-crk avian sarcoma virus CT10 oncogene homolog-like(Crkl)	Q5U2U2	-6.62	-6.69	-7.57	-6.41	-6.93	-6.97
14	p21 (RAC1) activated kinase 4(Pak4)	B5DF62	-6.34	-5.79	-6.09	-6.58	-6.19	-6.43
15	integrin subunit beta 4(Itgb4)	F1LSD3	-6.03	-5.99	-5.5	-6.28	-6.07	-6.71
16	integrin subunit alpha 6(Itga6)	G3V667	-7.47	-7.34	-7.69	-6.06	-5.89	-5.33
17	p21 (RAC1) activated kinase 1(Pak1)	P35465	-6.3	-5.66	-6.04	-6.71	-6.29	-6.36
18	integrin subunit beta 6(Itgb6)	Q6AYF4	-6.53	-5.8	-6.59	-8.09	-6.88	-6.99
19	IQ motif containing GTPase activating protein 1(Iqgap1)	G3V7Q7	-5.76	-5.33	-5.61	-6.63	-6.04	-6.28
20	mitogen activated protein kinase kinase 2(Map2k2)	P36506	-6.73	-5.96	-7.81	-7.16	-7.69	-7.52
21	cytoplasmic FMR1 interacting protein 1(Cyfip1)	A0A0G2K472	-7.37	-6.52	-6.79	-7.83	-7.95	-7.09

Continued

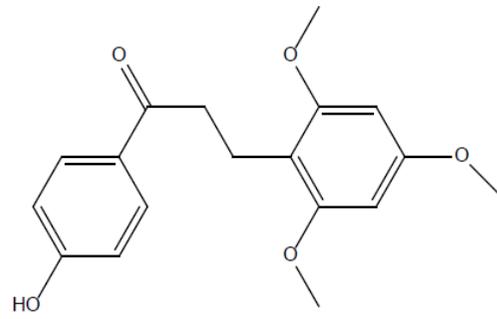
22	IQ motif containing GTPase activating protein 2(Iqgap2)	F1LW74	-6.28	-6.25	-6.11	-7.18	-5.96	-6.29
23	phosphatidylinositol-5-phosphate 4-kinase type 2 gamma(Pip4k2c)	O88370	-6.29	-5.62	-6.85	-6.98	-7.07	-6.81
24	ezrin(Ezr)	P31977	-5.52	-5.05	-5.47	-6.18	-5.8	-6.05
25	NCK-associated protein 1(Nckap1)	P55161	-6.03	-5.61	-5.99	-6.83	-6.02	-6.29
26	erb-b2 receptor tyrosine kinase 2(ErbB2)	A0A0G2JT61	-7.5	-7.11	-6.72	-6.75	-6.91	-6.45
27	filamin B(Flnb)	D4A8D5	-6.05	-5.35	-5.78	-6.68	-5.71	-6.1
28	laminin subunit beta 3(Lamb3)	F1LPI5	-7.87	-7.44	-7.39	-6.75	-6.61	-5.87
29	talin 1(Tln1)	G3V852	-5.92	-6	-6.36	-6.99	-6.28	-6.09
30	zyxin(Zyx)	D4A7U1	-6.28	-5.59	-5.77	-6.62	-5.8	-6.02
31	protein kinase C, alpha(Prkca)	F1M2P8	-6.59	-6.56	-6.62	-7.21	-6.5	-6.54
32	tight junction protein 1(Tjp1)	A0A0G2K2P5	-8.1	-7.5	-7.31	-7.04	-7.01	-7.11
33	cortactin(Cttn)	Q66HL2	-7.11	-6.78	-6.7	-6.31	-5.63	-5.33
34	claudin 2(Cldn2)	A0A0G2JYB2	-6.11	-6.21	-6.11	-6.31	-5.71	-5.96
35	tight junction protein 3(Tjp3)	A0A0G2K8M3	-6.49	-6.48	-6.3	-7.32	-6.47	-6.59
36	myosin heavy chain 14(Myh14)	F1LNF0	-7.22	-6.64	-6.62	-8.07	-7.61	-7.86
37	symplekin(Sympk)	F1LSH0	-6.55	-5.71	-6.54	-7.03	-6.34	-7.06
38	myosin, heavy chain 9, non-muscle-like 1(Myh911)	G3V6P7	-6.61	-6.11	-7.09	-7.06	-6.52	-6.79
39	tight junction protein 2(Tjp2)	Q3ZB99	-6.55	-6	-6.86	-7.27	-6.45	-6.53
40	protein phosphatase 2 scaffold subunit A beta(Ppp2r1b)	Q4QQT4	-5.35	-5.14	-5.82	-6.25	-6.19	-6.24
41	protein phosphatase 2 scaffold subunit A alpha(Ppp2r1a)	Q5XI34	-6.21	-6.03	-6.3	-6.24	-5.64	-6.01
42	claudin 3(Cldn3)	Q63400	-6.25	-5.98	-6.24	-7.04	-6.49	-6.44
43	catenin alpha 1(Ctnna1)	Q5U302	-6.61	-6.5	-6.66	-7.92	-7.49	-7.46
44	dynamamin 2(Dnm2)	A0A0A0MY48	-7.87	-5.78	-6.95	-8.23	-7.44	-7.79
45	engulfment and cell motility 1(Elmo1)	A0A0G2K4S6	-5.37	-4.55	-5.27	-6.13	-5.37	-5.56

Continued

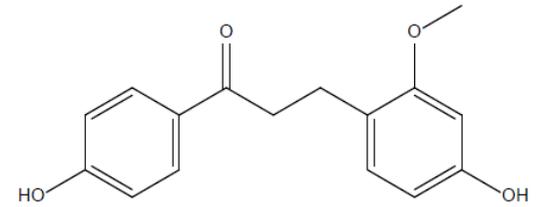
46	CD2-associated protein(Cd2ap)	F1LRS8	-6.32	-5.58	-5.94	-7.14	-6.96	-6.82
47	clathrin heavy chain(Cltc)	F1M779	-7.15	-7.05	-7.33	-7.17	-6.97	-6.96
48	engulfment and cell motility 3(Elmo3)	Q499U2	-6.06	-5.93	-6.04	-7.28	-6.65	-7.1
49	SMAD family member 4(Smad4)	A0A0G2JXW2	-6.17	-5.65	-6.49	-6.86	-6.5	-6.1
50	catenin delta 1(Ctnnd1)	D3ZZZ9	-6.11	-5.49	-6.91	-6.3	-6.29	-6.39
51	nectin cell adhesion molecule 3(Nectin3)	D4A5C0	-5.33	-5.09	-5.73	-6.21	-5.33	-5.42
52	protein tyrosine phosphatase, receptor type, F(Ptprf)	G3V8P4	-5.97	-5.05	-5.28	-6.72	-6.13	-6.07
53	Ras-related C3 botulinum toxin substrate 1 (Rac1)	Q6RUV5	-5.88	-5.88	-7.04	-6.15	-6.65	-6.12
54	Actin-related protein 3 (Arp3)	Q4V7C7	-8.09	-8.09	-8.35	-7.65	-7.83	-6.49
55	$\beta$ -catenin (Ctnnb)	Q9WU82	-5.17	-4.63	-5.2	-6.32	-5.63	-5.57
56	Occludin (Ocln)	Q6P6T5	-4.26	-3.87	-4.02	-5.21	-4.58	-4.73
57	Claudin-1 (Cldn)	P56745	-5.82	-5.57	-5.39	-6.66	-5.69	-5.89
58	E-Cadherin (Cdh1)	Q9R0T4	-7.38	-7.14	-7.71	-6.34	-6.74	-5.46



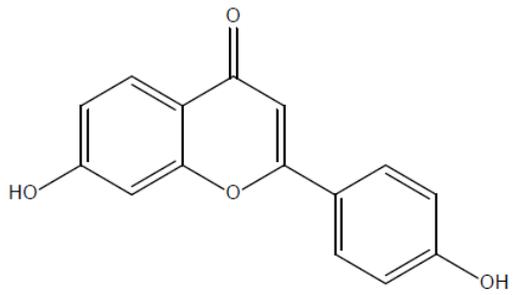
Loureirin A



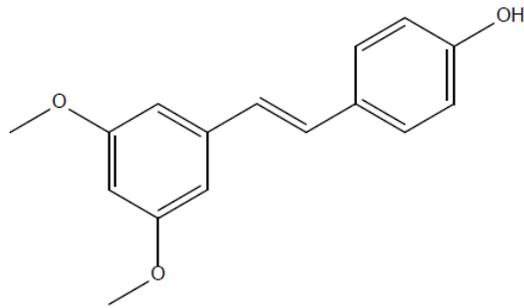
Loureirin B



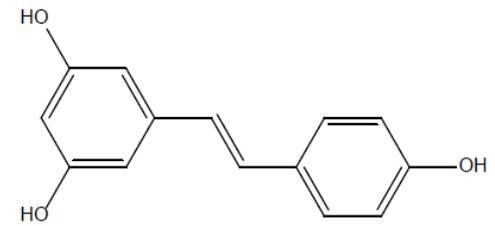
Loureirin C



7,4'-Dihydroxyflavone



Pterostilbene



Resveratrol