Figure S1

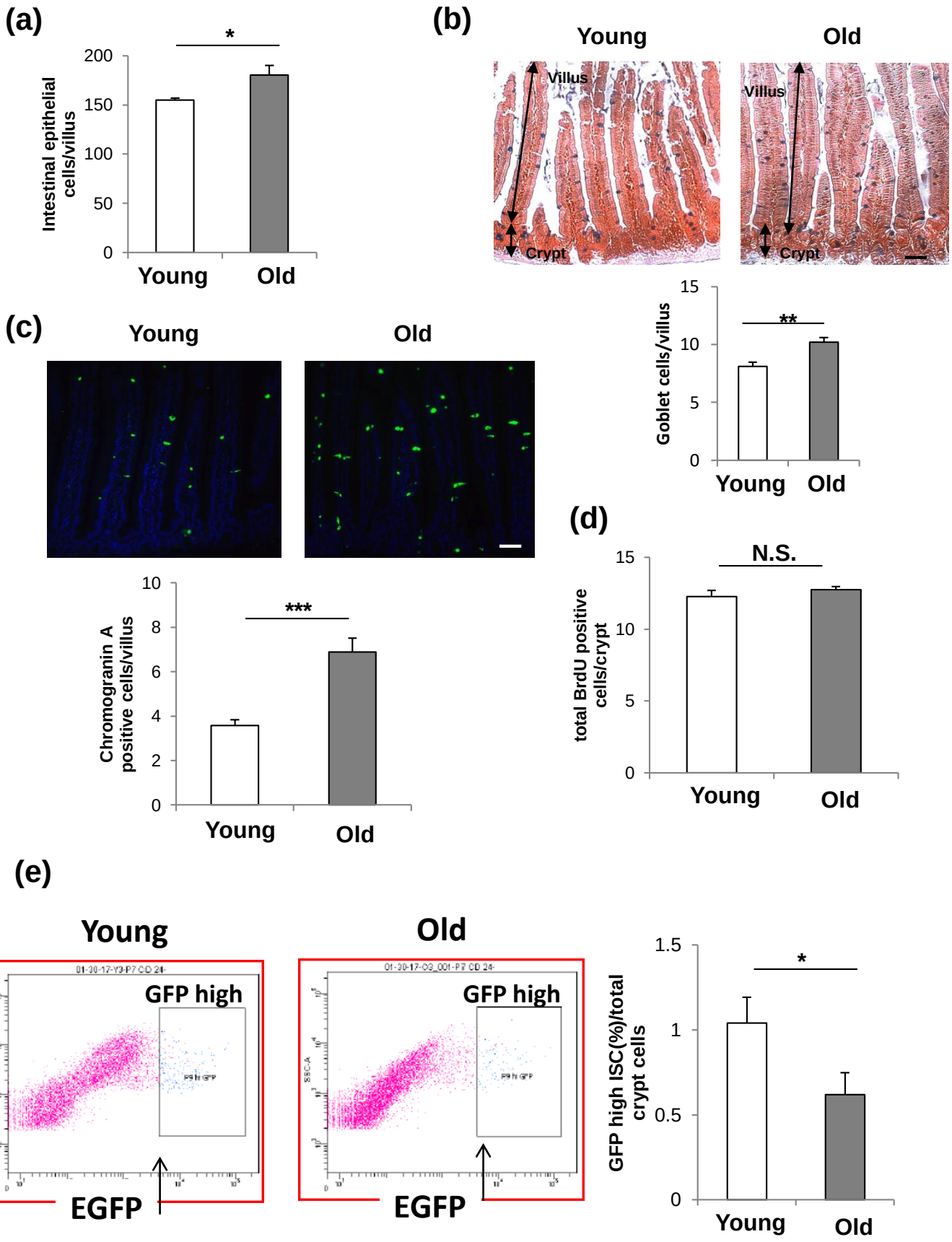

(a)
Intestinal epithelial cells/villus
200
150
100
50
0
*
Young
Old
(b)
Young
Old
Villus
Crypt
Villus
Crypt
(c)
Young
Old
Chromogranin A positive cells/villus
10
8
6
4
2
0
***
Young
Old
Goblet cells/villus
15
10
5
0
**
Young
Old
(d)
total BrdU positive cells/crypt
15
10
5
0
N.S.
Young
Old
(e)
Young
Old
GFP high
GFP high
EGFP
EGFP
GFP high ISC(%)/total crypt cells
1.5
1
0.5
0
*
Young
Old

Figure S2

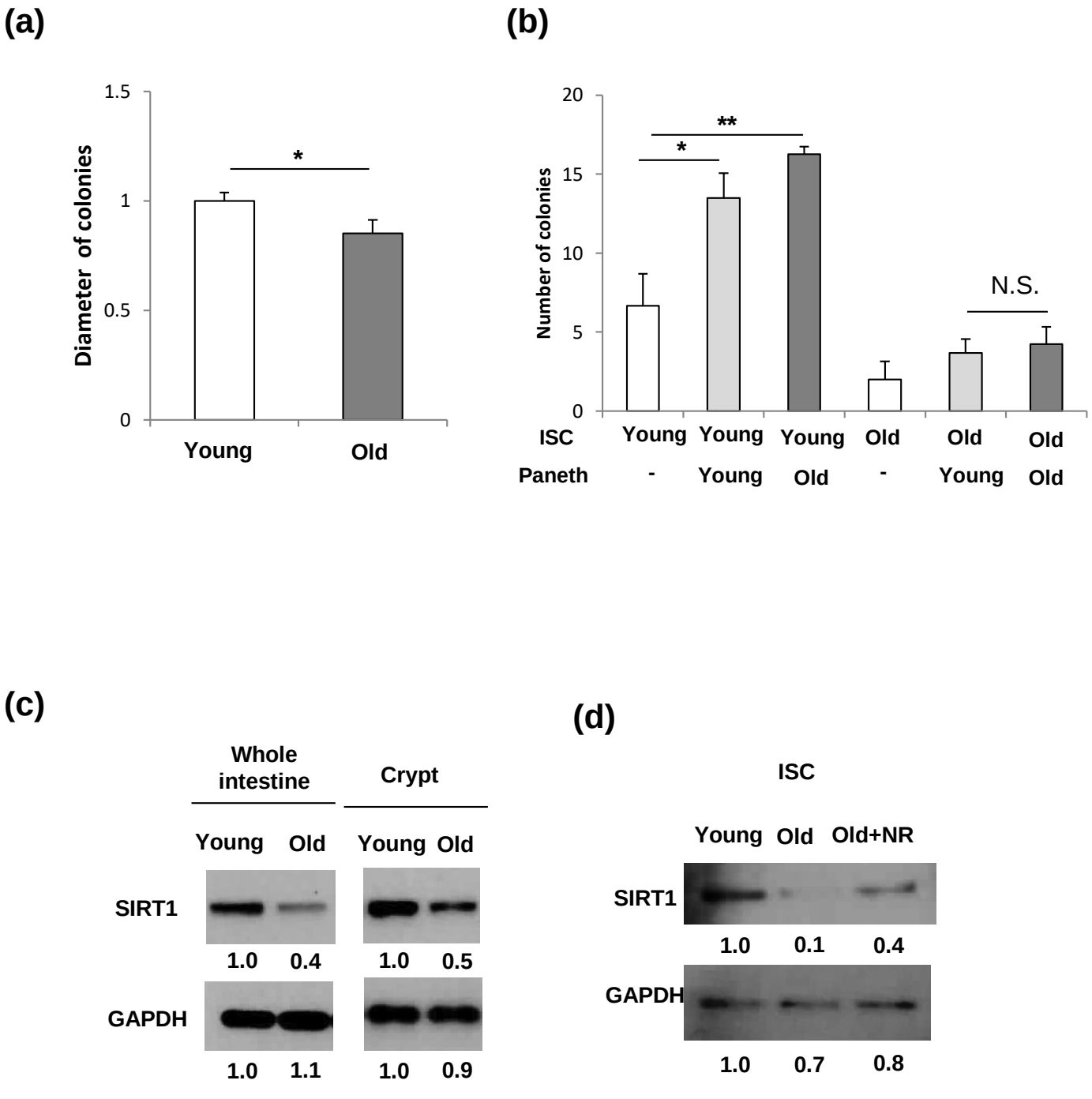
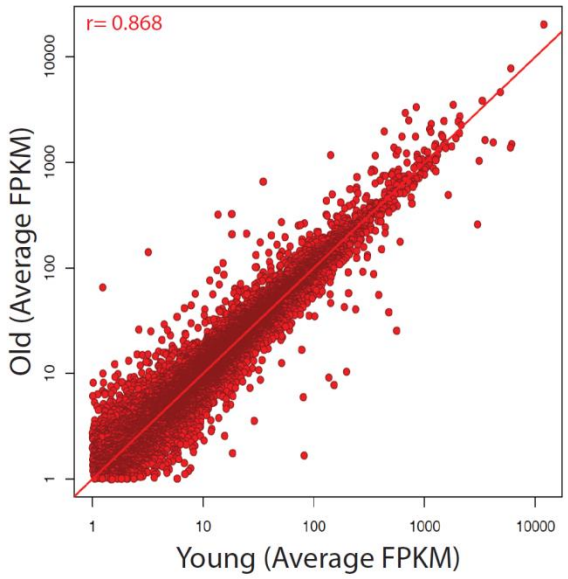

(a)
Diameter of colonies
1.5
1
0.5
0
*
Young
Old
(b)
Number of colonies
20
15
10
5
0
**
*
N.S.
ISC
Young
Young
Young
Old
Old
Old
Paneth
-
Young
Old
-
Young
Old
(c)
Whole intestine
Crypt
Young
Old
Young
Old
SIRT1
1.0
0.4
1.0
0.5
GAPDH
1.0
1.1
1.0
0.9
(d)
ISC
Young
Old
Old+NR
SIRT1
1.0
0.1
0.4
GAPDH
1.0
0.7
0.8

Figure S3

(a)



(b)

Gene ID	Young (Average FPKM)	Old (Average FPKM)	log2(fold_change)	q_value
Reg3b	670.052	2943.42	2.13515	0.00910147
Apoa1	715.457	2490.49	1.79949	0.00910147
Mir5121,Rpl13a,Snord33	1146.72	2321.22	1.01736	0.0350321
Apoa4	620.431	1768.78	1.51141	0.0430539
Fabp1	826.531	1768.72	1.09757	0.00910147
Rbp2	526.281	1377.22	1.38786	0.00910147
2210404O07Rik	554.189	1187.14	1.09904	0.0215895
2200002D01Rik	336.296	855.33	1.34675	0.00910147
Rabggtb,Snord45c	34.8038	655.257	4.23474	0.00910147
Mt1	242.162	580.198	1.26057	0.00910147
Guca2b	129.707	433.729	1.74154	0.00910147
Hipk3,Mir1902	13.6118	319.294	4.55196	0.00910147
Sis	72.2196	252.402	1.80526	0.00910147
Bpnt1	109.886	220.255	1.00317	0.0315765
Slc9a3r1	106.041	219.805	1.0516	0.0315765
Mt2	24.5766	213.1	3.11617	0.00910147
Coro2a	91.6118	206.147	1.17007	0.00910147
Slc5a1	78.0694	186.067	1.25299	0.0215895
Gstm1	46.2149	166.077	1.84542	0.00910147
Apob	51.2973	144.219	1.49131	0.0215895
Papss2	49.3341	133.235	1.43332	0.00910147
Kcne3	303.848	132.579	-1.1965	0.0275067
Enpep	49.3548	129.981	1.39704	0.00910147
Ifitm3	303.254	125.733	-1.27016	0.0154725
Aldh1a1	53.1201	120.043	1.17622	0.00910147
Acadl	60.4367	119.126	0.978994	0.0215895
Sepp1	39.6199	114.424	1.5301	0.00910147
Ces1f	50.0747	106.207	1.08473	0.0350321
Gpd1	49.1049	102.752	1.06523	0.0154725
Creb3l3	30.3965	102.534	1.75413	0.00910147
Ace	29.6539	102.433	1.78839	0.00910147
Slc6a6	40.6761	101.389	1.31765	0.00910147
Clca3	275.156	92.0953	-1.57905	0.00910147
Mia2	40.8711	91.7703	1.16695	0.00910147
Ms4a10	34.8073	91.4897	1.39422	0.0154725
Akr1b7	15.3488	86.3315	2.49176	0.00910147
Cyp4v3	33.814	84.8475	1.32725	0.00910147
Akr1c19	32.7456	83.3349	1.34762	0.00910147
Por	39.1708	81.4973	1.05697	0.0350321
Zfp36	36.0281	80.6137	1.1619	0.00910147
Slc7a8	39.5007	77.4992	0.972303	0.0430539
Ano6	34.0261	75.2988	1.14599	0.0154725
Xdh	30.8066	72.9073	1.24282	0.0154725
Ace2	29.3893	69.9477	1.25098	0.0154725
Cyp3a11	19.3146	63.7501	1.72273	0.00910147
Gpt	19.4496	63.0328	1.69636	0.00910147
Npc1l1	30.8624	62.98	1.02904	0.0460339
Cyp2c65	24.5379	62.8853	1.35771	0.00910147
Cdr2	21.4597	62.8084	1.54932	0.00910147
Tgfbi	26.9651	59.899	1.15144	0.0350321
Vat1	21.8065	59.4886	1.44785	0.00910147
Inpp5b,Mir698	20.6095	59.1636	1.5214	0.00910147
Cobl	18.9471	58.0816	1.6161	0.00910147
Ang4	204.753	57.9512	-1.82097	0.00910147
Cited2	25.6471	57.3092	1.15997	0.0275067
Pck1	8.48364	57.0149	2.74858	0.00910147
Fkbp5	12.1961	56.6774	2.21636	0.00910147
Axin2	112.343	56.2103	-0.999006	0.0499113

Gene ID	Young (Average FPKM)	Old (Average FPKM)	log2(fold_change)	q_value
Hsph1	139.538	56.1016	-1.31454	0.0460339
Lgals3	23.8038	55.0113	1.20854	0.0350321
Ggt1	20.1541	53.2701	1.40225	0.00910147
Cyp2b10	15.9021	48.4649	1.60772	0.00910147
Cyp3a13	19.4557	47.2981	1.28159	0.00910147
Hpgd	19.875	47.2711	1.25001	0.0154725
Cyp2d26	18.1035	45.3326	1.32428	0.0315765
Mir17hg,Mir19b-1	7.76562	44.5232	2.51939	0.0460339
Abcc2	14.7825	41.405	1.48591	0.00910147
Nr1d1	10.3352	40.6452	1.97552	0.00910147
Slc26a3	18.0152	40.1854	1.15746	0.0315765
Fbp1	13.8486	40.1738	1.53651	0.0315765
Slc25a24	15.3096	38.3472	1.32469	0.00910147
Mme	18.6712	37.3987	1.00217	0.0393845
Hsd17b13	10.217	35.6409	1.80256	0.0499113
Cirbp	5.81019	34.6005	2.57414	0.0154725
Slc6a8	16.0509	34.216	1.09202	0.0430539
Abcg8	13.2486	32.2835	1.28496	0.0154725
Dgat2	11.3642	31.911	1.48956	0.0215895
Maf	14.0848	31.7493	1.17259	0.0350321
Fmo5	15.0333	31.0948	1.04851	0.0275067
Slc2a2	7.74252	30.0048	1.95432	0.00910147
Mir3062,Pfas	12.7225	29.4883	1.21277	0.0393845
Akr1b8	4.44455	29.4738	2.72932	0.0315765
Slc15a1	8.97078	27.1441	1.59733	0.00910147
Myc	60.2757	25.8612	-1.22079	0.00910147
Iyd	3.36181	25.1313	2.90218	0.0154725
Sec24d	10.8971	24.7369	1.18273	0.0350321
Cyp27a1	6.87583	23.9324	1.79936	0.0430539
Slc6a19	5.07631	23.0961	2.1858	0.00910147
Prelp	52.0403	22.0911	-1.23616	0.0460339
Slfn9	50.3459	20.8801	-1.26974	0.00910147
Clec2e	6.5875	20.6252	1.64661	0.0315765
C530008M17Rik	7.12146	17.7403	1.31679	0.00910147
Mical2	8.19329	17.0683	1.0588	0.0460339
Per1	5.54937	16.4541	1.56805	0.00910147
Sowaha	6.11869	15.9557	1.38277	0.0499113
Slc2a5	4.6139	15.7766	1.77372	0.0315765
Kif21b	6.27432	15.7488	1.32771	0.00910147
Tef	2.5276	15.1986	2.5881	0.00910147
Sgk1	2.81979	15.0906	2.41999	0.0460339
Mafb	3.25584	12.7761	1.97234	0.00910147
Cd44	27.7856	11.2394	-1.30578	0.0154725
Clca2	25.7568	10.201	-1.33623	0.0215895
Zc3h6	2.21017	9.23341	2.06271	0.00910147
Dnaja1,Mir207	136.43	9.13623	-3.90042	0.00910147
Cd36	1.85075	8.24773	2.15589	0.0393845
Mir702,Plod3	80.1594	5.96569	-3.74811	0.00910147
Banp	11.7527	3.60826	-1.70362	0.0275067
Gsdmc4	28.8604	3.58221	-3.01017	0.00910147
Adamts15	8.21375	2.96564	-1.4697	0.0430539
Mir678,Prmt2	81.6631	1.68033	-5.60287	0.00910147

Figure S4

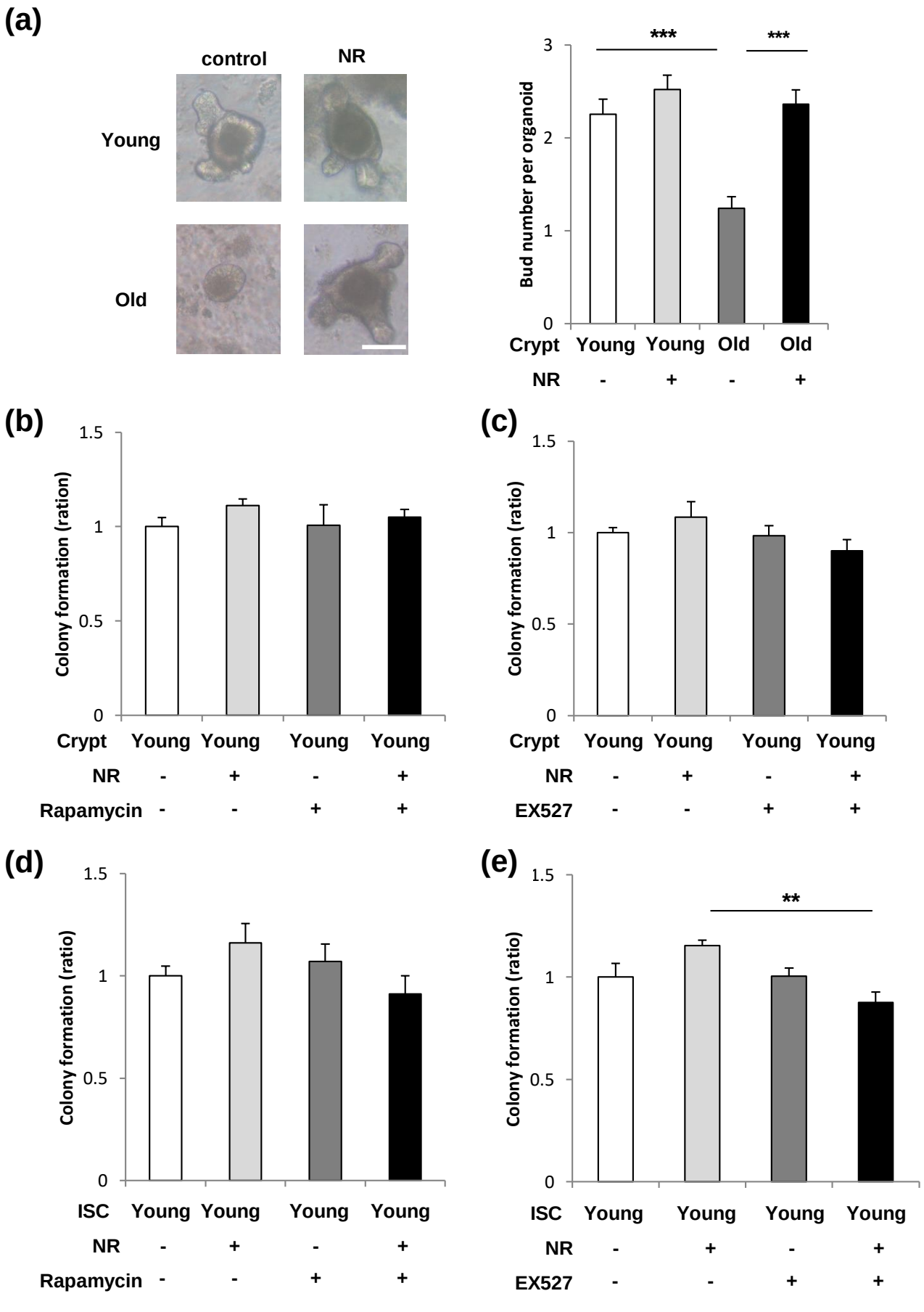

(a)
control
NR
Young
Old
***
***
Bud number per organoid
3
2
1
0
Crypt Young Young Old Old
NR - + - +
(b)
Colony formation (ration)
1.5
1
0.5
0
Crypt Young Young Young Young
NR - + - +
Rapamycin - - + +
(c)
Colony formation (ratio)
1.5
1
0.5
0
Crypt Young Young Young Young
NR - + - +
EX527 - - + +
(d)
Colony formation (ratio)
1.5
1
0.5
0
ISC Young Young Young Young
NR - + - +
Rapamycin - - + +
(e)
Colony formation (ratio)
**
1.5
1
0.5
0
ISC Young Young Young Young
NR - + - +
EX527 - - + +

Figure S5

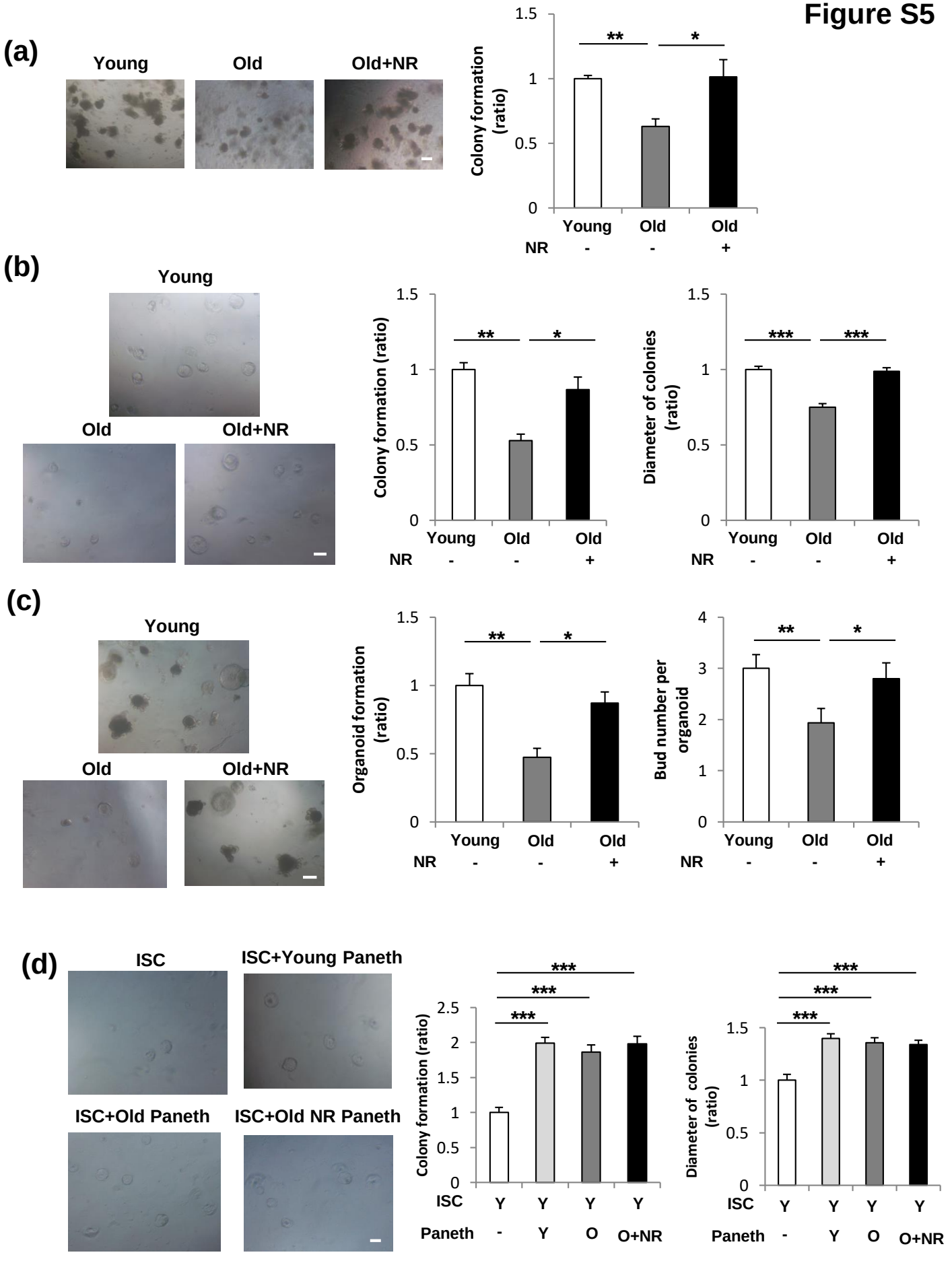
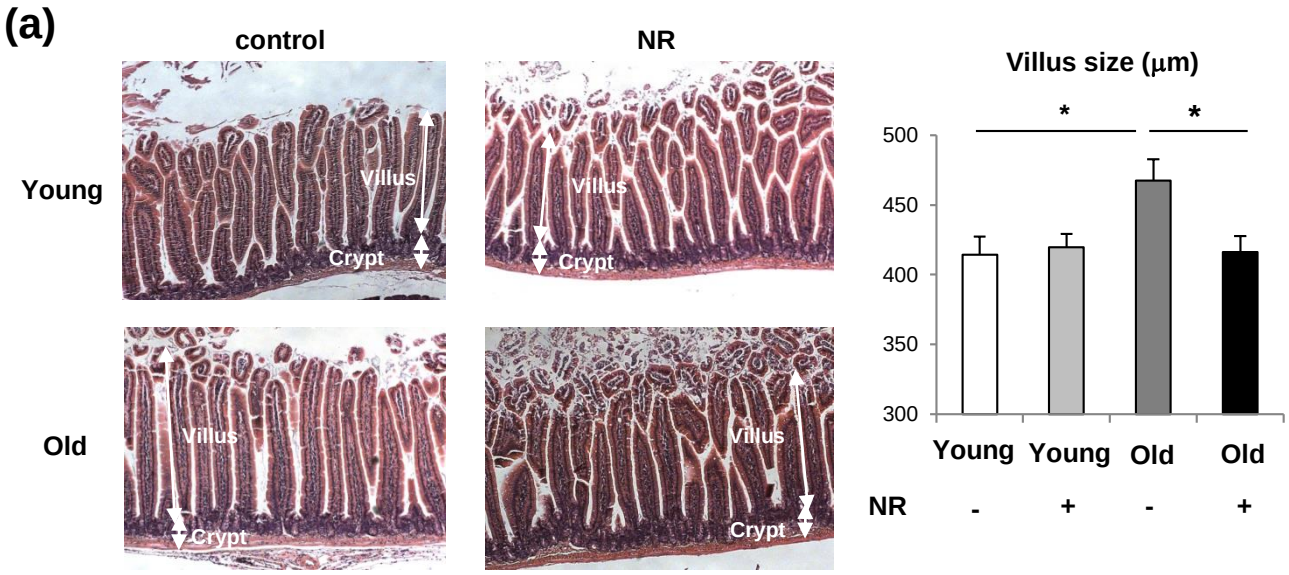
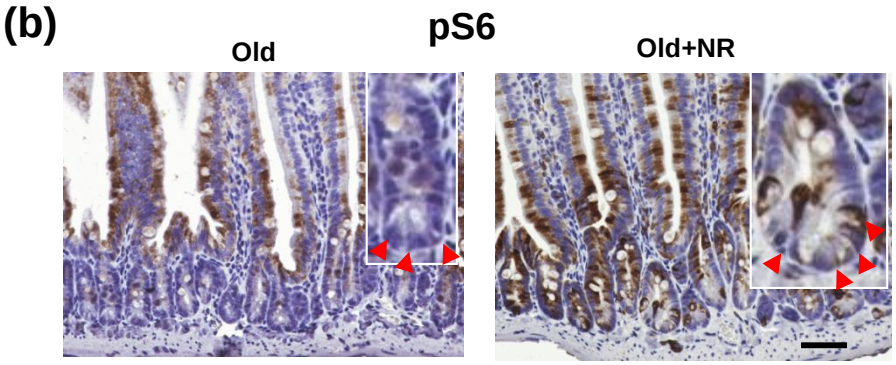

(a)
Young
Old
Old+NR
Colony formation (ratio)
1.5
1
0.5
0
**
*
Young
Old
Old
NR
-
-
+
(b)
Young
Old
Old+NR
Colony formation (ratio)
Diameter of colonies (ratio)
***
(c)
Organoid formation (ratio)
Bud number per organoid
4
3
2
(d)
ISC
ISC+Young Paneth
ISC+Old Paneth
ISC+Old NR Paneth
2.5
ISC
Y
Paneth
-
O
O+NR

Figure S6


(a)
control
NR
Young
Old
Villus
Crypt
Villus size (μm)
500
450
400
350
300
*
*
Young
Young
Old
Old
NR
-
+
-
+


(b)
pS6
Old
Old+NR