Supplementary data

Materials and methods

CpG genomic regions analyzed by pyrosequencing

Cdkn2a: cyclin-dependent kinase inhibitor 2A (also known as p16)

Rassf1a: RAS association domain family 1A gene

Mlh1: MutL homolog 1

Mgmt: O-6-methylguanine-DNA methyltransferase

Timp3: tissue inhibitor of metalloproteinase 3

Tmeff2: transmembrane protein with EGF-like and two follistatin-like domains 2 (also known as HPP1)

P2rx7: purinergic receptor P2X, ligand-gated ion channel, 7

Igf2-DMR1: insulin-like growth factor 2-differentially methylated region 1

Igf2-DMR2: insulin-like growth factor 2-differentially methylated region 2

Esr1: Estrogen receptor 1

Nkx2-5: NK2 transcription factor related, locus 5

Gpr37: G protein-coupled receptor 37

Prdm5: PR domain containing 5

Myod1: myogenic differentiation 1

Nptx2: neuronal pentraxin II

Supplementary Figure 1. Study design. Six week old wt female C57BL/6 mice were bred with male $Apc^{Min/+}$ mice. The $Apc^{Min/+}$ offspring were identified by allele-specific PCR . $Apc^{Min/+}$ and wt mice were randomized into 8 groups based on the genotype (wt or $Apc^{Min/+}$), the type of diet (BD or WD), and the beverage (water or APE) and treated for 12 weeks.

Supplementary Figure 2. Multiple regression analysis shows the strong effect of APE on polyp number. Leverage plot is displayed.

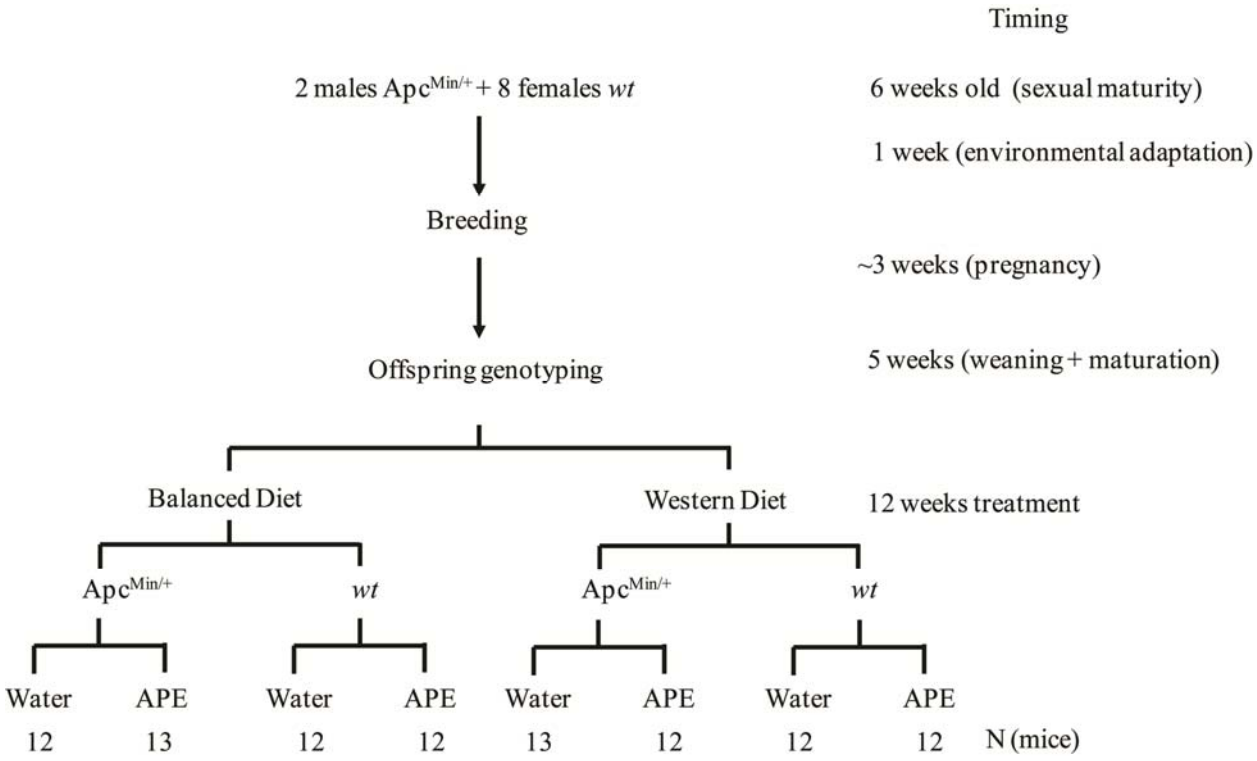
Supplementary Figure 3. APE prevents severe dysplasia. Representative H&E staining of the polyps. (A) colon (water, WD), high-grade; (B) colon (APE, WD), low-grade; (C) small intestine (wate, WD), high-grade; (D) small intestine (APE WD), low-grade; (E) colon (water BD), high-grade; (F) colon (APE BD), low-grade; (G) small intestine (water BD), high-grade; (H) small intestine (APE BD), low-grade.

Supplementary Figure 4. Multiple regression analysis shows the strong effect of APE on polyp load. Leverage plot is displayed.

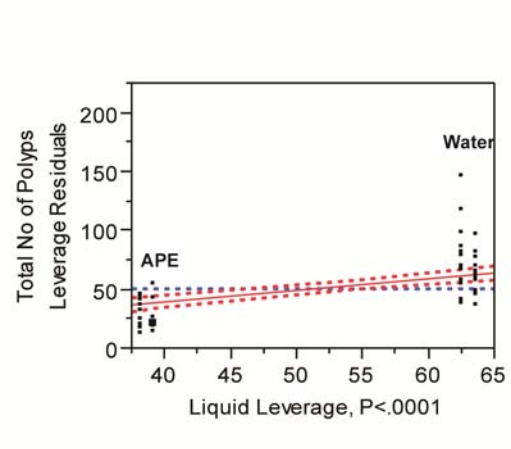
Supplementary Figure 5. Methylation of TSGs. Comparison of methylation changes in normal mucosa and polyps with different diets (BD or WD) and drinks (APE or water). Average methylation of Tmeff2, Mgmt, Mlh1, Cdkn2a, Timp3 and Rassf1a. TSGs show low levels of methylation, and no differences were found among the groups.

Supplementary Figure 6. Methylation of age-related hypermethylated genes. Comparison of methylation changes in normal mucosa and polyps, with different diets (BD or WD) and drinking (APE or water). Average methylation of Esr-1, Pcdh10, Nkx2-5, Gpr37, Prdm5, Myod1, Nptx2, Igf2-DMR2; no differences were found among groups.

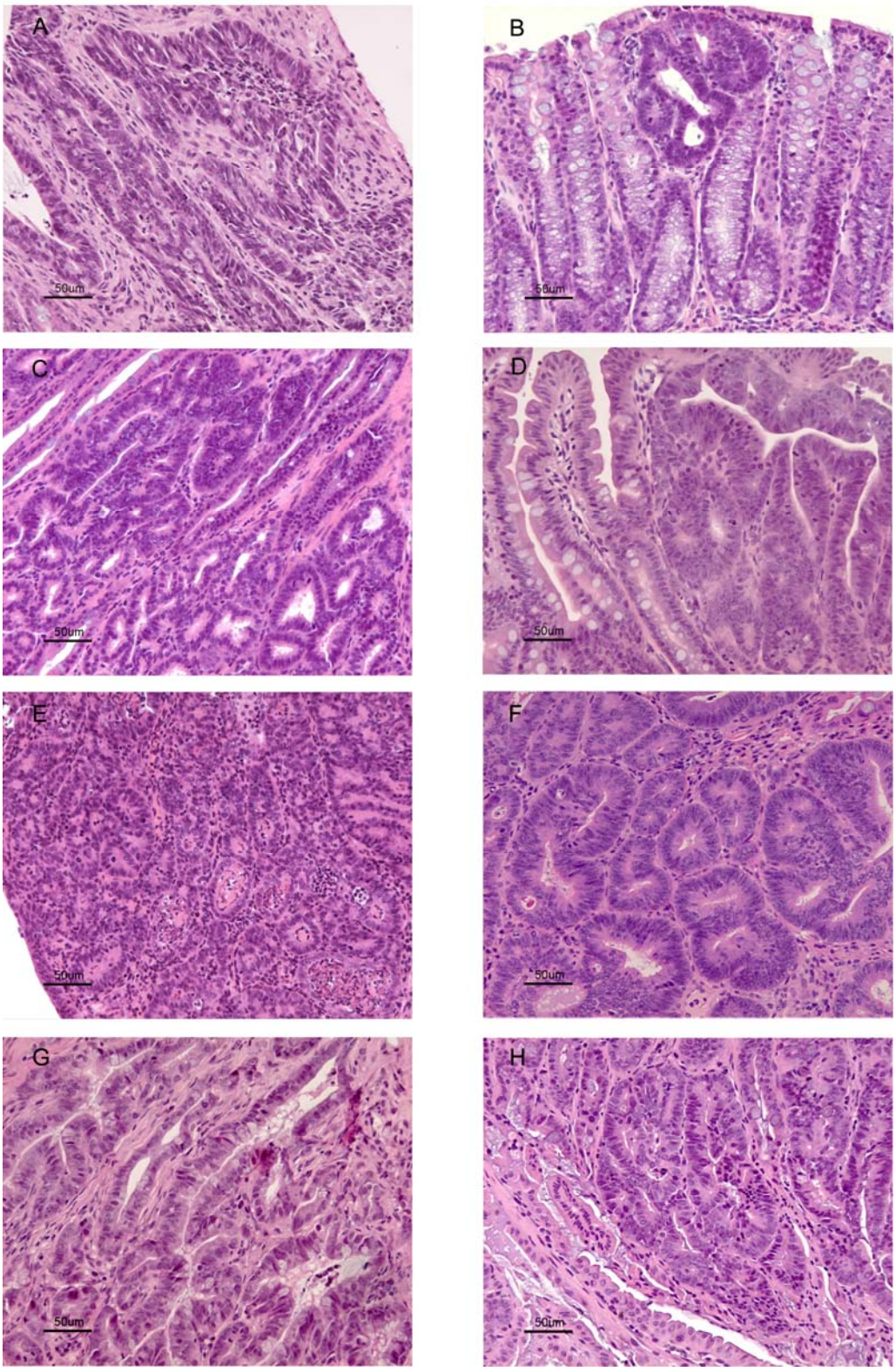
Supplementary Figure 1



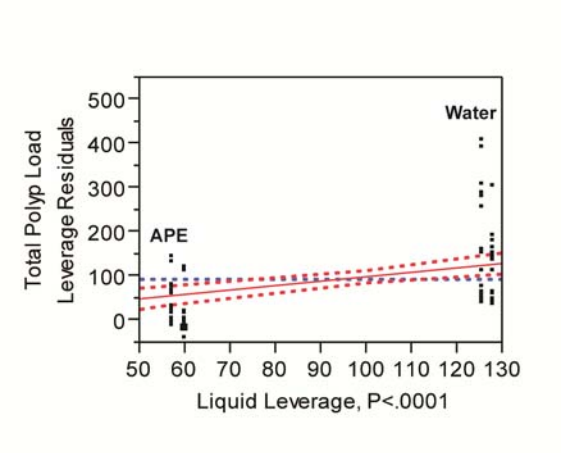
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4



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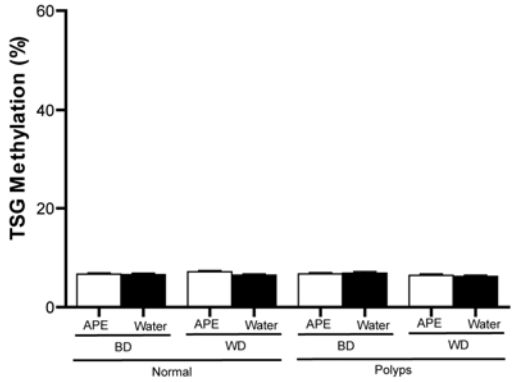
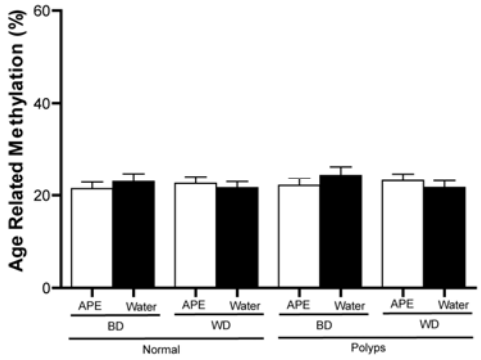


Supplementary Figure 6



Supplementary Table 1. Diet characteristics

Diet	**Western Diet**		**Balanced Diet (AIN-93G)**	
	gm%	Kcal%	gm%	Kcal%
Protein	24.4	19.5	24.4	19.5
Carbohydrate	45.6	40.5	73.8	65.5
Fat	**20**	40	**7.5**	15
Total		100		100
Kcal/gm	4.5		4.5	
Ingredient				
Casein, 80 Mesh	240	864	240	864
DL-Methionine	3.6	14.4	3.6	14.4
Corn Starch	75	300	500.5	2002
Maltodextrin 10	75	300	100	400
Sucrose	294.22	1176.9	125	500
Cellulose, BW200	**10**	0	**50**	0
Corn Oil	200	1800	75	675
Ethoxyquin	0.01	0	0.01	0
Mineral Mix S10001A	**21**	0	**0**	0
Mineral Mix S10001	**0**	0	**42**	0
Monosodium Phosphate	7.98	0	0	0
Monopotassium Phosphate	7.91	0	0	0
Calcium Carbonate	**0.88**	0	0	0
Vitamin Mix V10001	0	0	**12**	**48**
Vitamin Mix 13201	**12**	**48**	0	0
Vitamin D3 100,000 IU/gm	**0.0012**	0	0	0
Choline Bitartrate	2.4	0	2.4	0
Total	***950.0012***	***4503***	***1150.51***	***4503***

Mineral Mix S10001, gm of each component in 1000 gm of mix (Use at 35 gm/kg diet): Calcium phosphate dibasic 500, Magnesium Oxide 24 gm, Potassium Citrate 220 gm, Potassium Sulfate 52 gm, Sodium Chloride 74, Chromium Potassium Sulfate 0.55, Cupric Carbonate 0.3, Potassium Iodate 0.01, Ferric Citrate 6.0, Manganese Carbonate 3.5, Sodium Selenite 0.01, Zinc Carbonate 1.6, Sucrose 118.03.

Mineral Mix S10001A , gm of each component in 500 gm of mix (Use at 17.5 gm/kg diet)**:** Magnesium Oxide 24 gm, Potassium Citrate 220 gm, Potassium Sulfate 52 gm, Sodium Chloride 74, Chromium Potassium Sulfate 0.55, Cupric Carbonate 0.3, Potassium Iodate 0.01, Ferric Citrate 6.0, Manganese Carbonate 3.5, Sodium Selenite 0.01, Zinc Carbonate 1.6, Sucrose 118.03.

Vitamin mix, V10001 composition (amount in 10 grams): vitamin A palmitate, 20,000 IU; vitamin D-3, 1,000 IU; vitamin E acetate, 50 IU; menadione sodium bisulfate, 0.5 mg; biotin, 0.3 mg; cyanocobalamin, 10 micrograms; folic acid, 6 mg; nicotinic acid, 30 mg; calcium pantothenate, 30 mg; pyridoxine-HCl, 6 mg; riboflavin, 6 mg; thiamine-HCl, 6 mg; ascorbic acid, 500 mg; Sucrose 9.7842.

Vitamin Mix V13201 (amounts in 10 grams): Vitamin A Palmitate 4.000 IU; Vitamin E Acetate 50 IU; Menadione Sodium Bisulfite (62.5% Menadione) 0.5 mg; Biotin (1.0%) 0.2 mg; Cyancocobalamin (0.1%) 10 ug;

Folic Acid 2 mg; Nicotinic Acid 30 mg; Calcium Pantothenate 16 mg; Pyridoxine-HCl 7 mg; Riboflavin 6 mg; Thiamine HCl 6 mg; Sucrose 9.79 gm.

Supplementary Table 2. Relative weight gain (in grams) over 12 weeks (T-01 to T-12, weeks 1-12)

Time period	$Apc^{Min/+}$ mice			
	APE-BD	**APE-WD**	**Water-BD**	**Water-WD**
T-01	8.5103± 2.212	17.703±3.733	8.4211±2.825	18.7619±4.863
T-02	15.03±1.561	26.036±4.482	12.1748±4.118	25.4689±7.701
T-03	21.312±1.591	31.151±4.668	17.3998±4.636	26.9959±8.49
T-04	25.614±1.28	37.655±3.841	21.1288±4.575	36.7626±6.913
T-05	27.059±2.302	44.045±4.487	20.2347±5.037	41.0345±7.243
T-06	31.21±1.461	45.249±4.647	26.5559±5.308	39.4188±6.979
T-07	36.927±2.687	51.03±5.043	30.2323±5.634	41.4439±6.483
T-08	40.222±2.763	55.261±4.771	33.2814±5.671	43.7313±7.246
T-09	42.403±3.066	61.363±4.456	38.4922±6.201	50.9297±8.658
T-10	43.941±3.632	64.904±4.608	36.3747±5.416	47.9309±8.642
T-11	45.294±3.709	60.076±4.573	33.3966±4.494	41.6226±7.413
T-12	45.798±3.807	64.352±4.937	33.3884±4.025	28.315±4.821

Time period	Wild-type mice			
	APE-BD	**APE-WD**	**Water-BD**	**Water-WD**
T-01	7.5019±3.484	16.701±3.659	11.7434±2.776	14.322±2.148
T-02	11.885±3.65	25.717±3.876	18.7059±2.304	22.1923±1.793
T-03	16.065±3.687	20.827±5.066	22.85±2.198	27.1896±1.605
T-04	22.533±4.201	31.201±4.222	26.4113±2.455	33.642±2.308
T-05	25.101±3.614	37.223±3.155	27.8412±2.005	36.5474±2.059
T-06	32.399±4.382	43.363±4.752	28.9278±2.389	28.3445±7.449
T-07	36.477±4.662	48.197±4.601	32.4179±2.487	38.3198±3.459
T-08	36.949±4.039	49.258±4.676	34.5499±3.157	41.9179±3.23
T-09	40.784±4.324	51.346±4.218	37.8282±3.327	43.3485±3.591
T-10	43.557±4.752	56.464±5.537	40.1516±3.718	44.5779±4.774
T-11	47.278±4.713	59.125±5.64	43.5613±3.734	46.5419±3.749
T-12	49.326±4.923	60.062±5.6	43.6659±3.757	45.3672±3.507