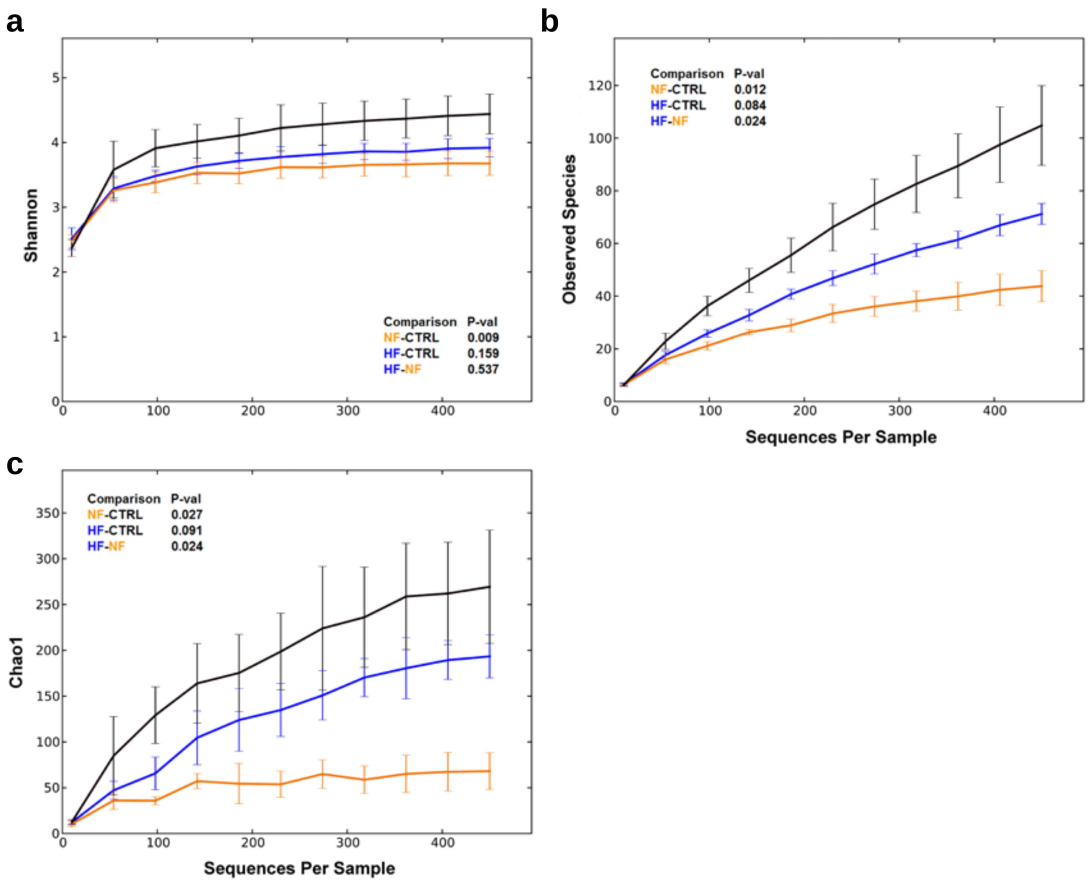
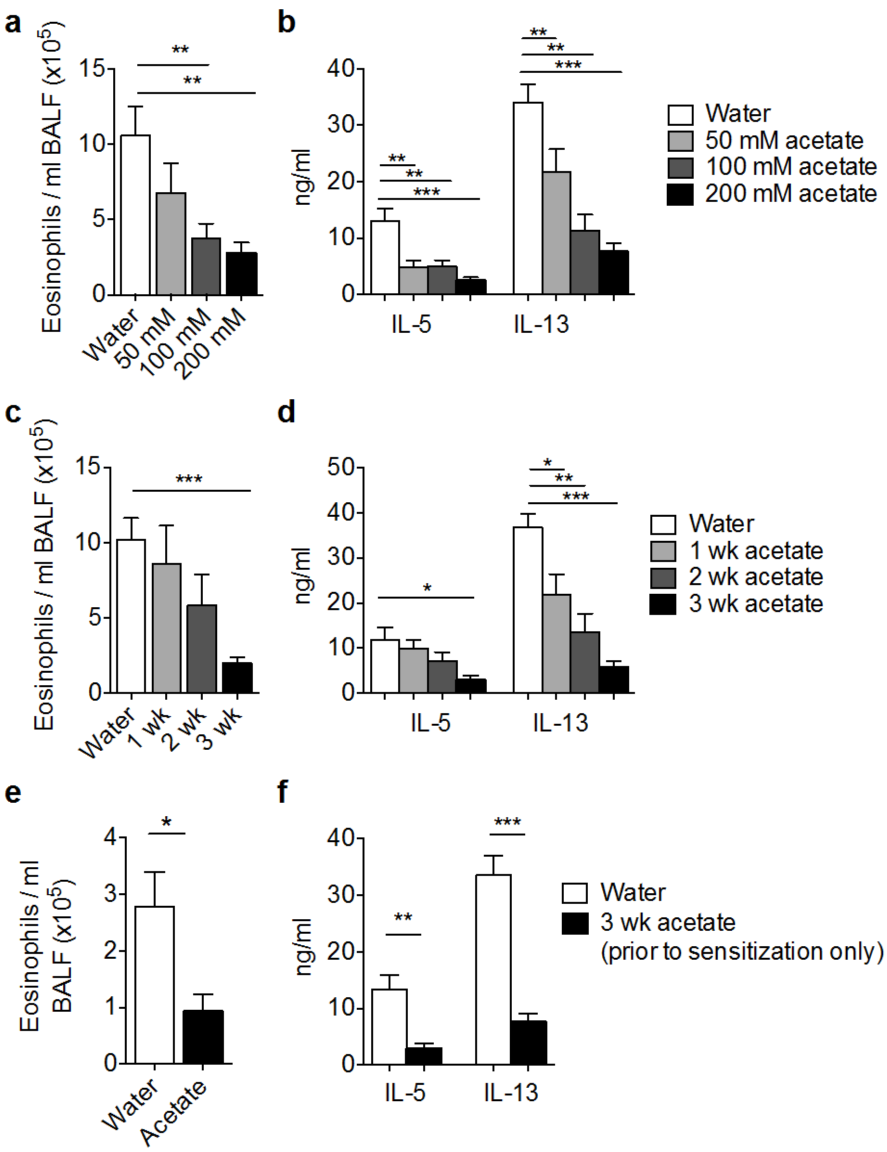
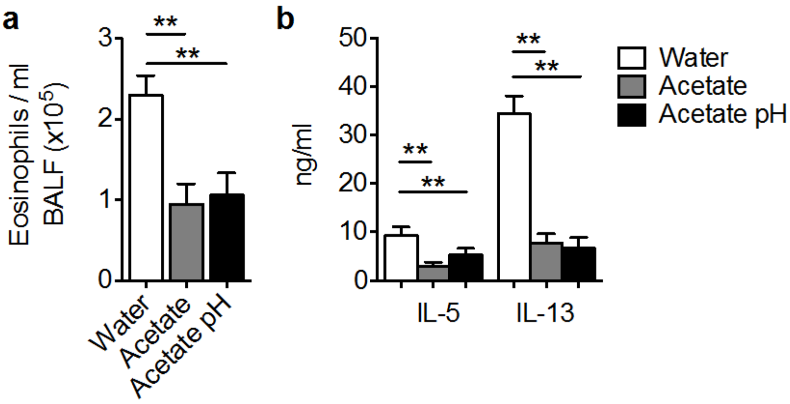


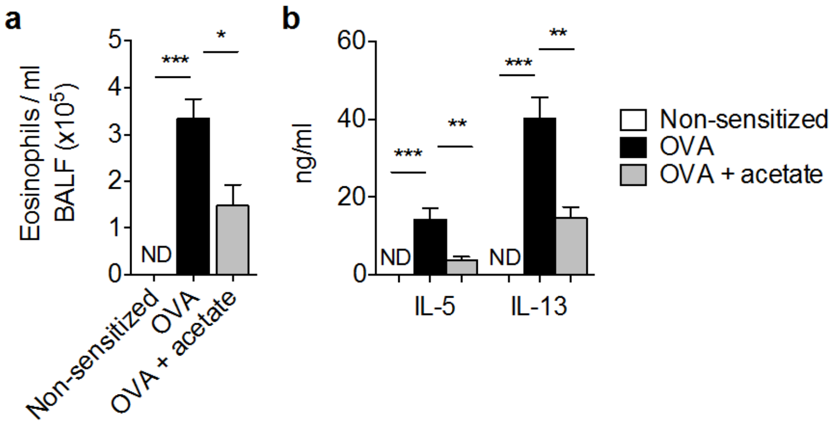
Supplementary Figure 1. The effect of different diets on Shannon index, number of species and equability. Adult mice were provided different diets for 3 weeks and then feces was collected. Microbiota composition was assessed by 16S sequencing using and final analysis used Qiime v1.6.0. The effect of the diets on alpha diversity metrics (Qiime) that showed significant differences between the groups **(a)** Shannon index, **(b)** number of observed species and **(c)** equability (Chao1). Control diet: black, high-fiber: blue, no-fiber: orange. Significance of individual comparisons was calculated in Qiime as nonparametric two-sample t-test using 1000 Monte Carlo permutations to calculate the p-value as per Qiime default.



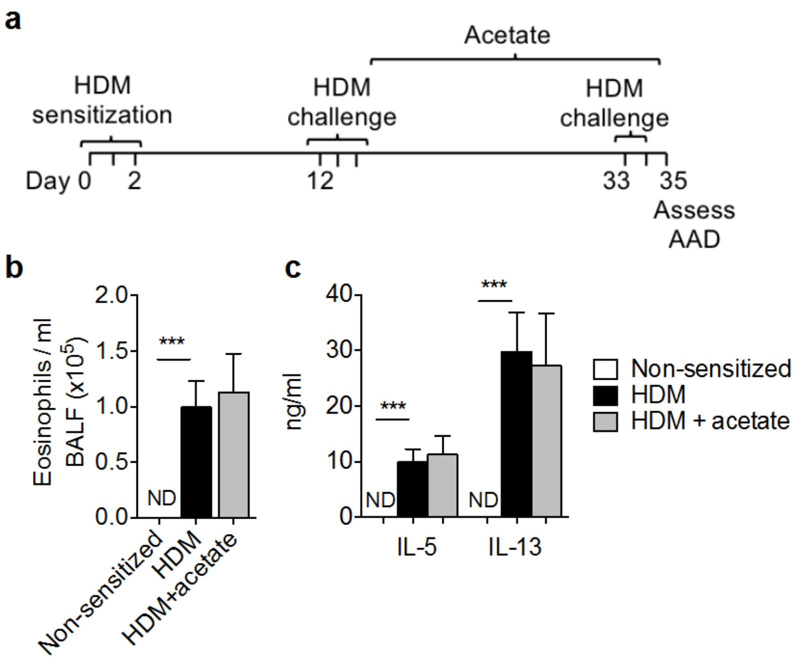
Supplementary Figure 2. The effect of acetate concentration, and time, on the development of AAD. Adult (6 week old female C57Bl6) mice were provided with acetate at different concentrations (50, 100 and 200 mM, from 3 weeks prior to sensitization) or different lengths of time prior to sensitization and challenged with HDM. The effect of acetate concentration on **(a)** eosinophil number in BALF and **(b)** IL-5 and IL-13 release from MLN T cells. The effect of different lengths of time prior to sensitization (1, 2 and 3 weeks) on **(c)** eosinophil number in BALF and **(d)** IL-5 and IL-13 release from MLN T cells. The effect of different acetate when provided for 3 weeks prior to sensitization only on **(e)** eosinophil number in BALF and **(f)** IL-5 and IL-13 release from MLN T cells. Data represent mean + SEM, n=6-8. Significance is represented by *p<0.05, **p<0.01, ***p<0.001, Student's t test. One representative experiment of two is shown.



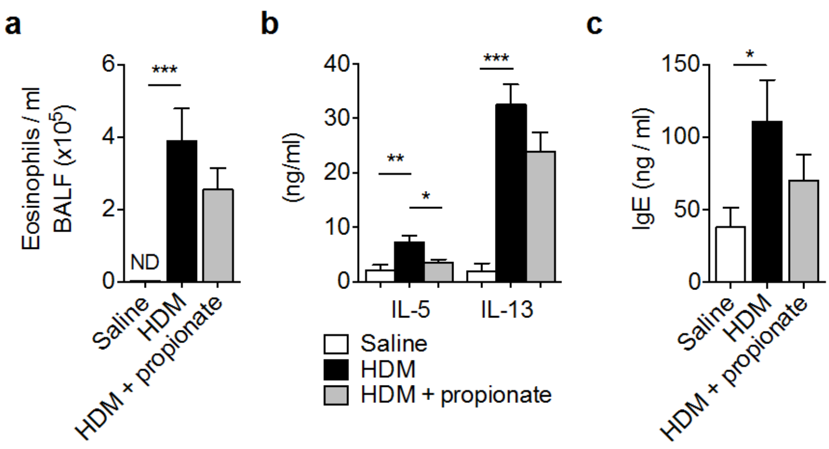
Supplementary Figure 3. The effect of adjusted pH of the acetate solution on the development of AAD. Adult (6 week old female C57Bl6) mice were provided with acetate or acetate pH adjusted to the same as water then sensitized and challenged with HDM. The effect of acetate with adjusted pH on **(a)** eosinophil number in BALF and **(b)** IL-5 and IL-13 release from MLN T cells. Data represent mean + SEM, n=8. Significance is represented by $^{**}p<0.01$, Student's t test. One representative experiment of two is shown.



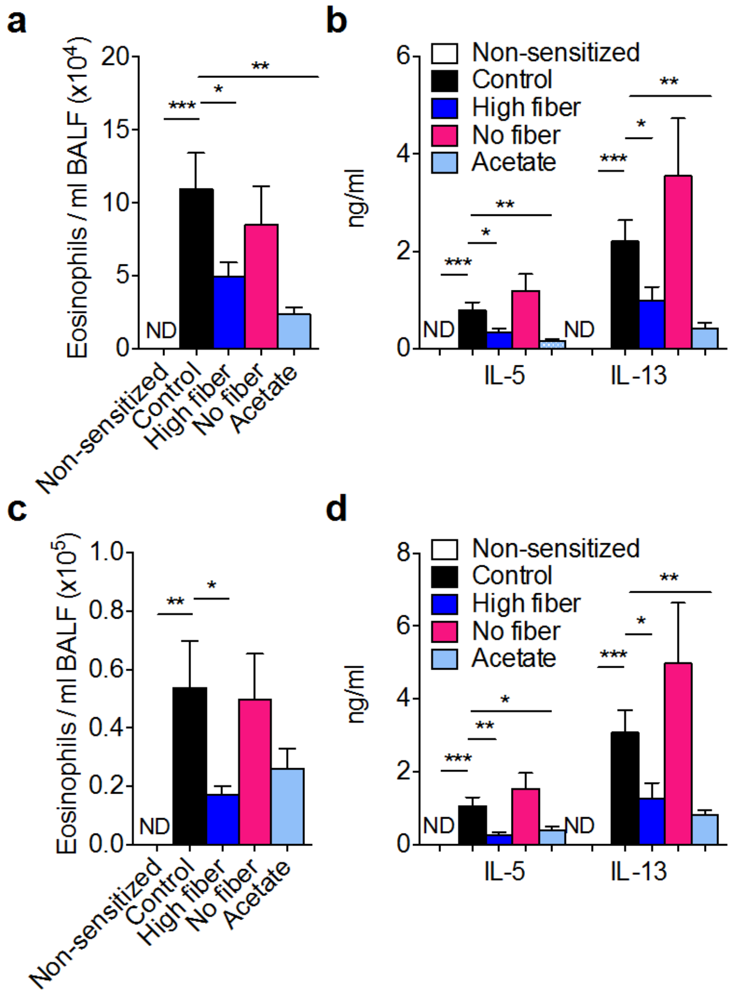
Supplementary Figure 4. The effect of acetate on the development of OVA-induced AAD. Adult (6 week old female C57Bl6) mice were provided with water or acetate then sensitized and challenged with OVA. The effect of acetate on **(a)** eosinophil number in BALF and **(b)** IL-5 and IL-13 release from MLN T cells. Data represent mean + SEM, n=8. Significance is represented by **p<0.05, **p<0.01, ***p<0.001, Student's t test. One representative experiment of two is shown. ND: not detected.



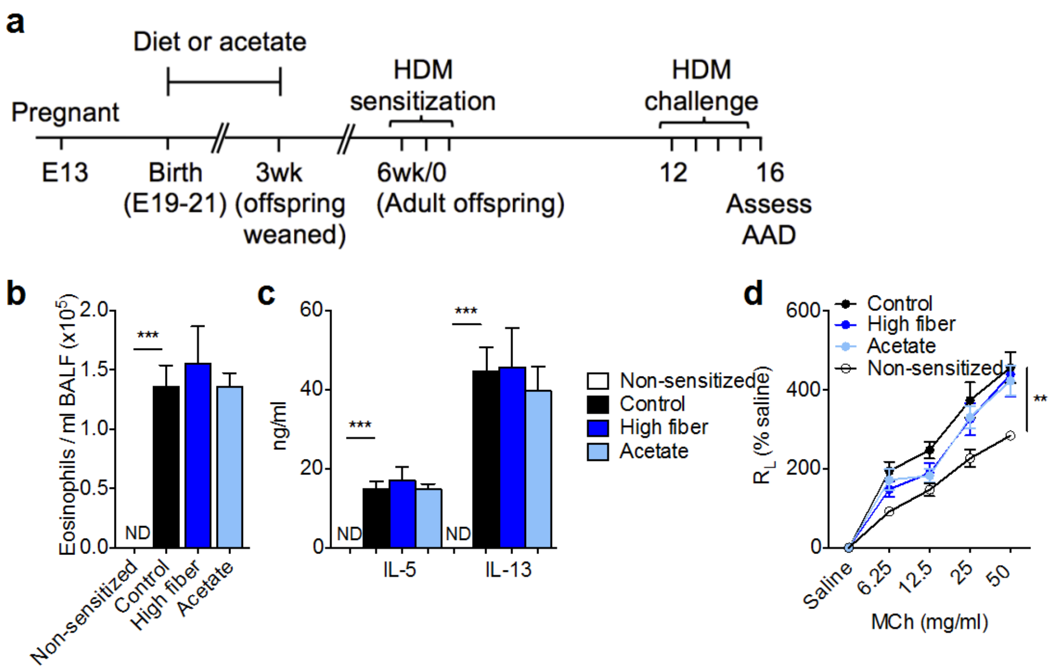
Supplementary Figure 5. The effect of acetate on established AAD. (a) Adult (6 week old female C57Bl6) mice were sensitized to HDM and challenged with HDM to induce AAD then provided acetate (or water as a control) before being challenged with HDM again to recapitulate AAD. The effect of acetate on **(b)** eosinophil number in BALF and **(c)** IL-5 and IL-13 release from MLN T cells. Data represent mean + SEM, n=8. Significance is represented by ***p<0.001, Student's t test. One representative experiment of two is shown. ND: not detected.



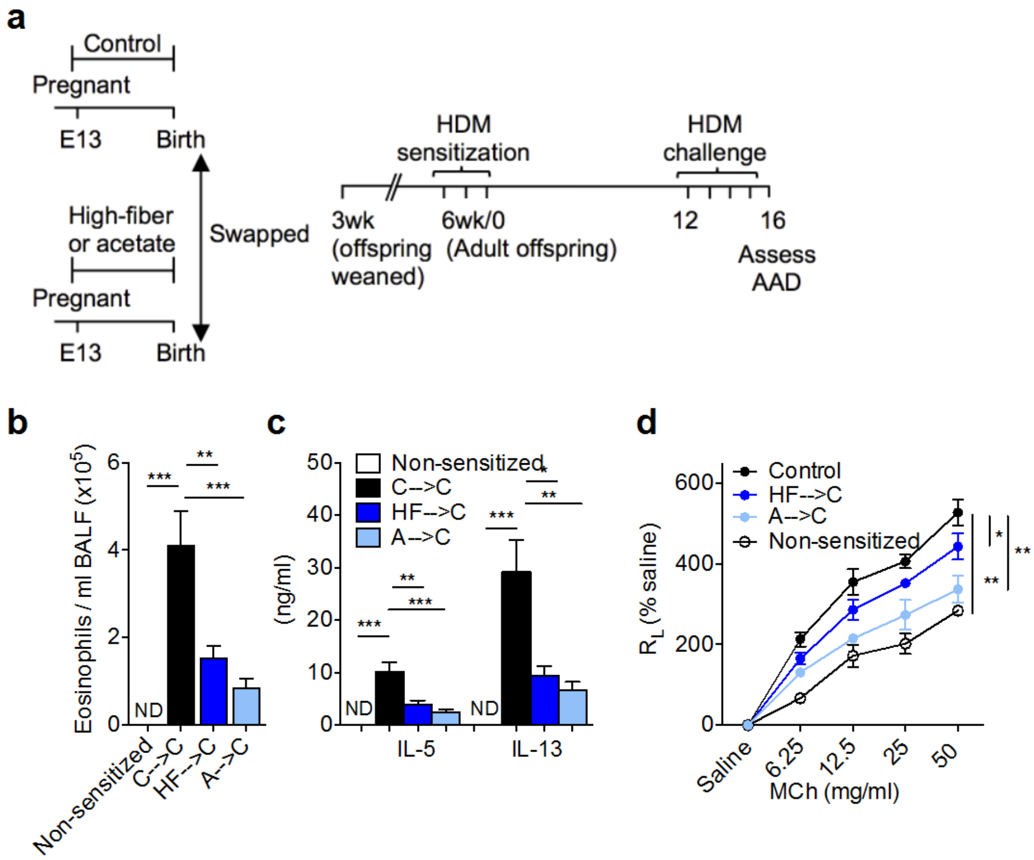
Supplementary Figure 6. The effect of propionate on the development of AAD. Adult (6 week old female Balb/c) mice were provided with propionate in their drinking water then sensitized and challenged with HDM. The effect of propionate on **(a)** eosinophil number in BALF, **(b)** IL-5 and IL-13 release from MLN T cells and **(c)** IgE. Data represent mean + SEM, n=8. Significance is represented by *p<0.05, Student's t test. One representative experiment of two is shown.



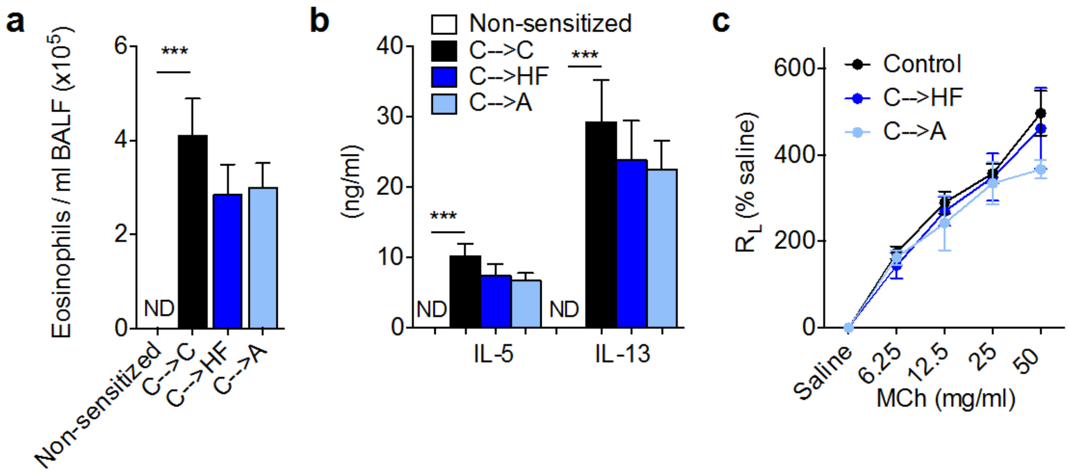
Supplementary Figure 7. The effect of maternal intake of high-fiber diet and acetate on the development of AAD in the offspring, at 3 and 16 weeks. Pregnant mice (E13, C57Bl6) were provided with control, high-fiber diet, no fiber diet, or acetate. Female offspring were weaned onto control diet and water at 3 weeks of age. The effect of high-fiber diet or acetate, when AAD is induced at 3 weeks, on **(a)** eosinophil number in BALF and **(b)** IL-5 and IL-13 release from MLN T cells. The effect of high-fiber diet or acetate, when AAD is induced at 16 weeks, on **(c)** eosinophil number in BALF and **(d)** IL-5 and IL-13 release from MLN T cells. Data represent mean + SEM, n=8. Significance is represented by *p<0.05, **p<0.01, ***p<0.001, Student's t test. One representative experiment of two is shown. ND: not detected.



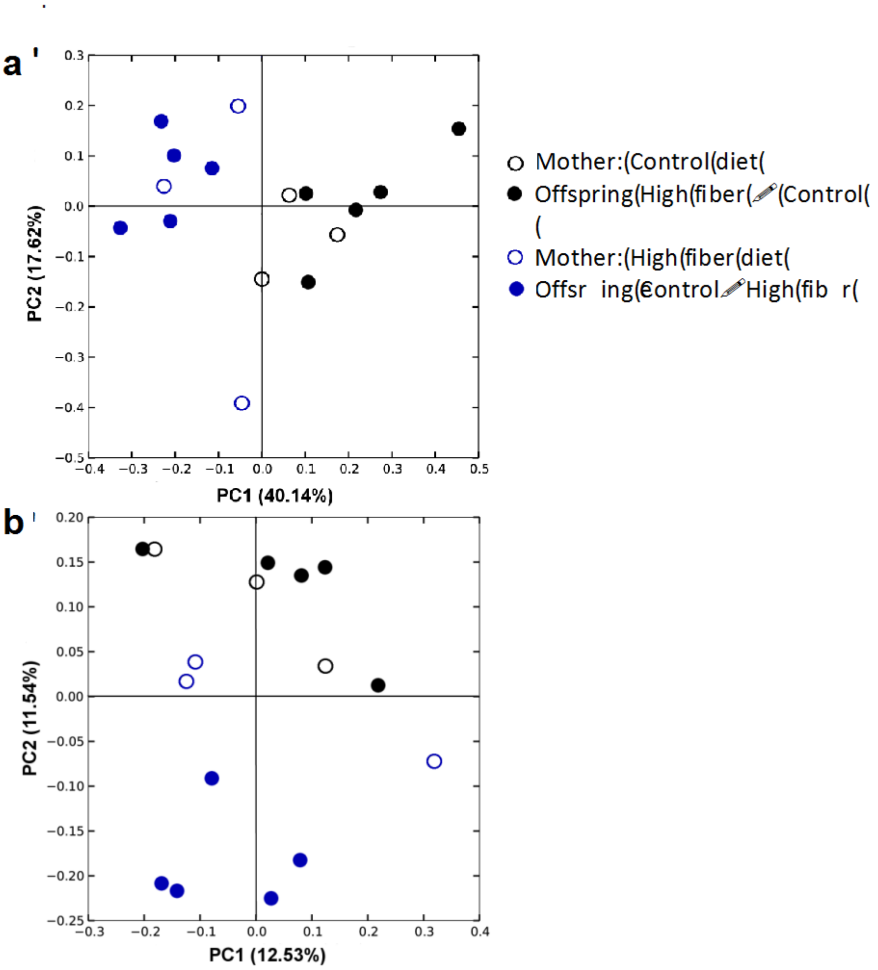
Supplementary Figure 8. The effect of maternal high-fiber diet and acetate during lactation on the development of AAD in the offspring. (a) Lactating mice (E13, C57Bl6) were provided with control, high-fiber diet, or acetate. Female offspring were weaned onto control diet and water at 3 weeks of age and at 6 weeks, sensitized and challenged with HDM. The effect of high-fiber diet or acetate during lactation on **(b)** eosinophil cell number in BALF, **(c)** IL-5 and IL-13 release from MLN T cells, and **(e)** airway hyperresponsiveness in terms of airway resistance (R_L). Data represent mean + SEM, n=8. Significance is represented by **p<0.01, ***p<0.001, Student's t test. One representative experiment of two is shown. ND: not detected.



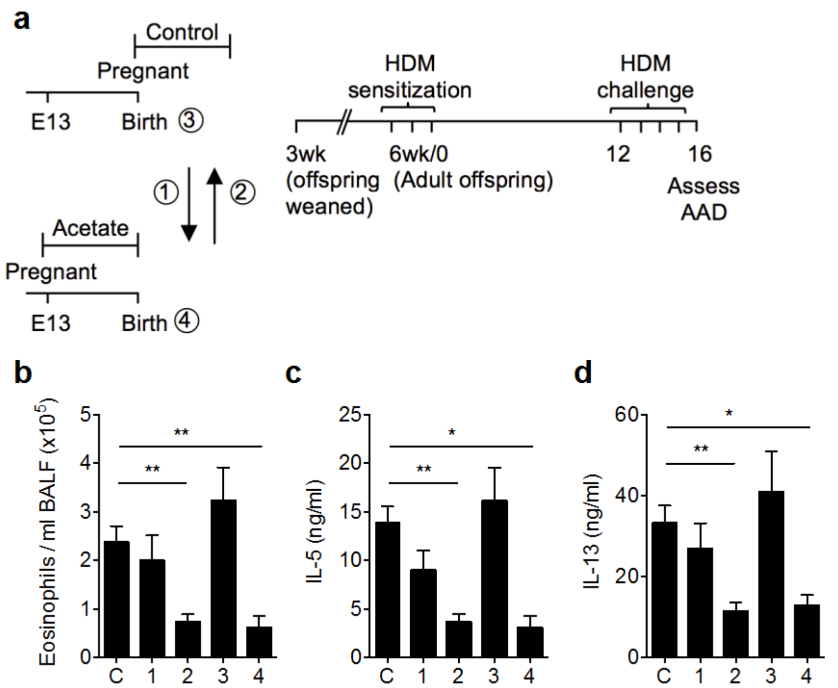
Supplementary Figure 9. The effect of maternal high-fiber diet and acetate on the development of AAD in the offspring, swapped at birth. (a) Pregnant mice (E13, Balb/c) were provided with control, high-fiber diet, or acetate. At birth, offspring were swapped to a mother that had received a control diet. Female offspring were weaned onto control diet and water at 3 weeks of age and at 6 weeks, sensitized and challenged with HDM. The effect of high fiber diet or acetate during on **(b)** eosinophil cell number in BALF, **(c)** IL-5 and IL-13 release from MLN T cells, **(e)** airway hyperresponsiveness in terms of airway resistance (R_L). Data represent mean + SEM, n=8. Significance is represented by *p<0.05, **p<0.01, ***p<0.001, Student's t test. One representative experiment of two is shown. ND: not detected.



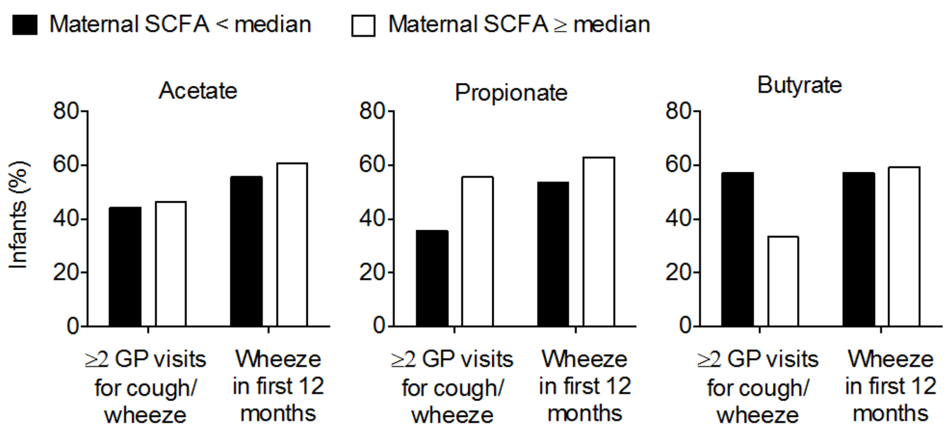
Supplementary Figure 10. The effect of maternal high-fiber diet and acetate on the development of AAD in the offspring, swapped at birth. (a) Pregnant mice (E13, Balb/c) were provided with control, high-fiber diet, or acetate. At birth, offspring from mothers that received a control diet were swapped to mothers on high-fiber diet or acetate (Supplementary Figure 7a). Female offspring were weaned onto control diet and water at 3 weeks of age and at 6 weeks, sensitized and challenged with HDM. The effect on **(b)** eosinophil cell number in BALF, **(c)** IL-5 and IL-13 release from MLN T cells, **(e)** airway hyperresponsiveness in terms of airway resistance (R_L). Data represent mean + SEM, n=8. Significance is represented by ***p<0.001, Student's t test. One representative experiment of two is shown. ND: not detected.



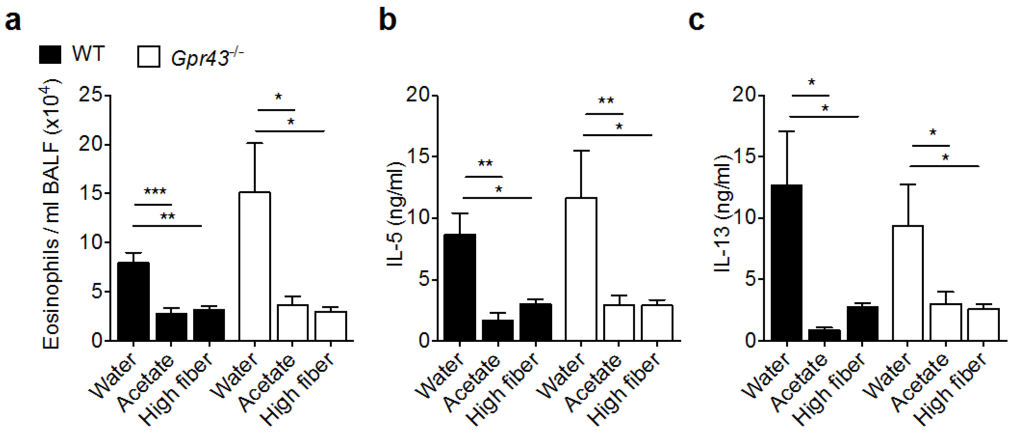
Supplementary Figure 11. Microbiota analysis of mothers and transferred offspring. The composition of the microbiota was determined to be significantly different using **(a)** unweighted (p = 0.0003) and **(b)** weighted UniFrac (p = 0.0002) analysis. Mother (Balb/c) on control diet (black empty circles), mother on high fiber (blue empty circles), female offspring high-fiber to control (black filled circles), offspring control to high-fiber (blue filled circles).



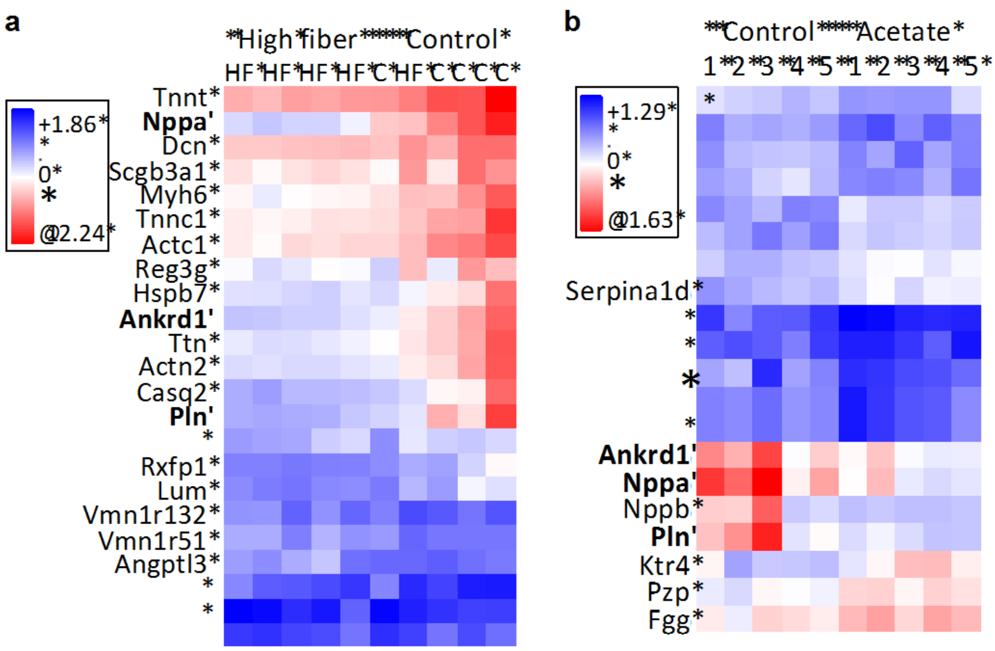
Supplementary Figure 12. Effect of co-housing offspring on the development of AAD. (a) Pregnant mice (E13, Balb/c) were provided with water or acetate from E13. Offspring were transferred from control mother to control mother (C), 1. Control mother to mother on acetate, 2. Mother on acetate to control mother or 3. Remained with control mother or 4. Remained with mother on acetate. All offspring were housed at a 1:1 ratio (kept:swapped). Female offspring were weaned at 3 weeks of age and at 6 weeks, sensitized and challenged with HDM. The effect of high-fiber diet or acetate on **(b)** eosinophil number in BALF, **(c)** IL-5 and **(d)** IL-13 release from MLN T cells. Data represent mean + SEM, n=8. Significance is represented by *p<0.05, **p<0.01, Student's t test. One representative experiment of two is shown.



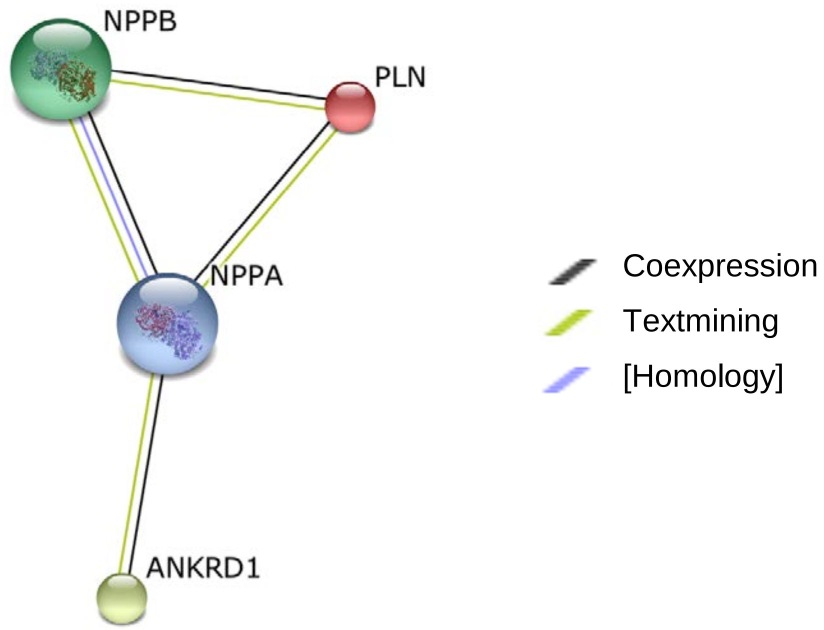
Supplementary Figure 13. Percentage of infants with 2 or more general practitioner (GP) visits for cough or wheeze and percentage of infants with parent-reported wheeze in the first 12 months of life (mothers asthmatic, see Supplementary Table 4). Solid bars represent the group with SCFA concentrations below median (0.0514mM for acetate, 0.0371mM for propionate and 0.03558mM for butyrate) open bars represent the group with SCFA concentrations greater than or equal to median, n=55.



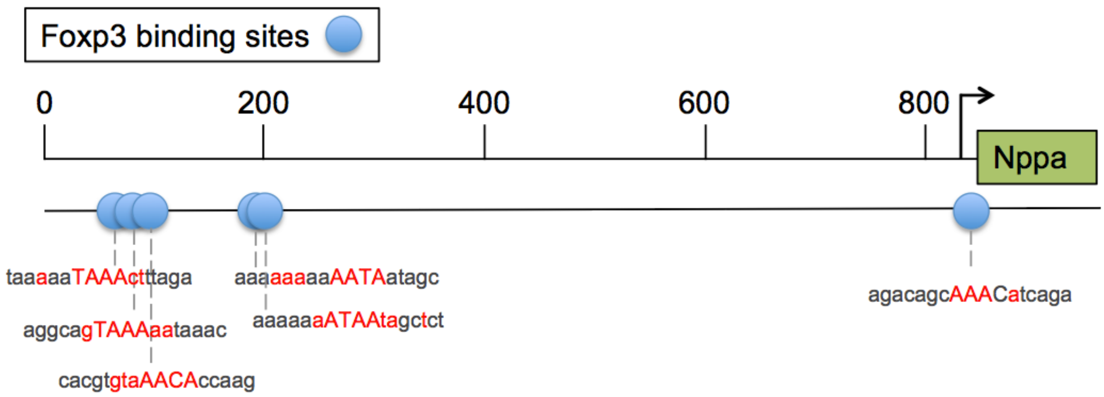
Supplementary Figure 14. The effect of a high-fiber diet and acetate on WT (C57Bl6) versus *Gpr43*$^{-/-}$ mice (6 week old female). (a) Eosinophil number in BALF, **(b)** IL-5 and **(c)** IL-13 release from MLN T cells. Data represent mean + SEM, n=10. Significance is represented by *p<0.05, **p<0.01, ***p<0.001, Student's t test. One representative experiment of three is shown.



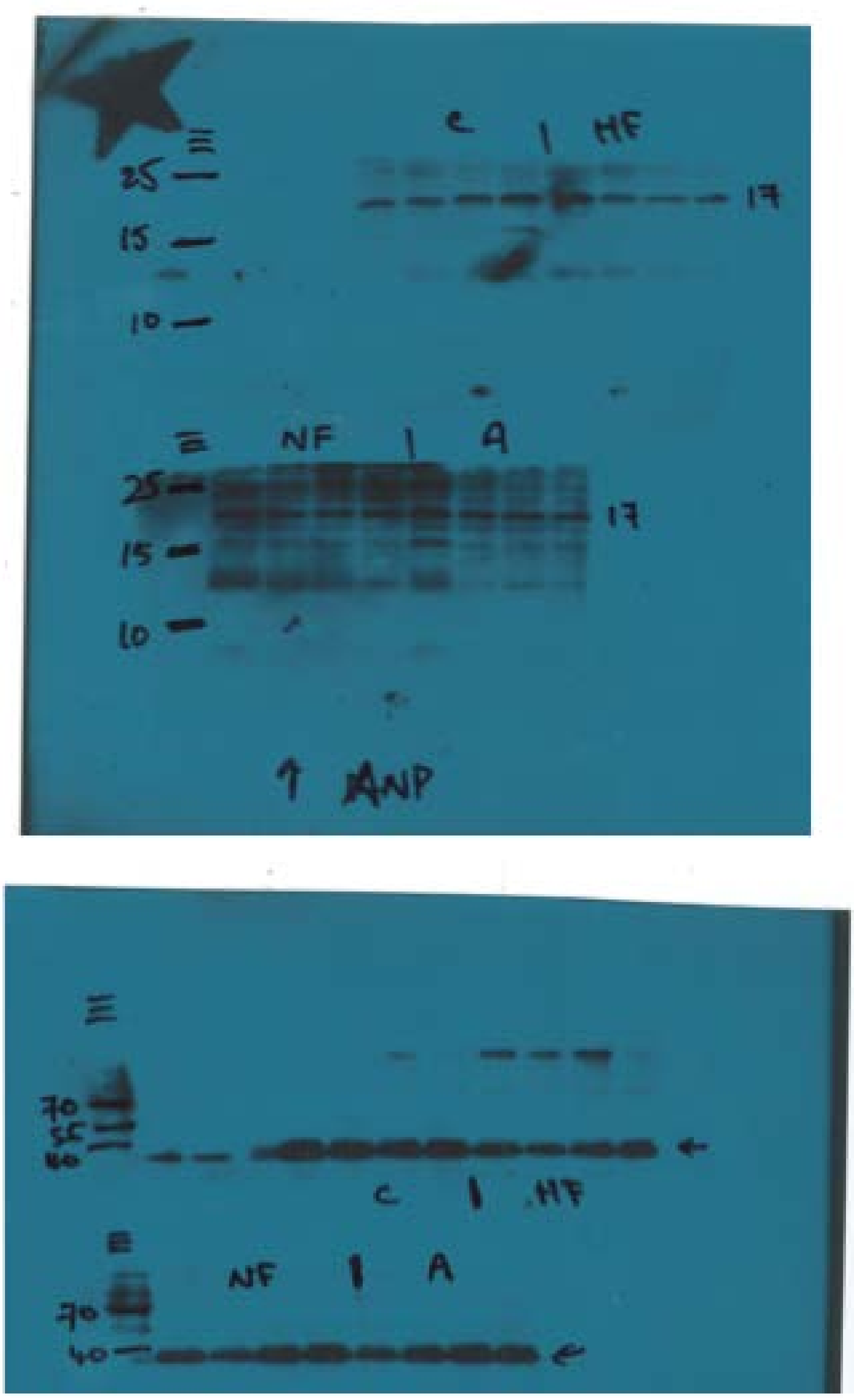
Supplementary Figure 15. Gene array heat map of lung tissue from fetus of mother (C57Bl6) mice fed control, high-fibre diet or acetate. **(A)** High-fiber versus control, and **(B)** Acetate versus control. Bolded names are shared between the high fiber and acetate groups. Gene arrays were performed using Affymetrix microarrays, and data was analysed using Affymetrix Transcriptome Analysis Console (TAC) 2.0 software.



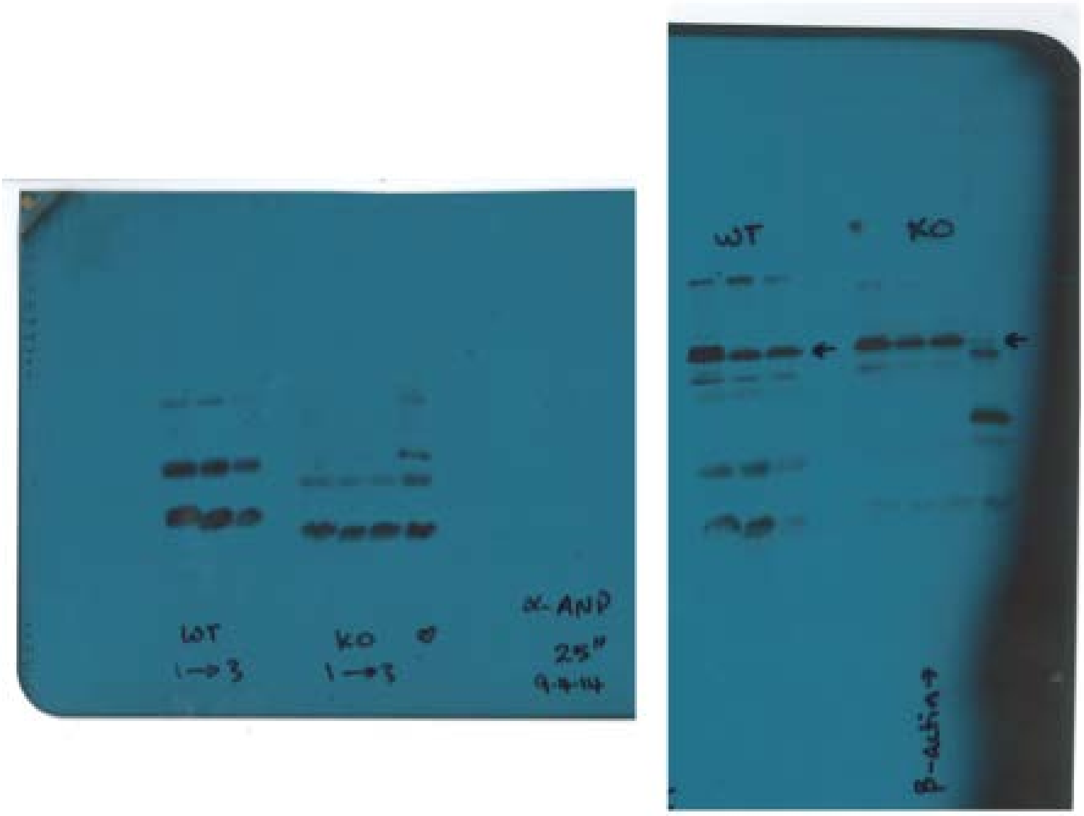
Supplementary Figure 16. Evidence of known protein-protein interactions between top regulated genes (STRING9.1).



Supplementary Figure 17. Putative binding sites for Foxp3 in the Nppa promoter region as determined by Genomatrix software suite v3.1 maptInspector.



Supplementary Figure 18. Full size Western Blot image for Figure 8d ANP (top) and beta actin (bottom).



Supplementary Figure 19. Full size Western Blot image for Figure 8f ANP (left) and beta actin (right).

Supplementary Table 1. Calculated nutritional parameters for diets used in this study.

	Control (8720310)	**High fiber (SF11-025)**	**No fiber (SF09-028)**
Crude Fiber	3.2 %	4.7 %	0 %
AD Fiber	4.2 %	4.7 %	0 %
ND Fiber	11.2 %	n/a	n/a
Starch	29 %	63 % (all resistant)	0 %
Total fiber/starch	47.6 %	72.7 %	0 %
Protein	20 %	19.4 %	19.4 %
Total Fat	6 %	7 %	7 %
Digestible Energy	12.8 MJ/kg	16.3 MJ/kg	16.9 MJ/kg
Total calculated digestible energy from:			
Lipids	19 %	16 %	16 %
Protein	31 %	21 %	21 %
Carbohydrate	50 %	62 %	Replaced with dextrose monohydrate (62%)

AD: acid detergent

ND: Neutral detergent

Supplementary Table 2. Participant characteristics for pregnant women with and without asthma who provided dietary data

	Maternal Asthma (n=42)	No Asthma (n=19)
Maternal age at recruitment (years); median (IQR)	28 (25, 31)	28 (23.5, 32.5)
Maternal self-reported smoking; n (%)	8/42 (19%)	3/19 (15.8%)
Gravida; median (IQR)	2 (1, 4)	2 (1, 2.5)
Parity; median (IQR)	1 (0, 1)	0 (0, 1.5)
Early pregnancy BMI; median (IQR)	25.5 (22.9, 30.7)	29.5 (25.6, 32.1)
Gestational age at serum collection (weeks); median (IQR)	36 (35.3, 37)	36 (35, 36)
Dietary Fiber (g); median (IQR)	18.5 (13.2, 25.7)	18.7 (15.5, 22.5)

IQR Interquartile range

Supplementary Table 3. Participant characteristics for pregnant women without asthma and their infants

Maternal age at recruitment (years); median (IQR)	28.6 (27.7, 31.9)
Maternal self-reported smoking; n (%)	5/40 (12.5%)
Gravida; median (IQR)	2 (1, 2)
Parity; median (IQR)	1 (0, 1)
Early pregnancy BMI; median (IQR)	25.6 (23.7, 30.1)
Gestational age at serum collection (weeks); median (IQR)	37.6 (36.6, 38.4)
Infant age at assessment (months); median (IQR)	12.1 (12.0, 12.8)

IQR Interquartile range

Supplementary Table 4. Participant characteristics for pregnant women with asthma and their infants

Maternal age at recruitment (years); median (IQR)	27.5 (24.7, 32.0)
Maternal self-reported smoking; n (%)	4/55 (7.3%)
Gravida; median (IQR)	2 (1, 3)
Parity; median (IQR)	1 (0, 1)
Early pregnancy BMI; median (IQR)	28.0 (24.1, 31.7)
Gestational age at serum collection (weeks); median (IQR)	35.9 (33.9, 37.1)
Infant age at assessment (months); median (IQR)	12.3 (12.0, 12.8)

IQR Interquartile range

Supplementary Table 5. Gene expression (by microarray) relative to control (increase or decrease > 2-fold change, p<0.05)

	High fiber vs. Control		**Acetate vs. Control**	
Up-regulated	Vmn1r132	+2.18	Krt4	+3.32
	Vmn1r151	+2.08	Pzp	+2.18
	Angptl3	+2.01	Serpina1	+2.14
			Fgg	+2.03
Down-regulated	**Nppa**	**-9.91**	**Nppa**	**-10.71**
	Pln	**-4.94**	**Pln**	**-4.13**
	Ankrd1	**-4.26**	Nppb	-3.87
	Actn2	-3.26	**Ankrd1**	**-3.46**
	Actc1	-3.01		
	Ttn	-2.92		
	Tnnt2	-2.84		
	Reg3g	-2.77		
	Casq2	-2.70		
	Myh6	-2.68		
	Scgb3a1	-2.42		
	Lum	-2.38		
	Tnnc1	-2.26		
	Rxfp1	-2.09		
	Hspb7	-2.04		
	Dcn	-2.01		

Bolded names are shared between the high fiber and acetate groups

Supplementary Table 6. Ingenuity systems analysis of down-regulated genes (decrease > 1.5-fold, $p<0.05$)

	High-fiber vs. Control	**Acetate vs. Control**
Top networks	1. **Cardiovascular Disease**, Skeletal and Muscular Disorders, Cardiovascular System Development and Function (48) 2. Cellular Development, Cell Morphology, Cancer (12) 3. Cell-To-Cell Signaling and Interaction, Cancer (3) 4. Organ Morphology, Reproductive System Development and Function, **Developmental Disorder** 2 5. Amino Acid Metabolism, Molecular Transport, Small Molecule Biochemistry (2)	1. Cardiac Hypertrophy, **Cardiovascular Disease**, **Developmental Disorder** (22) 2. Embryonic Development, Hair and Skin Development and Function, Organ Development (3)
Diseases and disorders	**Cardiovascular Disease** (16) **Skeletal and Muscular Disorders** (10) **Developmental Disorder** (13) Organismal Injury and Abnormalities (17) Cancer (16)	**Cardiovascular Disease** (4) **Skeletal and Muscular Disorders** (4) **Developmental Disorder** (4) Connective Tissue Disorders (1) Hereditary Disorder (3)

Molecular and Cellular Functions	Cell Death and Survival (14) Cell Morphology (13) Cellular Assembly and Organization (13) Cellular Function and Maintenance (13) Cell Signaling (10)	Lipid Metabolism (2) Small Molecule Biochemistry (3) Drug Metabolism (3) Molecular Transport (4) Nucleic Acid Metabolism (2)
Physiological System Development and Function	**Cardiovascular System Development and Function** (16) Organ Morphology (17) Skeletal and Muscular System Development and Function (18) **Embryonic Development (**13) **Organ Development** (16)	Endocrine System Development and Function (2) **Cardiovascular System Development and Function** (4) Tissue Morphology (3) **Embryonic Development** (6) **Organ Development** (6)
Top Canonical Pathways	Calcium Signaling Cellular Effects of Sildenafil (Viagra) Epithelial Adherens Junction Signaling ILK Signaling Actin Cytoskeleton Signaling	Cardiomyocyte Differentiation via BMP Receptors Granzyme A Signaling Protein Kinase A Signaling Nitric Oxide Signaling in the Cardiovascular System Sperm Motility
Top upstream regulators	MEF2C – inhibited ($p=3.03x10^{-20}$) TBX5 – inhibited ($p=1.09x10^{-19}$) **GATA4 – inhibited** ($p=5.45x10^{-17}$) HAND2 – inhibited ($p=6.16x10^{-16}$)	**GATA4 – inhibited** ($p=5.35x10^{-8}$) YAP1 – inhibited ($p=1.51x10^{-7}$) NKX2-5 – inhibited ($p=3.13x10^{-7}$) Hdac9 – inhibited ($p=3.81x10^{-7}$)

	MYOCD – inhibited ($p=2.15x10^{-14}$)	MYOZ2 – inhibited ($p=3.81x10^{-7}$)
Top Tox Lists	**Cardiac Hypertrophy** **Cardiac Fibrosis** **Cardiac Necrosis/Cell Death** Hepatic Fibrosis **Increases Bradycardia**	**Cardiac Hypertrophy** **Cardiac Fibrosis** **Increases Bradycardia** Increases Heart Failure **Cardiac Necrosis/Cell Death**

Data are listed in order of statistical significance.

(Number) = score/number of molecules related to the result.

Bolded names are shared between the high fiber and acetate groups.

Supplementary Table 7. Ingenuity systems analysis of up-regulated genes (increase > 1.5-fold, p<0.05)

	High-fiber vs. Control	**Acetate vs. Control**
Top networks	1. Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry (25) 2. Embryonic Development, **Hair and Skin Development and Function**, Organ Development (3) 3. Organ Morphology, Embryonic Development, Organ Development (3) 4. Hereditary Disorder, Neurological Disease, Carbohydrate Metabolism (3)	1. Developmental Disorder, Hematological Disease, Hereditary Disorder (39) 2. Cell-To-Cell Signaling and Interaction, Digestive System Development and Function, Gastrointestinal Disease (26) 3. **Hair and Skin Development and Function**, Dermatological Diseases and Conditions, Developmental Disorder (2)
Diseases and disorders	Inflammatory Response (3) Neurological Disease (3) Cardiovascular Disease (5) **Developmental Disorder** (4) Endocrine System Disorders (1)	**Developmental Disorder** (12) Hematological Disease (9) Hereditary Disorder (15) Immunological Disease (9) Cancer (19)
Molecular and Cellular Functions	Cellular Assembly and Organization (3) **Lipid Metabolism** (5) **Small Molecule Biochemistry** (6)	Cell-To-Cell Signaling and Interaction (13) **Cell Death and Survival** (11) Protein Synthesis (10)

	Vitamin and Mineral Metabolism (3) **Cell Death and Survival** (2)	**Lipid Metabolism** (14) **Small Molecule Biochemistry** (15)
Physiological System Development and Function	**Tissue Development** (4) **Hematological System Development and Function** (3) Connective Tissue Development and Function (2) Digestive System Development and Function (2) Hepatic System Development and Function (2)	**Hematological System Development and Function** (14) **Tissue Development** (12) Immune Cell Trafficking (11) Organismal Functions (6) Cardiovascular System Development and Function (5)
Top Canonical Pathways	**Acute Phase Response Signaling** **LXR/RXR Activation** FXR/RXR Activation Hepatic Cholestasis PPAR□□ RXR□□Activation	**Acute Phase Response Signaling** **LXR/RXR Activation** Coagulation System Extrinsic Prothrombin Activation Pathway Intrinsic Prothrombin Activation Pathway
Top upstream regulators	**HNF1A** ($p=3.41\times10^{-6}$) **Tcf 1/3/4** ($p=4.81\times10^{-6}$) Acetaminophen ($p=7.06\times10^{-5}$) Hmgn3 ($p=1.48\times10^{-4}$) Methotrexate ($p=3.27\times10^{-4}$)	**HNF1A** ($p=8.88\times10^{-20}$) Nitrofurantoin ($p=1.58\times10^{-15}$) **Tcf 1/3/4** ($p=7.61\times10^{-15}$) Methapyrilene ($p=2.61\times10^{-14}$) Ciprofibrate ($p=3.33\times10^{-12}$)
Top Tox Lists	**LXR/RXR Activation** **Negative Acute Phase Response**	**LXR/RXR Activation** Positive Acute Phase Response

	Proteins LPS/IL-1 Mediated Inhibition of RXR Function Cytochrome P450 Panel - Substrate is a Xenobiotic (Mouse) Cytochrome P450 Panel - Substrate is a Xenobiotic (Rat)	Proteins **Negative Acute Phase Response Proteins** FXR/RXR Activation Liver Necrosis/Cell Death

Data are listed in order of statistical significance.

(Number) = score/number of molecules related to the result.

Bolded names are shared between the high fiber and acetate groups.

Supplementary Table 8. Ingenuity systems analysis of all differentially regulated genes (decrease or increase > 1.5-fold change, p<0.05)

	High-fiber vs. Control	**Acetate vs. Control**
Top networks	1. **Cardiovascular Disease**, Skeletal and Muscular Disorders, Cardiovascular System **Development and Function** (57) 2. Cellular Assembly and Organization, Cellular Function and Maintenance, Embryonic Development (24) 3. **Embryonic Development, Hair and Skin Development and Function, Organ Development** (3) 4. Cell Cycle, Cell Death and Survival, Gastrointestinal Disease (3) 5. **Cell-To-Cell Signaling and Interaction**, Cancer (3)	1. **Cardiovascular Disease**, Hematological Disease, Hematological System **Development and Function** (35) 2. **Cell-To-Cell Signaling and Interaction**, Inflammatory Response, Developmental Disorder (19) 3. Cardiac Hypertrophy, Cardiovascular Disease, Developmental Disorder (11) 4. Lipid Metabolism, Molecular Transport, Small Molecule Biochemistry (11) 5. **Embryonic Development, Hair and Skin Development and Function, Organ Development** (3)
Diseases and disorders	Cardiovascular Disease (21) Skeletal and Muscular Disorders (12)	**Cancer** (26) Gastrointestinal Disease (20) Hepatic System Disease (13)

	Developmental Disorder (17) Organismal Injury and Abnormalities (18) **Cancer** (18)	Developmental Disorder (11) Hematological Disease (12)
Molecular and Cellular Functions	Cell Morphology (12) Cellular Assembly and Organization (14) **Cell Death and Survival** (16) Cellular Function and Maintenance (14) **Cell Signaling** (10)	Lipid Metabolism (19) Small Molecule Biochemistry (21) Vitamin and Mineral Metabolism (11) Cell-To-**Cell Signaling** and Interaction (17) **Cell Death and Survival** (17)
Physiological System Development and Function	**Cardiovascular System Development and Function** (18) Organ Morphology (19) Skeletal and Muscular System Development and Function (18) Embryonic Development (15) Organ Development (19)	Hematological System Development and Function (19) Organismal Functions (9) Tissue Development (18) Immune Cell Trafficking (14) **Cardiovascular System Development and Function** (11)
Top Canonical Pathways	Calcium Signaling Cellular Effects of Sildenafil (Viagra) Epithelial Adherens Junction Signaling Acute Phase Response Signaling ILK Signaling	Acute Phase Response Signaling LXR/RXR Activation Coagulation System Intrinsic Prothrombin Activation Pathway Extrinsic Prothrombin Activation

		Pathway
Top upstream regulators	MEF2C – inhibited (p=4.83x10^{-18}) TBX5 – inhibited (p=1.01x10^{-17}) GATA4 – inhibited (p=4.94x10^{-15}) HAND2 – inhibited (p=2.04x10^{-14}) MYOCD – inhibited (p=7.02x10^{-18}3	HNF1A – activated (p=2.82x10^{-18}) Hmgn3 – activated (p=4.59x10^{-14}) Tcf1/3/4 –activated (p=5.43x10^{-14}) Methapyrilene – inhibited (p=1.11x10^{-12}) Ciprofibrate – inhibited (p=1.74x10^{-12})
Top Tox Lists	Cardiac Hypertrophy **Cardiac Fibrosis** Cardiac Necrosis/Cell Death Hepatic Fibrosis LPS/IL-1 Mediated Inhibition of RXR Function	LXR/RXR Activation Positive Acute Phase Response Proteins Negative Acute Phase Response Proteins FXR/RXR Activation **Cardiac Fibrosis**

Data are listed in order of statistical significance.

(Number) = score/number of molecules related to the result.

Bolded names are shared between the high fiber and acetate groups.