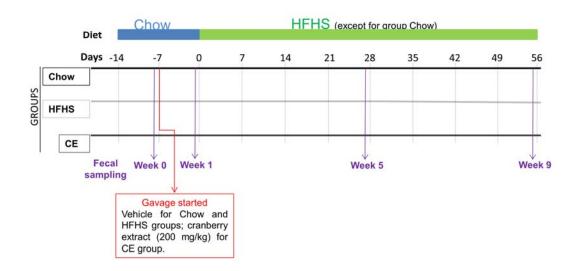
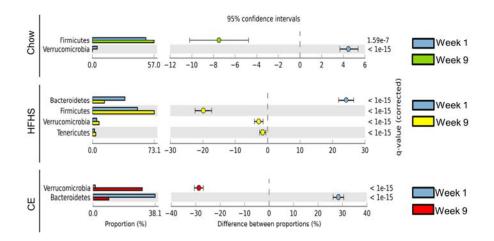
Supplementary Figure S1. Experimental Design. Eight-week-old C57Bl/6J male mice (n=36, Jackson, USA) were bred two animals per cage in a controlled environment with food and water ad libitum. After two weeks of acclimation (week 0 and week 1) on a normal-chow diet (Teklad 2018, Harlan), mice were fed either a chow or a high-fat high-sucrose (HFHS) diet containing 65% lipids, 15% proteins and 20% carbohydrates. Animals were randomly divided in three groups of 12 mice, and one group (assigned as CE) started to receive daily doses (200 mg/kg) of cranberry extract (CE) by gavage, whereas the other two groups (assigned as Chow and HFHS) received the vehicle (water). Feces were collected by the end of weeks 0, 1, 5 and 9 for subsequent metagenomic analysis. Body weight gain and food intake were assessed twice a week. After 8 weeks of HFHS feeding, animals were anesthetized in chambers saturated with isoflurane and then sacrificed by cardiac puncture. Tissues and blood were collected for subsequent analysis.

Figure S1 Experimental Design

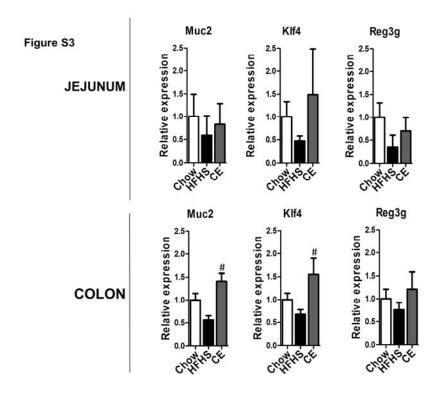


Supplementary Figure S2. Statistical comparisons of gut metagenomic profiles at the phylum level. Plots showing significant differences in abundance of reads assigned to a given bacterial phylum between week 1 and week 9 for Chow, HFHS and CE mice. The bar graphs on the left side display the mean proportion of sequences assigned to each phylum. The dot plots on the right side display the difference in mean proportions between the week 1 and week 9 with associated q-value. Error bars on both sides of dots represent the 95% confidence intervals. Only features (genus) with a q-value of >0.05 and a difference between proportions value >1 were considered.

Figure S2



Supplementary Figure S3. Muc2, Klf4 and Reg3g mRNA expression in the jejunum and proximal colon. Mucin 2 (Muc2), Kruppel-like factor 4 (Klf4) and Regenerating islet-derived 3 gamma (Reg3g) mRNA expressions were analysed by qPCR. Total RNA was extracted from jejunum and proximal colon and used for cDNA synthesis. Hprt (hypoxanthine guanine phosphoribosyl transferase) was used as the housekeeping gene. Data were calculated according to the $2-\Delta\Delta$ Ct method. Primer sequences for targeted mouse gene are available in Table S3. n=6-8. Data are expressed as the mean \pm SEM. *p<0.05 vs. Chow controls; #p<0.05 vs. HFHS controls.



Supplementary Figure S4. Statistical comparisons of gut metagenomic profiles during adaptation period (week 0 and week 1). Plots showing significant differences in abundance of reads assigned to a given bacterial genus between week 0 and week 1 for Chow, HFHS and CE groups. The bar graphs on the left side display the mean proportion of sequences assigned to each genus. The dot plots on the right side display the difference in mean proportions between week 0 and week 1 with associated q-value. Error bars on both sides of dots represent the 95% confidence intervals. Only features (genus) with a q-value of >0.05 and a difference between proportions value >1 were considered.

Figure S4

