Description of Additional Supplementary Files

File Name: Supplementary Data 1

Description: Baseline characteristics of the MetaSalt study participants

Normally distributed variables are presented as mean ± standard deviation, and the differences were tested using t-test; skewed distributed variables are presented as median (inter-quartile range), and the differences were tested using Wilcoxon rank sum test; categorical variables are presented as frequency (proportion), and the differences were tested using Chi-square test or Fisher's test. *p*-values are two-sided. BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MAP, mean arterial pressure; SBP, systolic blood pressure; SR, salt resistance; SS, salt sensitivity; SSBP, salt sensitivity of blood pressure; TC, total cholesterol; TG, triglycerides; UK, urinary potassium; UNa, urinary sodium.

File Name: Supplementary Data 2

Description: Identification of salt-related gut-microbial species

Differences in gut-microbial species between the low-salt and high-salt interventions were examined using linear mixed models with the random intercepts of individuals and families. Those species with Bonferroni significance [i.e., $p < 9.42\times10^{-5}$ (0.05/531 included species)] were defined as salt-related species. *p*-values are two-sided. CI, confidence interval.

File Name: Supplementary Data 3

Description: Identification of salt-related KEGG pathways

Differences in KEGG pathways between the low-salt and high-salt interventions were examined using linear mixed models with the random intercepts of individuals and families. Those metabolites with Bonferroni significance [i.e., $p < 2.63\times10^{-4}$ (0.05/190 included pathways)] were defined as salt-related KEGG pathways. *p*-values are two-sided. CI, confidence interval; KEGG, the Kyoto Encyclopedia of Genes and Genomes database.

File Name: Supplementary Data 4

Description: Identification of salt-related CAZy families

Differences in CAZy families between the low-salt and high-salt interventions were examined using linear mixed models with the random intercepts of individuals and families. Those metabolites with Bonferroni significance [i.e., $p < 3.76\times10^{-4}$ (0.05/133 included CAZy families)] were defined as salt-related CAZy families. *p*-values are two-sided. CAZy, the Carbohydrate-Active EnZymes database; CI, confidence interval.

File Name: Supplementary Data 5

Description: Identification of salt-related metabolites

Differences in metabolites between the low-salt and high-salt interventions were examined using linear mixed models with the random intercepts of individuals and families. Those metabolites with Bonferroni significance [i.e., $p < 2.25\times10^{-4}$ (0.05/222 included metabolites)] were defined as salt-related metabolites. *p*-values are two-sided. CI, confidence interval; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; GLCA-3S, glycolithocholic acid 3-sulfate; HMDB, the Human Metabolome Database; isoLCA, isolithocholic acid; KEGG, the Kyoto Encyclopedia of Genes and Genomes database; NA, no available; TMA, trimethylamine; TMAO, trimethylamine-N-oxide.

File Name: Supplementary Data 6

Description: Origin of salt-related metabolites annotated by MetOrigin

* The associations of salt-related metabolites with salt-related gut-microbial species and functions were assessed using LMMs, and metabolites with $p < 0.05$ were considered to be significantly associated with gut microbiome (see Supplementary Fig. 8-9 for details. *p*-values are two-sided. MetOrigin was used to annotate the origins of metabolites. DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; GLCA-3S, glycolithocholic acid 3-sulfate; isoLCA, isolithocholic acid; TMA, trimethylamine; TMAO, trimethylamine-N-oxide.

File Name: Supplementary Data 7

Description: Identification of SSBP-related gut-microbial species and functions

The changes in salt-related gut-microbial species and KEGG pathways from the low-salt to the high-salt intervention were calculated, and their associations with SSBP were assessed using LMMs by including SSBP as an ordinal variable. Those species with $p < 0.05$ were defined as SSBP-related species or KEGG pathways, and those that were associated with SSBP in the same direction as the effects of the high-salt intervention on them were further focused. The associations of the changes in species or KEGG pathways with categorical SSBP groups were further assessed using LMMs, with SR individuals as reference. Covariates included age, sex, field centers, body mass index, smoking, hypertension, and total cholesterol, and the random intercepts of families were included. *p*-values are two-sided. CI, confidence interval; KEGG, the Kyoto Encyclopedia of Genes and Genomes database; LMM, linear mixed model; SR, salt resistance; SS, salt sensitivity; SSBP, salt sensitivity of blood pressure.

File Name: Supplementary Data 8

Description: Identification of SSBP-related metabolites

The changes in salt-related metabolites from the low-salt to the high-salt intervention were calculated, and their associations with SSBP were assessed using LMMs by including SSBP as an ordinal variable. Those metabolites with $p < 0.05$ were defined as SSBP-related metabolites, and those that were associated with SSBP in the same direction as the effects of the high-salt intervention on them were further focused. The associations between the changes in metabolites and categorical SSBP groups were further assessed using LMMs, with SR individuals as the reference. Covariates included age, sex, field centers, body mass index, smoking, hypertension, and total cholesterol, and the random intercepts of families were included. *p*-values are two-sided. CI, confidence interval; HMDB, the Human Metabolome Database; KEGG, the Kyoto Encyclopedia of Genes and Genomes database; LMM, linear mixed model; SR, salt resistance; SS, salt sensitivity; SSBP, salt sensitivity of blood pressure.

File Name: Supplementary Data 9

Description: Associations between SSBP-related gut-microbial species and SSBP-related metabolites

The associations between the changes in SSBP-related gut-microbial species and the changes in SSBP-related metabolites were estimated using linear mixed models with the random intercepts of families, adjusted for age, sex, field centers, body mass index, smoking, hypertension, total cholesterol. *p*-values are two-sided.

File Name: Supplementary Data 10

Description: Associations of microbial genes with isovalerylcarnitine and its related gut-microbial species

The microbial genes that were related to the biosynthesis and metabolism of carnitine/acylcarnitine were extracted from the metagenome data of the MetaSalt study, and the associations of the relative abundance of these microbial genes with the plasma levels of the isovalerylcarnitine and the relative abundance of isovalerylcarnitine-related gut-microbial species were assessed using linear mixed model, adjusted for study phases, age, sex, field centers, body mass index, smoking, hypertension, total cholesterol, and the random intercepts of individuals and families were included. *p*-values are two-sided.

File Name: Supplementary Data 11

Description: SSBP-related biomarkers replicated using SBP or DBP to determine SSBP groups

SSBP-related biomarkers identified using MAP to determine SSBP groups were replicated when using SBP or DBP to determine SSBP groups. Linear mixed models were used to conduct analyses. Covariates included age, sex, field centers, body mass index, smoking, hypertension, and total cholesterol, and the random intercepts of families were included. *p*-values are two-sided. 28 of 32 and 13 of 32 biomarkers were replicated when using SBP or DBP to reclassify participants, respectively. CI, confidence interval; DBP, diastolic blood pressure; KEGG, the Kyoto Encyclopedia of Genes and Genomes database; MAP, mean arterial pressure; SBP, systolic blood pressure; SSBP, salt sensitivity of blood pressure.

File Name: Supplementary Data 12

Description: Baseline characteristics of the GenSalt study participants

Normal distributed variables are presented as mean ± standard deviation, and the differences were tested using paired t-test; skewed distributed variables are presented as median (inter-quartile range), and the differences were tested using Wilcoxon signed-rank test; categorical variables are presented as frequency (proportion), and the differences were tested using McNemar's Chi-square test. *p*-values are two-sided. BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MAP, mean arterial pressure; NA, no available; SBP, systolic blood pressure; SR, salt resistance; SS, salt sensitivity; SSBP, salt sensitivity of blood pressure; TC, total cholesterol; TG, triglycerides; UK, urinary potassium; UNa, urinary sodium.

File Name: Supplementary Data 13

Description: Replication of salt-related metabolites in the GenSalt study

The differences in metabolites between the low-salt and high-salt interventions were examined using linear mixed models with the random intercepts of individuals. Those metabolites with $p < 0.05$ were defined as salt-related metabolites. *p*-values are two-sided. CI, confidence interval; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; GLCA-3S, glycolithocholic acid 3-sulfate; HMDB, the Human Metabolome Database; KEGG, the Kyoto Encyclopedia of Genes and Genomes; NA, no available; TMA, trimethylamine; TMAO, trimethylamine-N-oxide.

File Name: Supplementary Data 14

Description: Replication of SSBP-related metabolites in the GenSalt study

The changes in salt-related metabolites from the low-salt to the high-salt intervention were calculated, and their associations with SSBP were assessed using LMMs. Those metabolites with $p < 0.05$ were defined as SSBP-related metabolites. *p*-values are two-sided. Covariates included body mass index, smoking, and total cholesterol, and the random intercepts of pairs were included. CI, confidence interval; HMDB, the Human Metabolome Database; LMM, linear mixed model; KEGG, the Kyoto Encyclopedia of Genes and Genomes database; SR, salt resistant; SS, salt sensitivity; SSBP, salt sensitivity of blood pressure.

File Name: Supplementary Data 15

Description: Differences in body weight, feed intake, and urinary indicators between different groups of Dahl SS rats at the end of the intervention

The information on body weight, feed intake, urinary volume, and urinary sodium was collected at the end of the intervention. Differences between groups were tested using ANOVA and t-test. p-values are two-sided, and $p < 0.05$ indicates a significant difference.

File Name: Supplementary Data 16

Description: Baseline characteristics of the prospective cohort participants

Normal distributed variables are presented as mean ± standard deviation; skewed distributed variables are presented as median (inter-quartile range); categorical variables are presented as frequency (proportion). BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MAP, mean arterial pressure; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides.