

Supplementary Material

Supplementary Table S1. Student's t-test shows significant ($p < 0.05$) and almost significant ($p < 0.1$) alterations in kidney and plasma metabolites between GC-treated and control mice.

| Kidney | 8W | p-values | 12W | p-values | 16W | p-values |
|--------|------------|----------|----------|----------|---------------|----------|
| | Fumarate | 0.031 | | | 2-HB | 0.044 |
| | Inosine | 0.046 | | | 4-AB | 0.055 |
| | Xanthine | 0.078 | | | Uridine | 0.064 |
| | Uracil | 0.041 | | | Acetone | 0.069 |
| | | | | | 3-HB | 0.072 |
| | | | | | Citrate | 0.083 |
| Plasma | Creatine | 0.013 | Tyrosine | 0.037 | Creatinine | 0.016 |
| | Creatinine | 0.066 | Valine | 0.080 | Phenylacetate | 0.036 |
| | Choline | 0.078 | Acetate | 0.047 | Proline | 0.038 |
| | | | | | 4AB | 0.049 |
| | | | | | 2AB | 0.050 |
| | | | | | Taurine | 0.079 |

Supplementary Table S2. Plasma fold change values of metabolites (GC-treated/control) that were identified by 1D ¹H NMR metabolomics. All values are reported in log2 base. Negative values indicate lower concentrations, while values with + sign indicates higher concentration level in the GC-treated group for a given metabolite.

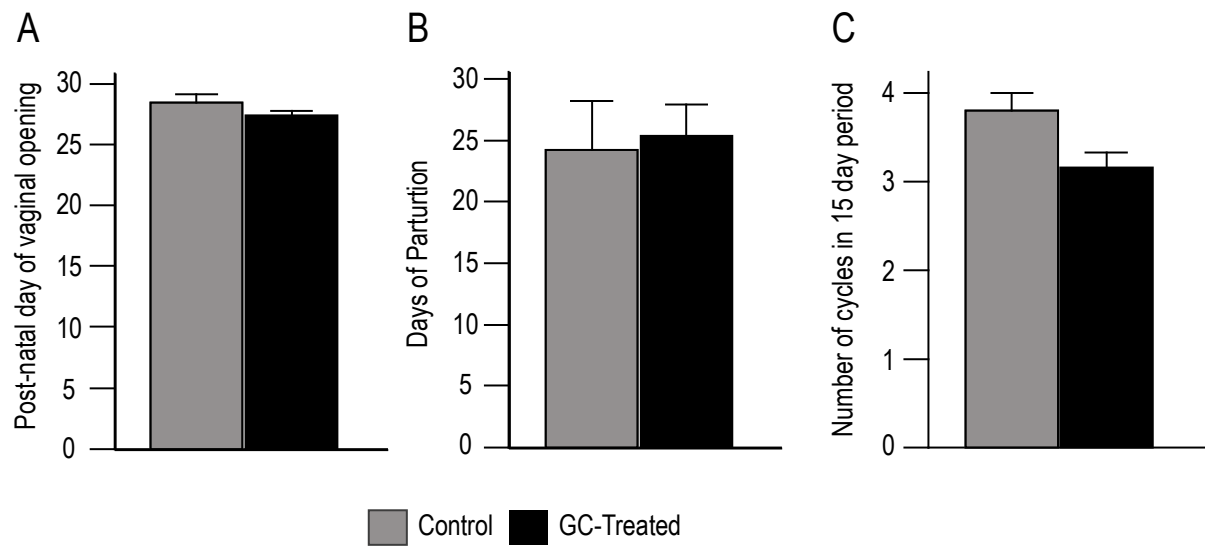
| Major pathway | Metabolite | 8W | 12W | 16W |
|---------------|-------------------|-------|-------|-------|
| Lipid | 3-Hydroxybutyrate | +0.01 | +0.40 | +0.23 |
| Lipid | Acetate | -0.29 | -0.27 | -0.12 |
| Lipid | Acetone | +0.54 | +0.76 | +0.04 |
| Lipid | Carnitine | -0.03 | -0.10 | -0.47 |
| Lipid | Choline | -0.30 | -0.22 | -0.25 |
| Lipid | Glycerol | -0.29 | -0.25 | -0.25 |
| Energy | Citrate | -0.27 | +0.21 | +0.07 |
| Energy | Creatine | +0.59 | -0.15 | -0.27 |
| Energy | Creatinine | +0.70 | +0.04 | -0.25 |
| Energy | Glucose | -0.10 | -0.38 | -0.15 |
| Energy | Lactate | +0.10 | +0.04 | -0.30 |
| Energy | Pyruvate | -0.36 | -0.23 | -0.10 |
| Energy | Succinate | -0.84 | +0.20 | +0.14 |
| Amino acid | 2-Aminobutyrate | -0.30 | -0.03 | -0.43 |
| Amino acid | 2-Hydroxybutyrate | -0.09 | -0.29 | +0.03 |
| Amino acid | 4-Aminobutyrate | -0.06 | -0.71 | -0.22 |
| Amino acid | Alanine | -0.09 | -0.04 | -0.29 |
| Amino acid | Asparagine | 0.07 | 0.01 | -0.12 |
| Amino acid | Glutamate | -0.51 | -0.12 | -0.62 |
| Amino acid | Glutamine | -0.01 | -0.10 | -0.09 |

| | | | | |
|------------|---------------|-------|-------|-------|
| Amino acid | Glycine | 0.00 | -0.17 | -0.17 |
| Amino acid | Isoleucine | +0.01 | -0.03 | +0.06 |
| Amino acid | Leucine | -0.09 | -0.12 | -0.01 |
| Amino acid | Lysine | -0.07 | -0.01 | -0.36 |
| Amino acid | Methionine | +0.01 | -0.10 | -0.34 |
| Amino acid | Phenylalanine | -0.07 | -0.20 | -0.09 |
| Amino acid | Proline | +0.06 | +0.07 | -0.36 |
| Amino acid | Serine | -0.09 | -0.23 | -0.22 |
| Amino acid | Taurine | +0.01 | -0.15 | -0.51 |
| Amino acid | Threonine | -0.15 | -0.18 | -0.36 |
| Amino acid | Tryptophan | -0.06 | +0.11 | -0.22 |
| Amino acid | Tyrosine | +0.10 | -0.22 | -0.09 |
| Amino acid | Valine | -0.18 | -0.34 | -0.23 |

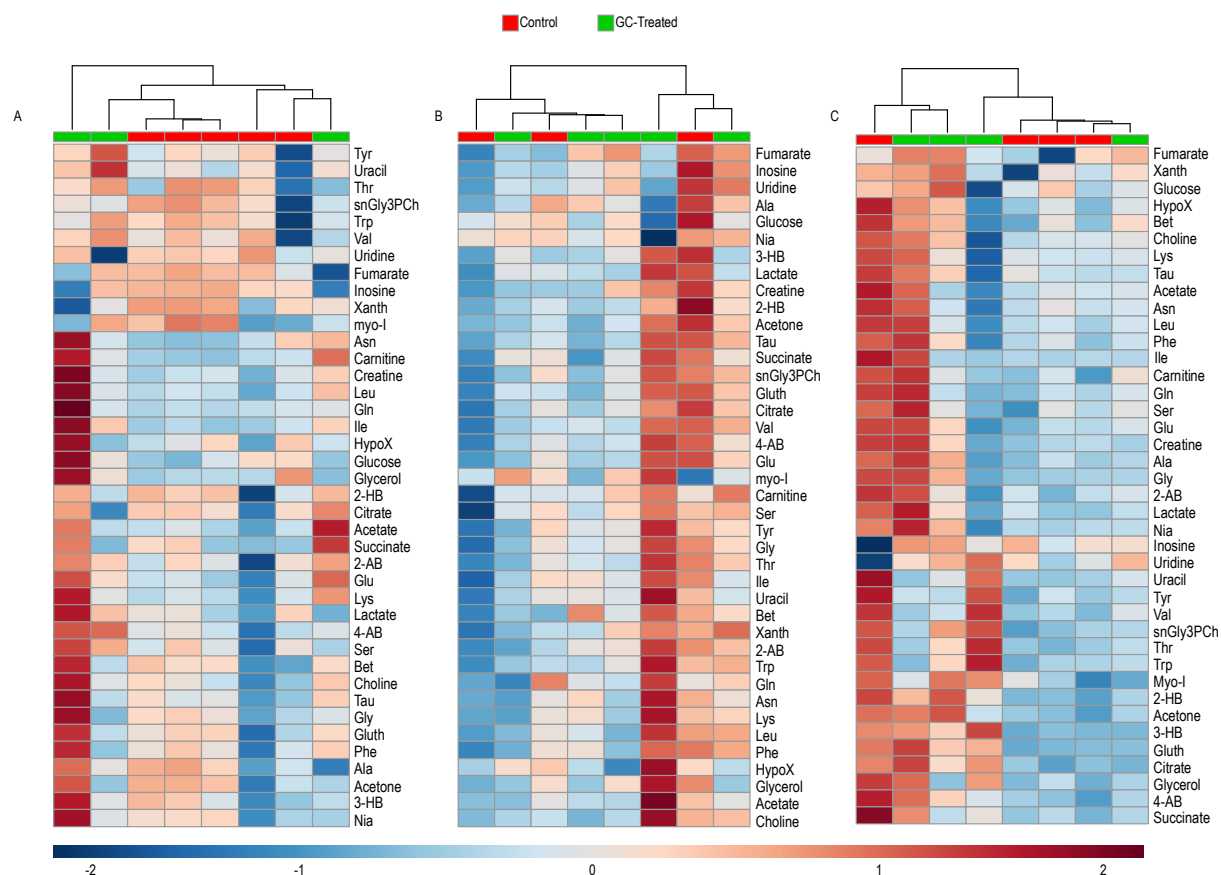
Supplementary Table S3. Kidney fold change (GC-treated/control) values of metabolites that are identified by 1D ¹H NMR metabolomics. All values are reported in log2 base. Negative values indicate lower concentrations in the GC-treated group for a given metabolite, while + values indicate higher concentration levels in the GC-treated group.

| Major PW | Metabolite | 8W | 12W | 16W |
|----------------------|----------------------------|-------|-------|-------|
| Lipid | 3-Hydroxybutyrate | +0.26 | -0.06 | +1.11 |
| Lipid | Acetate | +0.89 | +0.49 | +0.89 |
| Lipid | Acetone | -0.15 | -0.16 | +1.53 |
| Lipid | Carnitine | +0.76 | +0.59 | +1.59 |
| Lipid | Choline | +0.39 | +0.11 | +0.85 |
| Lipid | Glycerol | +0.57 | +0.01 | +1.34 |
| Lipid | snGlycero-3-PhosphoCholine | +0.12 | +0.03 | +1.58 |
| Energy | Glucose | +0.69 | -0.81 | +0.28 |
| Energy | Lactate | +0.16 | -0.02 | +0.79 |
| Energy | Citrate | +0.41 | 1.00 | +1.44 |
| Energy | Succinate | +0.71 | +0.03 | +0.91 |
| Energy | Fumarate | -1.21 | +0.20 | +0.50 |
| Pentose Phosphate PW | Hypoxanthine | 0.00 | +0.05 | +0.47 |
| Pentose Phosphate PW | Xanthine | -2.48 | +0.36 | +1.77 |
| Pentose Phosphate PW | Inosine | -1.80 | -0.53 | +0.49 |
| Pentose Phosphate PW | Uracil | +1.45 | +0.28 | +0.72 |
| Pentose Phosphate PW | Uridine | -1.04 | -0.23 | +1.45 |
| Pentose Phosphate PW | Myo-Inositol | +0.27 | +0.52 | +1.73 |
| Amino acid | Glutathione | +0.33 | +0.05 | +1.04 |
| Amino acid | 2-Aminobutyrate | +0.36 | +0.27 | +1.11 |

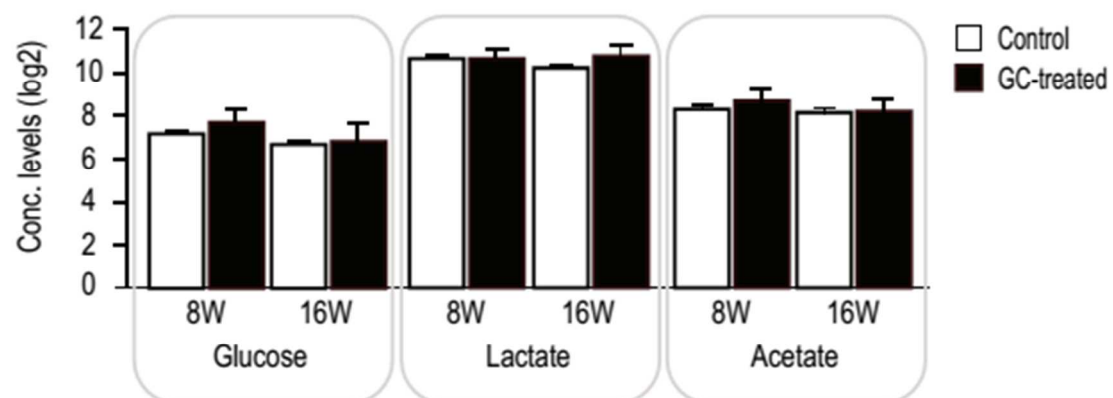
| | | | | |
|------------|-------------------|-------|-------|-------|
| Amino acid | 2-Hydroxybutyrate | -0.07 | -0.36 | +1.40 |
| Amino acid | 4-Aminobutyrate | +0.74 | +0.03 | +1.16 |
| Amino acid | Alanine | -0.30 | -0.27 | +1.30 |
| Amino acid | Asparagine | +1.17 | +0.11 | +0.65 |
| Amino acid | Betaine | +0.74 | +0.61 | +1.02 |
| Amino acid | Creatine | +0.83 | +0.02 | +0.91 |
| Amino acid | Glutamate | +0.40 | -0.07 | +1.18 |
| Amino acid | Glutamine | +0.72 | +0.01 | +1.18 |
| Amino acid | Glycine | +0.24 | +0.12 | +0.97 |
| Amino acid | Isoleucine | +1.29 | +0.11 | +0.89 |
| Amino acid | Leucine | +0.89 | +0.10 | +0.83 |
| Amino acid | Lysine | +0.62 | +0.16 | +0.64 |
| Amino acid | Niacinamide | +0.18 | -0.43 | +0.78 |
| Amino acid | Phenylalanine | +0.22 | +0.03 | +1.05 |
| Amino acid | Serine | +0.15 | +0.28 | +1.08 |
| Amino acid | Taurine | +0.61 | -0.01 | +0.55 |
| Amino acid | Threonine | -0.05 | +0.09 | +1.16 |
| Amino acid | Tryptophan | +0.59 | +0.29 | +0.94 |
| Amino acid | Tyrosine | +1.25 | +0.14 | +0.95 |
| Amino acid | Valine | +0.83 | +0.09 | +0.85 |



Supplementary Figure S1: Differences in vaginal opening, estrous cycle and parturition between GC-treated and control groups. **(A)** The day of vaginal openings **(B)** Number of estrous cycles in a 15 day period and **(C)** Parturition time of female mice after introducing to males in GC-treated (light-gray) and control (dark gray) groups.



Supplementary Figure S2. Heatmap representation of kidney metabolome profiles at: **(A)** eight weeks of age (8W), **(B)** 12 weeks of age (12W) and **(C)** 16 weeks of age (16W) labeled in the heatmap. Individual samples are represented by group labels and are shown as top row in the heatmaps. Red squares denote a mouse in control group, green denotes a mouse in GC-Treated group.



Supplementary Figure S3. Relative concentrations levels of glycolytic substrates between GC-treated and control groups are shown for at all-time points.