SUPPLEMENTARY TABLES

Supplementary Table 1. LC-MS-based metabolomic analysis results of metabolic genes related to glutathione metabolism in mouse kidney tissue.

| rt    | mz     | Metabolite                | Wilcox_p | t-test_p | FC  |
|-------|--------|---------------------------|-----------|----------|-----|
| 1.53  | 307.0843| Oxidized glutathione      | 0.01      | 0.00     | 2.77|
| 1.12  | 308.0915| Glutathione               | 0.03      | 0.03     | 2.37|
| 0.61  | 148.0603| L-Glutamic acid           | 0.01      | 0.01     | 0.91|
| 3.71  | 261.1447| Y-glutamylisoleucine      | 0.04      | 0.04     | 0.86|
| 2.26  | 247.1285| Y-glutamylvaline          | 0.01      | 0.00     | 0.82|
| 2.3   | 279.1007| Y-glutamylmethionine      | 0.02      | 0.01     | 0.66|
| 1.29  | 497.1009| Bis-Y-glutamylcystine     | 0.01      | 0.01     | 0.64|

The retention times (rt) and detected mass over charge (mz) values of metabolites are shown. Fold changes (FCs) were calculated by dividing the mean relative intensity values of identified metabolites from the old group ($n = 8$) by those from the young group ($n = 7$). P-values were determined by the Wilcoxon rank sum test (Wilcox_p) and t-test (t-test_p) using R.

Supplementary Table 2. Metaboanalyst results.

| Metabolic Pathway                          | Total Cmpd | Hits | Raw p      | FDR       | Impact |
|-------------------------------------------|------------|------|------------|-----------|--------|
| Riboflavin metabolism                     | 4          | 2    | 0.00078    | 0.00397   | 0.5    |
| Nicotinate and nicotinamide metabolism    | 15         | 2    | 0.00004    | 0.00095   | 0.4290 |
| Glutathione metabolism                    | 28         | 4    | 0.00043    | 0.00281   | 0.3026 |
| Purine metabolism                         | 65         | 6    | 0.00037    | 0.00281   | 0.2061 |
| Alanine, aspartate and glutamate metabolism | 28       | 2    | 0.00820    | 0.01066   | 0.1971 |
| Citrate cycle (TCA cycle)                 | 20         | 2    | 0.00337    | 0.00572   | 0.1345 |
| Arginine and proline metabolism           | 38         | 2    | 0.00140    | 0.00438   | 0.0860 |
| Glyoxylate and dicarboxylate metabolism   | 32         | 3    | 0.00204    | 0.00482   | 0.0318 |
| Pyrimidine metabolism                     | 39         | 2    | 0.00092    | 0.00397   | 0.0202 |

The number of total annotated compounds in each metabolic pathway (Total Cmpd) and the number of identified metabolites (Hits) were used for the hypergeometrical test-based pathway enrichment test. According to the test results, raw p-values (Raw p) and FDR values were calculated. Additionally, the estimated impact parameters in the Metaboanalyst results are shown.

Supplementary Table 3. Transcriptomic results of metabolic genes related to glutathione metabolism in mouse kidney tissue.

| Gene_Sym | Description                                  | FC  | Adjusted p-value |
|----------|----------------------------------------------|-----|------------------|
| Ggct     | gamma-glutamyl cyclotransferase              | 0.55| 1.49E-06         |
| Opr2h    | 5-oxoprolinase (ATP-hydrolysing)             | 1.38| 0.0406977        |
| Gss      | glutathione synthetase                       | 0.8 | 0.0608817        |
| Chac2    | ChaC, cation transport regulator 2           | 0.78| 0.0956953        |
| Ggt1     | gamma-glutamyltransferase 1                  | 0.87| 0.3969397        |
| Anpep    | alanyl (membrane) aminopeptidase             | 0.79| 0.1122825        |
| Gclc     | glutamate-cysteine ligase, catalytic subunit | 0.74| 0.4305143        |
| Dpep1    | dipeptidase 1                               | 0.75| 0.4100684        |

Fold changes (FCs) were calculated by dividing the mean FPKM values of genes from the old group ($n = 3$) by those from the young group ($n = 3$). Adjusted p-values were calculated by using the Deseq2 R package.
Supplementary Table 4. Gene Set Enrichment Analysis results of transcriptome data from mouse kidney tissue.

| Gene Set                                      | ES  | NES  | NOM p-val | FDR q-val |
|-----------------------------------------------|-----|------|-----------|-----------|
| GSE17721_LPS_VS_POLYC_1H_BMDC_DN              | -0.96 | -1.53 | 0         | 0.046     |
| GSE14308_TH1_VS_NAIVE_CD4_TCELL_DN           | -0.9 | -1.46 | 0         | 0.046     |
| GSE43955_10H_VS_30H_ACT_CD4_TCELL_DN         | -0.96 | -1.42 | 0         | 0.046     |
| GSE14308_INDUCTED_VS_NATURAL_TREG_UP         | -0.98 | -1.36 | 0         | 0.069     |
| GSE14769_UNSTIM_VS_120MIN_LPS_BMDC_DN        | -0.98 | -1.36 | 0         | 0.055     |
| CAIRO_LIVER_DEVELOPMENT_DN                   | -0.91 | -1.35 | 0         | 0.054     |
| OHGUICH_LIVER_HNF4A_TARGETS_DN                | -0.96 | -1.34 | 0         | 0.078     |
| GSE19198_6H_VS_24H_IL21_TREATED_TCELL_DN     | -0.93 | -1.33 | 0         | 0.074     |

Nominal p-values (NOM p-val) were adjusted as FDR q-values. Only the gene sets with FDR q-values less than 0.1 are shown above. Enrichment scores (ES) and negative enrichment scores (NES) are also shown.

Supplementary Table 5. Body weights of the young and old mice.

| Young (3 months) | BW (g) |
|------------------|--------|
| Y1               | 25.2   |
| Y2               | 25.8   |
| Y3               | 28.4   |
| Y5               | 21.6   |
| Y7               | 23.5   |
| Y8               | 22.4   |
| Y9               | 24.3   |
| Old (24 months)  |        |
| O1               | 37.7   |
| O2               | 45.3   |
| O3               | 35.6   |
| O4               | 49.6   |
| O5               | 31.0   |
| O7               | 35.6   |
| O8               | 45.1   |
| O9               | 41.7   |

Young group (n = 7) and old group (n = 8).