Supplementary Figure 1

- 28361 Affimetrix probes

- 22126 filtered genes
  - 6267 differentially expressed genes with p-value < 0.05

- 3025 differentially expressed genes with FDR < 0.05
  - 1398 up-regulated genes
  - 1627 downregulated genes
Supplementary Figure 3

A

**Fn14**

\[
\begin{array}{ccc}
\text{WT} & \text{Pgc-1α−/−} \\
0 & 0 & 0
\end{array}
\]

\[
\begin{array}{ccc}
**F4/80** & \text{CD3} \\
0 & 0 & 0
\end{array}
\]

\[
\begin{array}{ccc}
\text{Tnfa} & \text{Ccl2} & \text{Tnfa} \\
0 & 0 & 0
\end{array}
\]

B

**Cell number/hpf**

\[
\begin{array}{ccc}
\text{WT} & \text{Pgc-1α−/−} \\
0 & 0 & 0
\end{array}
\]

\[
\begin{array}{ccc}
\text{F4/80+ macrophages} & \text{CD3+ lymphocytes} & \text{F4/80+ macrophages} \\
0 & 0 & 0
\end{array}
\]

C

**NGAL mRNA levels**

\[
\begin{array}{ccc}
\text{WT} & \text{Pgc-1α−/−} \\
0 & 0 & 0
\end{array}
\]

\[
\begin{array}{ccc}
\text{uNGAL (ng/mL)} & \text{uNGAL (ng/mL)} & \text{uNGAL (ng/mL)} \\
0 & 0 & 0
\end{array}
\]

D

**TUNEL+ nuclei/hpf**

\[
\begin{array}{ccc}
\text{WT} & \text{Pgc-1α−/−} \\
0 & 0 & 0
\end{array}
\]

E

**Albuminuria (µg/mL)**

\[
\begin{array}{ccc}
\text{WT} & \text{Pgc-1α−/−} \\
0 & 0 & 0
\end{array}
\]

**Legend:**

- WT: Wild Type
- Pgc-1α−/−: PGC-1α knockout
- **: p < 0.01
- *: p < 0.05

**Notes:**

- F4/80: Macrophages
- CD3: Lymphocytes
- FN14: FASL
- IL-6: Interleukin-6
- TNFα: Tumor Necrosis Factor alpha
- CCL2: Chemokine (C-C motif) ligand 2
- NGAL: Neutrophil gelatinase-associated lipocalin
- Fas: Fas antigen
- Albuminuria: Proteinuria
Supplementary Figure 4

The image shows a bar graph illustrating mtDNA deletion (% change vs WT control) over time, categorized by WT and Pgc-1α<sup>−/−</sup> genotypes. The x-axis represents time points: Control, AKI 24 h, and AKI 72 h. The y-axis indicates the percentage change in mtDNA deletion.

Key findings:
- In the Control group, there is a slight increase in mtDNA deletion for both WT and Pgc-1α<sup>−/−</sup> genotypes.
- At AKI 24 h, there is a notable increase in mtDNA deletion for Pgc-1α<sup>−/−</sup> compared to WT.
- At AKI 72 h, mtDNA deletion is significantly higher for Pgc-1α<sup>−/−</sup> compared to WT.

Statistical significance is indicated by asterisks (*) and a plus symbol (+), suggesting a significant difference between groups.
Supplementary Figure 6

WT

Pgc-1α−/−

Control AKI 24 h AKI 72 h

Control AKI 24 h AKI 72 h

Tubular PCNA+ nuclei/hpf

WT Pgc-1α−/−

Control AKI 24 h AKI 72 h

WT Pgc-1α−/−

Interstitial PCNA+ nuclei

Control AKI 24 h AKI 72 h
Supplementary Figure 7

A

![Graph showing the expression of Arginase 2 protein](image)

<table>
<thead>
<tr>
<th>PGC-1α</th>
<th>Control</th>
<th>AKI 24 h</th>
<th>AKI 72 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>+/+</td>
<td><img src="image" alt="Bar graph" /></td>
<td><img src="image" alt="Bar graph" /></td>
<td><img src="image" alt="Bar graph" /></td>
</tr>
<tr>
<td>-/-</td>
<td><img src="image" alt="Bar graph" /></td>
<td><img src="image" alt="Bar graph" /></td>
<td><img src="image" alt="Bar graph" /></td>
</tr>
</tbody>
</table>

Arginase 2 protein (± change vs WT control)

** = P < 0.01 vs WT control
*** = P < 0.001 vs WT control
† = P < 0.05 vs WT control

B

![Graph showing the expression of Arginase 1 protein](image)

<table>
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<th>AKI 72 h</th>
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</tr>
</tbody>
</table>

Arginase 1 protein (± change vs control)

# = P < 0.01 vs WT control
** = P < 0.001 vs WT control
† = P < 0.05 vs WT control
Early decrease in mitochondrial mass

Increased inflammatory status
- ↑ Fn14, TNFα
- ↑ NGAL
- trend to ↑ IL-6, CCL2
- ↑ macrophages, lymphocytes

Mild kidney inflammation

Spontaneous

Pgc-1α deficiency

AKI

More severe AKI and decreased survival

Early decrease in mitochondrial mass

More severe inflammation
- NFκB activation
- ↑↑ inflammatory cytokines
- ↑↑ leukocyte infiltration (macrophages, lymphocytes)

↑ cell death

Supplementary Figure 8