Supplementary Figure 1

AKI cortex → Control cortex

LC/MS-MS →
- 41235 peptides
- 6516 unique proteins
- 1480 unique proteins

p<0.05 AND (FC≤0.5 or ≥2.0)

Bioinformatics analysis

Focused data mining and validation

Significant dataset
- 1449 upregulated
- 31 downregulated

KEGG signaling pathways: MAPK, ubiquitin-mediated proteolysis, chemokines, NFκB, apoptosis and others (Table 1)

Selection of a pathway: Non-canonical NFκB activation through ubiquitin-mediated proteolysis

Identification of further non-canonical NFκB pathway proteins: MAP3K14, NFκB2, RelB, Ube2m and Cullin1

Validation of observed changes: Western blot, immunohistochemistry, qRT-PCR

Selection of the apical MAPK of non-canonical NFκB activation protein for functional studies: MAP3K14

Selection of potential targets: chemokines, apoptosis

In culture
- Selection of cell type: tubular cells
- Targeting method: siRNA

In vivo: aly/aly mice with point mutation in MAPK14 gene
Supplementary Figure 3

A) % cullin-1 protein levels

<table>
<thead>
<tr>
<th></th>
<th>Vehicle</th>
<th>24 hours</th>
<th>72 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI</td>
<td></td>
<td></td>
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</tbody>
</table>

* indicates a significant difference.

B) Immunohistochemistry images

Control

AKI
Supplementary Figure 5

A) 

![Graph showing mortality percentage for different conditions.]

B) 

![Graph showing serum creatinine levels for different conditions.]

**A)** 

<table>
<thead>
<tr>
<th>Condition</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP3K14&lt;sup&gt;aly/aly&lt;/sup&gt; BM</td>
<td>5</td>
</tr>
<tr>
<td>Wild-type BM</td>
<td>5</td>
</tr>
<tr>
<td>MAP3K14&lt;sup&gt;aly/aly&lt;/sup&gt; BM</td>
<td>3</td>
</tr>
<tr>
<td>Wild-type BM</td>
<td>3</td>
</tr>
</tbody>
</table>

**B)** 

<table>
<thead>
<tr>
<th>Condition</th>
<th>Serum creatinine (mg/dl)</th>
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</thead>
<tbody>
<tr>
<td>MAP3K14&lt;sup&gt;aly/aly&lt;/sup&gt; BM</td>
<td>1.7 ± 0.2</td>
</tr>
<tr>
<td>Wild-type BM</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td>MAP3K14&lt;sup&gt;aly/aly&lt;/sup&gt; BM</td>
<td>1.8 ± 0.3</td>
</tr>
<tr>
<td>Wild-type BM</td>
<td>1.6 ± 0.2</td>
</tr>
</tbody>
</table>

**Legend:**
- MAP3K14<sup>aly/aly</sup> BM
- Wild-type BM

**Notes:**
- n values are indicated for each condition.
Supplementary Figure 6

A) % MCP1 mRNA levels

<table>
<thead>
<tr>
<th>TWEAK</th>
<th>Scramble siRNA</th>
<th>MAP3K14 siRNA</th>
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</thead>
<tbody>
<tr>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

* P < 0.05
** P < 0.01