Data Supplement

Canagliflozin Prevents Intrarenal Angiotensinogen Augmentation and Mitigates Kidney Injury and Hypertension in Mouse Model of Type 2 Diabetes Mellitus

Fig. S1

a. Effects of low and high doses of CANA on hyperglycemia in a DM mouse. Blood glucose levels measured by a telemetry system were plotted every minute. The mouse was treated every day from 10:00 am - 10:30 am. After the baseline measurements, the mouse was treated with 5 mg/kg/day CANA for two days followed by 10 mg/kg/day CANA for three days.

b. Urinary glucose excretion in DM mice. ND+Veh: N=12, ND+CANA: N=11, DM+Veh: N=10-12, DM+CANA: N=14-16. Dotted lines show results in ND mice. Solid lines indicate results in DM mice. Open circles and closed squares are vehicle- and CANA-treated groups, respectively. Mean ± SE. Asterisk (p < 0.05) indicates significant difference among groups.
Fig. S2
Effects of CANA on body weight gain in T2DM mice. ND+Veh: N=9, ND+CANA: N=8, DM+Veh: N=7, DM+CANA: N=7. Mean ± SE. Dotted lines show results in ND mice. Solid lines indicate results in DM mice. Open circles and closed squares are vehicle- and CANA-treated groups, respectively. Asterisk (p < 0.05) indicates significant difference among groups.
Fig. S3

**a.** Effect of CANA on SBP. SBP were measured by a tail-cuff system. ND+Veh: N=4-5, ND+CANA: N=5, DM+Veh: N=6-7, DM+CANA: N=5-7. Dotted lines show results in ND mice. Solid lines indicate results in DM mice. Open circles and closed squares are vehicle- and CANA-treated groups, respectively. Mean ± SE. Panel **b** (day time) and **c** (night time) show changes in SBP monitored by a telemetry system during 6 week of treatment. Open circles and closed
squares are vehicle- and CANA-treated DM groups, respectively. Panel d indicates SBP during 24 hours on week 6. Mean ± SE. N=4 in Vehicle group, N=5 in CANA group. Asterisk (p < 0.05)

**Fig. S4**

a

![Graph showing urinary sodium excretion](image)

b

![Graph showing urinary potassium excretion](image)

indicates significant difference between groups.

**Fig. S4**

b. Changes in urinary K+ levels on week 6. Mean ± SE. Asterisk (p < 0.05) indicates significant difference among groups.

**Fig. S5**

Effects of CANA on AGT levels in liver, adipose tissue and plasma in T2DM mice. ND+Veh: N=8, ND+CANA: N=8, DM+Veh: N=9, DM+CANA: N=10. AGT mRNA levels in liver (a) and adipose tissue (b). c. Plasma AGT levels. Mean ± SE. Asterisk (p < 0.05) indicates significant difference among groups.
Fig. S6

a. Urinary albumin and protein levels, respectively. Panels a. and b. show urinary albumin and protein levels normalized based on 24-hour urine volume. ND+Veh: N=4-8, ND+CANA: N=5-8, DM+Veh: N=5-7, DM+CANA: N=6. Dotted lines show results in ND mice. Solid lines indicate results in DM mice. Open circles and closed squares are vehicle- and CANA-treated groups, respectively. Mean ± SE. Asterisk (p < 0.05) indicates significant difference among groups.
Fig. S6

a. b. c. and d. Urinary albumin and protein levels, respectively. Panels c. and d. show urinary albumin and protein levels normalized based on urinary creatinine concentrations. ND+Veh: N=4-8, ND+CANA: N=5-8, DM+Veh: N=5-7, DM+CANA: N=6. Dotted lines show results in ND mice. Solid lines indicate results in DM mice. Open circles and closed squares are vehicle- and CANA-treated groups, respectively. Mean ± SE. Asterisk (p < 0.05) indicates significant difference among groups.
Table S1

Gene copies in renal cortex (copies in 1 ng RNA)

<table>
<thead>
<tr>
<th></th>
<th>ND+Veh</th>
<th>ND+CANA</th>
<th>DM+Veh</th>
<th>DM+CANA</th>
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<tr>
<td>N</td>
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<td>8</td>
<td>9</td>
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</tr>
<tr>
<td>Renin</td>
<td>258 ± 41</td>
<td>371 ± 33</td>
<td>430 ± 55</td>
<td>621 ± 31*</td>
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<tr>
<td>ACE</td>
<td>313 ± 27</td>
<td>274 ± 36</td>
<td>261 ± 22</td>
<td>309 ± 22</td>
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<tr>
<td>AT1a</td>
<td>869 ± 37</td>
<td>927 ± 22</td>
<td>803 ± 57</td>
<td>825 ± 38</td>
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<tr>
<td>SGLT2</td>
<td>5314 ± 291</td>
<td>5079 ± 116</td>
<td>6472 ± 260*</td>
<td>5782 ± 342</td>
</tr>
</tbody>
</table>

*: p<0.05 vs ND+Veh

Table S1
Number of renin, ACE, AT1a and SGLT2 mRNA copies in renal cortex. ND+Veh: N=8, ND+CANA: N=8, DM+Veh: N=9, DM+CANA: N=9. Mean ± SE. Asterisk (p < 0.05) indicates significant difference compared to ND+Veh group.