A Tbc1d1Ser231Ala-knockin mutation partially impairs AICAR- but not exercise-induced muscle glucose uptake in mice

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Figure 1

(a) Skeletal muscle

<table>
<thead>
<tr>
<th>AMPKα1/α2 f/f</th>
<th>AMPKα1/α2 mKO</th>
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<tbody>
<tr>
<td>pS231-TBC1D1</td>
<td></td>
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<tr>
<td>TBC1D1</td>
<td></td>
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<tr>
<td>AS160</td>
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<tr>
<td>pT172-AMPK</td>
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<tr>
<td>AMPKα</td>
<td></td>
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<tr>
<td>AMPKα1</td>
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<td>AMPKα2</td>
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<td>GAPDH</td>
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(b) Heart

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<th>AMPKα1/α2 f/f</th>
<th>AMPKα1/α2 mKO</th>
</tr>
</thead>
<tbody>
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<tr>
<td>TBC1D1</td>
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<tr>
<td>AMPKα</td>
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<tr>
<td>GAPDH</td>
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</table>

(c) Liver

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<th>AMPKα1/α2 mKO</th>
</tr>
</thead>
<tbody>
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<tr>
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<td>AMPKα</td>
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<tr>
<td>GAPDH</td>
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</tbody>
</table>

(d) Blood glucose (mmol/l)

Time after AICAR injection (min)

(e) Glucose uptake in soleus (µmol/g/h)

(f) Glucose uptake in EDL (µmol/g/h)

(g) PM GLUT4 (fold)

h

<table>
<thead>
<tr>
<th>AMPKα1/α2 f/f</th>
<th>AMPKα1/α2 mKO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td></td>
</tr>
<tr>
<td>AICAR</td>
<td></td>
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</tbody>
</table>

Basal

AICAR

**Basal**

AICAR

**Basal**

AICAR

**Basal**

AICAR

**NS**

†
Figure 3

(a) Glucose uptake in EDL and Soleus muscle with different AICAR concentrations. 

(b) Comparison of glucose uptake in Soleus muscle between WT and TBC1D1\textsuperscript{S231A} at basal and AICAR conditions. 

(c) Glucose uptake in EDL muscle with varying AICAR concentrations. 

Key:
- **WT**
- **TBC1D1\textsuperscript{S231A}**

Statistical significance:
- *: p < 0.05
- †: p < 0.01
- ‡: p < 0.001
- NS: non-significant
Figure 4

(a) Images of Soleus and EDL muscles from WT and TBC1D1<sup>S231A</sup> mice.

(b) Bar charts showing the percentage of Type I and Type II fibres in the soleus muscle for WT and TBC1D1<sup>S231A</sup> mice. There is no significant difference (NS).

(c) Bar charts showing the percentage of Type IIa and Type IIb/IIx fibres in the EDL muscle for WT and TBC1D1<sup>S231A</sup> mice. There is no significant difference (NS).
Figure 5

(a) Western blots showing the expression levels of various proteins in different conditions. IB: Immunoblotting for:
- pS231-TBC1D1
- TBC1D1
- pS212-ACC
- ACC
- pT172-AMPK
- AMPKα
- GLUT4
- FLOT1

(b) Graph showing the total GLUT4 expression levels in different conditions.

(c) Graph showing the PM GLUT4 expression levels in different conditions.
Figure 6

(a) WT vs. TBC1D1S231A

(b) Resting vs. Running

(c) WT vs. TBC1D1S231A

(d) Running distance (m)

(e) IB: WT vs. TBC1D1S231A

(f) Glucose uptake (DPM/g in 35 min)

(g) WT vs. TBC1D1S231A NS