**Supplementary Table 1.** Characteristics of human subjects.

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>No. and Sex of Subjects</th>
<th>Aβ40- pg/ml (range)</th>
<th>Aβ42- pg/ml (range)</th>
<th>Age-year (range)</th>
<th>Glucose- mmol/L (range)</th>
<th>Triglycerides- mmol/L (range)</th>
<th>Cholesterol- mmol/L (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euglycemia (controls)</td>
<td>26 (17 M/9 F)</td>
<td>101.8±10.8 (25.8-200.4)</td>
<td>145.0±19.1 (29.0-365.2)</td>
<td>58.6±1.1 (51-76)</td>
<td>5.3±0.1 (4.2-5.9)</td>
<td>1.24±0.09 (0.66-2.54)</td>
<td>4.99±0.11 (3.96-5.84)</td>
</tr>
<tr>
<td>Hyperglycemia (IFG and diabetes)</td>
<td>35 (21 M/14 F)</td>
<td>159.2±20.8* (2.2-509.6)</td>
<td>258.0±38.1* (25.8-814.2)</td>
<td>59.6±1.1 (42-70)</td>
<td>8.1±0.4*** (4.5-14.8)</td>
<td>1.77±0.13# (0.56-3.49)</td>
<td>4.59±0.15** (2.13-5.85)</td>
</tr>
</tbody>
</table>

Blood was drawn with the subject after an overnight fasting. Data are presented as mean and s.e.m. IFG: impaired fasting glucose. *P < 0.05, **P < 0.01, ***P < 0.001. #P = 0.053.
Supplementary Figure 1. The metabolic phenotype of APP/PS1 transgenic mice. A: Body weight of male APP/PS1 mice (n = 9) and wild-type littermates (n = 8) from 10 to 19 weeks of age. B-D: Food intake (B), total body fat content (C) and lean content (D) of male APP/PS1 mice (n = 9) and wild-type littermates (n = 8) at 12 or 16 weeks of age. E and F: Plasma alanine transaminase (ALT) and aspartate transaminase (AST) activity (E), and plasma triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) levels (F) in male APP/PS1 mice (n = 4) and wild-type littermates (n = 6) at 20 weeks of age. Data are presented as mean and s.e.m.
**Supplementary Figure 2.** Aβ induces insulin resistance in HepG2 cells. *A* and *B*: The dose and time response of Aβ on insulin signaling, including the phosphorylation of insulin receptor (InsR), Akt and GSK-3β in HepG2 cells was analyzed by immunoblot. Cells were incubated with indicated doses of Aβ25-35 for 60 h (*A*) or with 10 μM Aβ25-35 for indicated times (*B*), followed by treatment with or without 100 nM insulin for 20 min.

**Supplementary Figure 3.** The morphology and viability of primary hepatocytes treated with or without Aβ. *A*: The morphology of primary hepatocytes treated with or without 10 μM Aβ42 for 60 h. *B* and *C*: The viability of primary hepatocytes treated with or without Aβ. Cells were incubated with indicated doses of Aβ25-35 for 60 h (*B*) or with 10 μM Aβ25-35 for indicated times (*C*), and then measured by MTT assay. Data are presented as mean and s.e.m.
Supplementary Figure 4. Quantitative RT-PCR analysis of SOCS-1, SOCS-3 and inflammation-related gene expression in liver, muscle and white adipose tissue (WAT). A: Quantitative RT-PCR analysis of SOCS-1 and SOCS-3 expression in WAT (A) of APP/PS1 mice (n = 4) and wild-type littermates (n = 4) at 20 weeks of age. B-D: Quantitative RT-PCR analysis of inflammation-related gene expression in liver (B), muscle (C) and WAT (D) of APP/PS1 mice (n = 4) and wild-type littermates (n = 4) at 20 weeks of age. Data are presented as mean and s.e.m. *P < 0.05.
Supplementary Figure 5. Aggregation of Aβ42. Aβ peptides were incubated at the concentration of 2 mM in distilled water for 72 h in darkness at 37°C. The samples were examined on 15% SDS-PAGE and detected by immunoblot. A 6E10 antibody from Covance was used to detect Aβ.

Supplementary Figure 6. Immunoblot analysis of IRS1 and IRS2 protein levels in liver of AD mouse model and in hepatocytes treated with Aβ or SOCS-1 siRNA. A: Immunoblot analysis of IRS1 and IRS2 protein levels in liver of APP/PS1 mice and wild-type littermates at 20 weeks of age. B: Quantification of IRS1 and IRS2 levels in (A). The protein levels were normalized to tubulin. C: Immunoblot analysis of IRS1 and IRS2 protein levels in hepatocytes treated with or without 10 μM Aβ42 for 60 h. D: Immunoblot analysis of IRS1 and IRS2 protein levels in hepatocytes after transfection with the indicated siRNAs. Data are presented as mean and s.e.m.
Supplementary Figure 7. The purity and viability of isolated primary hepatocytes. 

A: The purity of isolated primary hepatocytes was verified by PAS staining to stain glycogen.

B: The viability of isolated primary hepatocytes was verified by trypan blue staining.