

## **Supplementary Information**

### **p66Shc Signaling Mediates Diabetes-Related Cognitive Decline**

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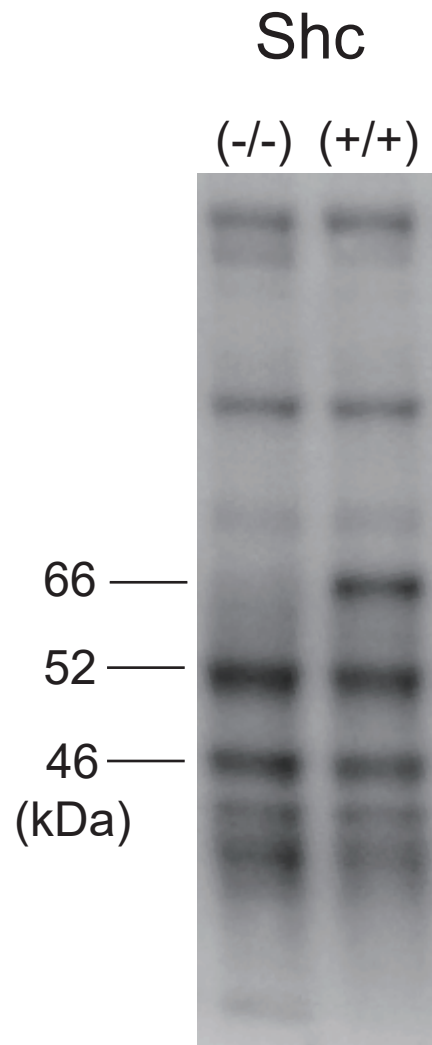
**Table S1: Nucleotide Sequences of Primers. Related to Figure 3, 5**

Gene	Forward primer (5'→3')	Reverse primer (5'→3')
<i>gp91phox</i>	ACTGCGGAGAGTTTGGGAAGA	GGTGATGACCACCTTTTGCT
<i>p22phox</i>	TGGCTACTGCTGGACGTTTCAC	CTCCAGCAGACAGATGAGCACAC
<i>IL-1<math>\beta</math></i>	AAATACCTGTGGCCTTGGGC	CTTGGGATCCACACTCTCCAG
<i>TNF-<math>\alpha</math></i>	CTCCTGGCCAACGGCATGGAT	ATCGGCTGACGGTGTGGGTG
<i>p66Shc</i>	CCCCAAGCCGAAGTACAACCCA	TCCGGGGAAAGAAGGAACACAGG
<i><math>\beta</math>-Actin</i>	TGACAGGATGCAGAAGGAGA	GCTGGAAGGTGGACAGTGAG

**Table S2: Body Weight and Blood Glucose in Type 1 and Type 2 diabetic mice. Related to Figure 1 to 3.**

	age (weeks)	body weight (g)	Blood glucose (mg/dL)
Type 1 diabetic mice (ICR)			
diabetic (STZ-induced), n = 9	7weeks aged	33.6±0.3	133.0±5.6
control (vehicle), n = 9	(before STZ)	33.8±0.5	137.8±8.3
diabetic (STZ-induced), n = 9	21weeks aged	41.4±1.3*	681.2±27.9*
control (vehicle), n = 9	(14 weeks after STZ)	48.0±0.6	164.3±3.8
Type 2 diabetic mice (db/db)			
diabetic (db/db), n = 10	10 weeks aged	44.9±0.5*	543.9±14.7*
control (db/+), n = 6		27.6±0.2	128.7±13.6
diabetic (db/db), n = 10	30weeks aged	57.0±2.4*	487.4±128.0*
control (db/+), n = 6		32.3±0.3	116.5±8.8

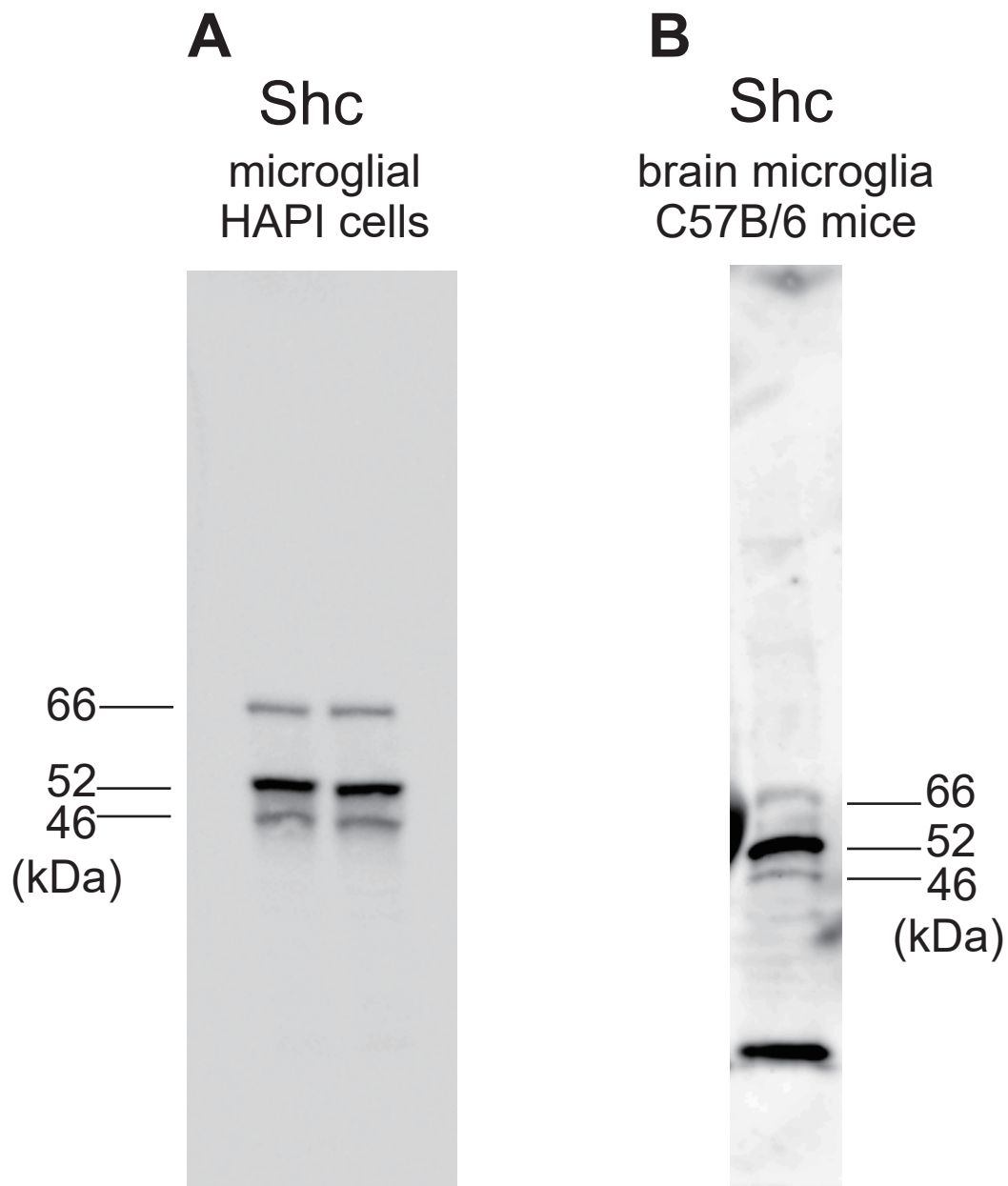
Body weight and blood glucose concentrations in type 1 and type 2 diabetic mice. Data are means  $\pm$  SE. \*P < 0.05 vs. control.



**Figure S1: Western blot analysis to confirm deleted protein expression of p66Shc.**

**Related to Figure 4.**

Western blotting results using anti-Shc protein antibody, with total protein extracted from liver homogenates of *p66Shc* (-/-) and *p66shc* (+/+) mice.



**Figure S2: Western blot analysis of microglial cells.**

**Related to Figure 6.**

Western blotting results using anti-Shc protein antibody, (A) with total protein extracted from microglial HAPI (highly aggressively proliferating immortalized) cells, and (B) with total protein extracted from brain microglia of C57B/6 mice.