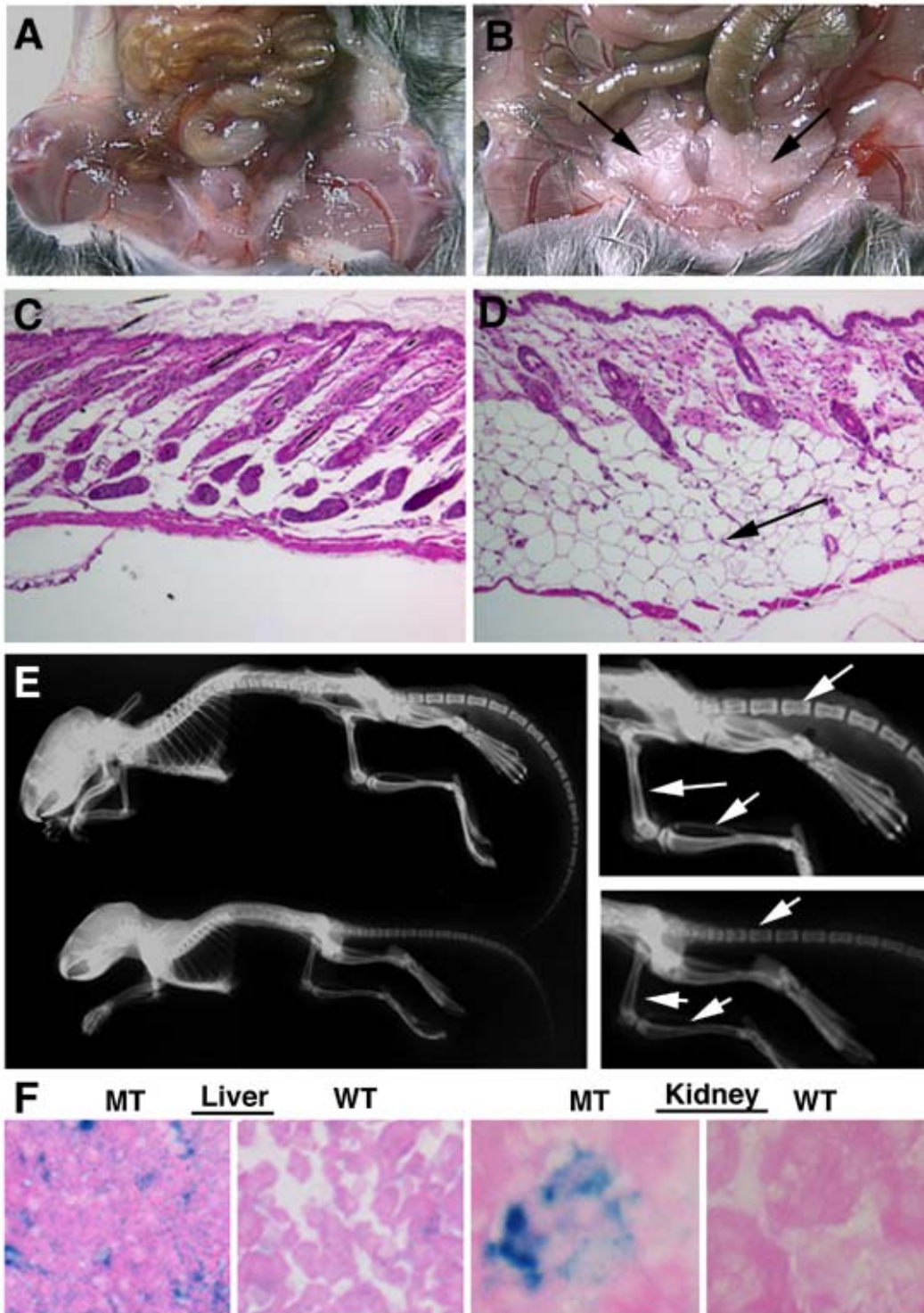


**SIRT6 DEFICIENCY RESULTS IN SEVERE HYPOGLYCEMIA BY ENHANCING
BOTH BASAL AND INSULIN-STIMULATED GLUCOSE UPTAKE IN MICE**

**Cuiying Xiao^{1,4}, Hyun-Seok Kim^{1,3,4}, Tyler Lahusen^{1,4}, Rui-Hong Wang¹, Xiaoling Xu¹,
Oksana Gavrilova², William Jou², David Gius³, and Chu-Xia Deng¹**

Supplemental Figures



Supplemental FIGURE. 1. Phenotypic analysis of *Sirt6* ^{$\Delta 2-3/\Delta 2-3$} mice. *A-B*. Visceral fat (arrows in *B*) was missing in the SIRT6 mutant mouse (*A*) at P25. *C-D*. H&E skin sections of SIRT6 mutant (*C*) and wild-type control (*D*) mice at P20. Arrow in (*D*) points to subcutaneous fat. *E*.

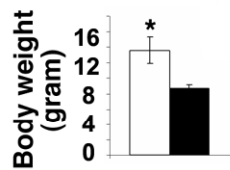
X-ray image of SIRT6 wild-type (upper) and mutant (lower) mice at P28. SIRT6 mutant mice have reduced bone density compared with control mice (arrows). *F*. SIRT6 mutant mice exhibit increased staining for acidic β -galactosidase revealed by senescence-associated β -gal staining in the liver and kidney at P15.

A

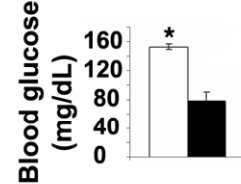
	Sirt6 ^{+/+} ; p53 ^{-/-} (1/16)	Sirt6 ^{+/+} ; p53 ^{+/-} (1/8)	Sirt6 Δ/Δ ; p53 ^{+/-} (1/8)	Sirt6 Δ/Δ ; p53 ^{-/-} (1/16)	Sirt6 Δ/Δ ; p53 ^{+/+} (1/16)	Sirt6 $\Delta/+$; p53 ^{-/-} (1/8)	Sirt6 $\Delta/+$; p53 ^{+/-} (1/4)	Sirt6 $\Delta/+$; p53 ^{+/+} (1/8)	Sirt6 ^{+/+} ; p53 ^{+/+} (1/16)	Total number of mice
No. of mice	3	19	18*	13*	10*	18	42	15	13	164

* These mice were morphologically similar irrespective of their p53 status

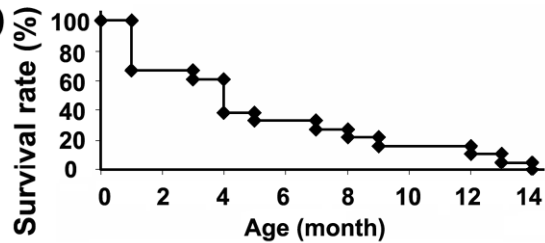
B



C

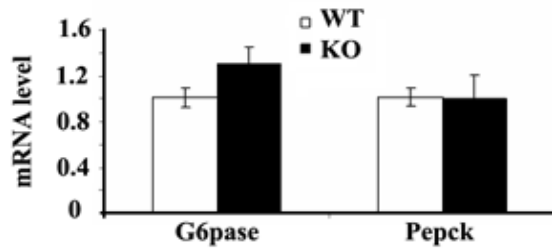


D



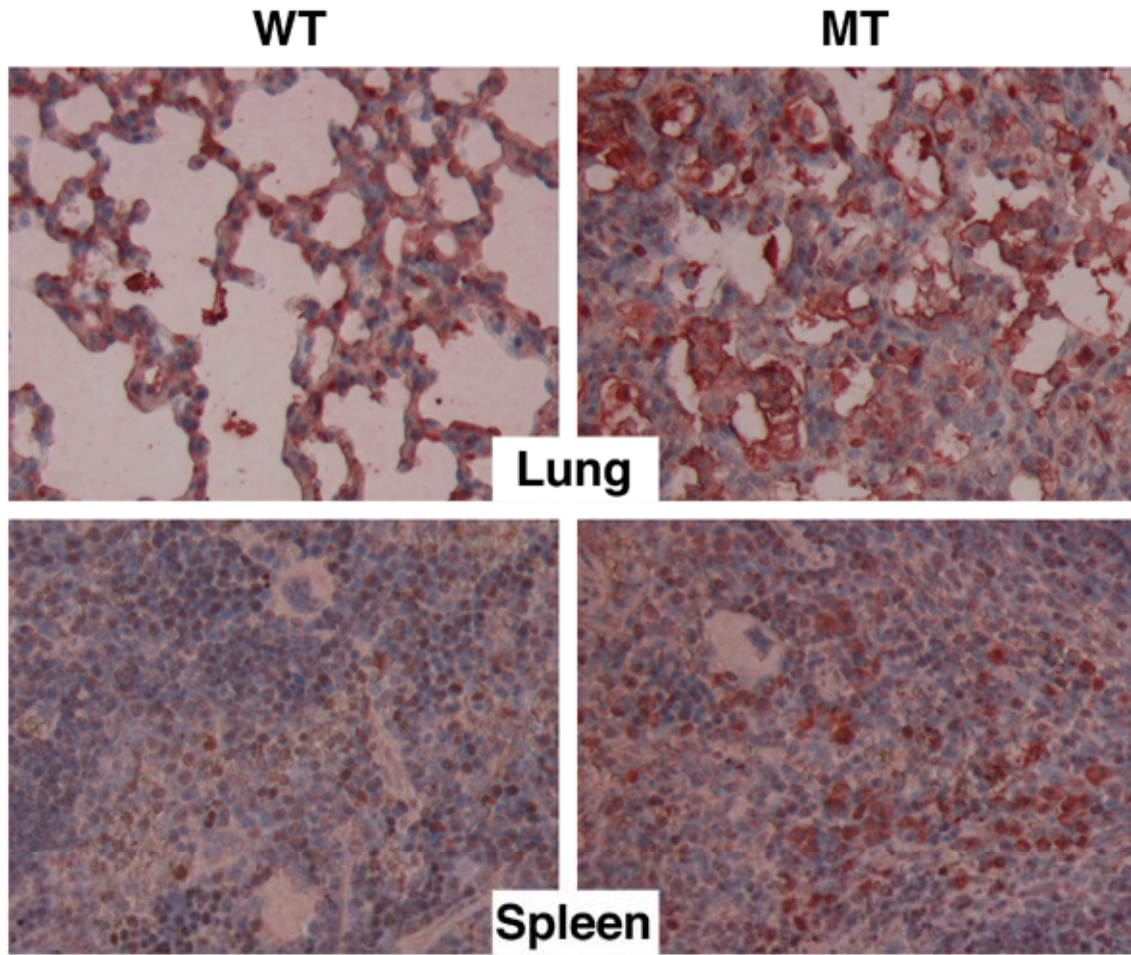
Supplemental FIGURE 2. Phenotype of *Sirt6* ^{$\Delta 2-3/\Delta 2-3$} mice in p53 mutant background. A.

Offspring of interbred between *Sirt6* ^{$\Delta 2-3/+$} ;*p53* ^{$+/-$} mice. *B-D*. Body weight (B) and blood glucose level (C), and viability (D) of *Sirt6* ^{$\Delta 2-3/\Delta 2-3$} ;*p53* ^{$+/-$} and *Sirt6* ^{$\Delta 2-3/\Delta 2-3$} ;*p53* ^{$-/-$} mice. Open bars in B and C are WT animals, black bars in B and C are mutants.

A**B**

	Food consumed (g/g BW/day)		
	P28-29	P32-39	P40-46
WT	0.22	0.19	0.20
MT	0.20	0.18	0.20

Supplemental FIGURE 3. Gluconeogenic gene expression and food intake of Sirt6 mutant and control mice. *A*. G6pase and Pepck mRNA levels in the liver. *B*. Food intake of Sirt6 mutant and WT control mice after normalized with their body weight. No difference was observed. At least 4 pairs of animals at each time point were used.



Supplemental FIGURE 4. Immunohistochemical staining of GLUT1 in lung and spleen of SIRT6 wild-type and mutant mice. Organs and genotypes were as indicated.