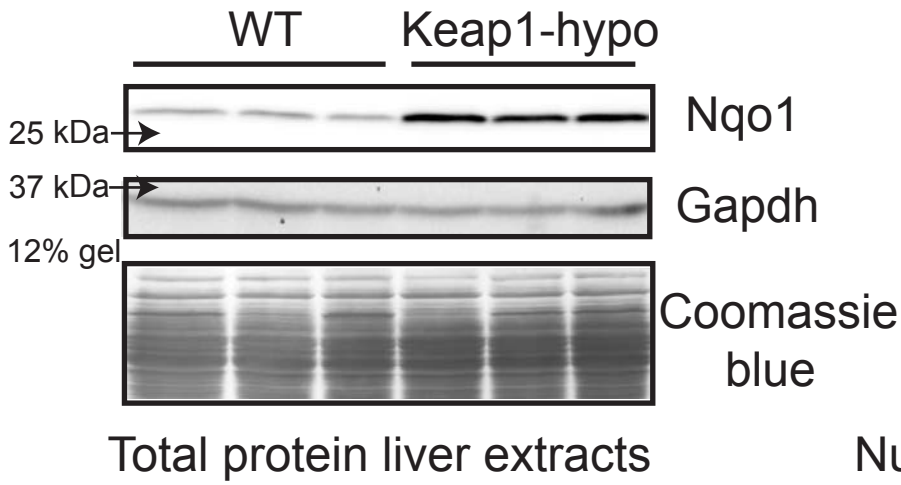
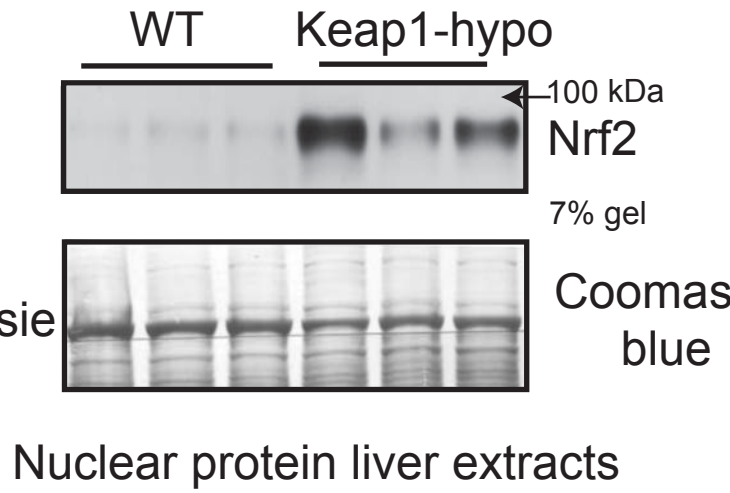


Supplementary Figure 1

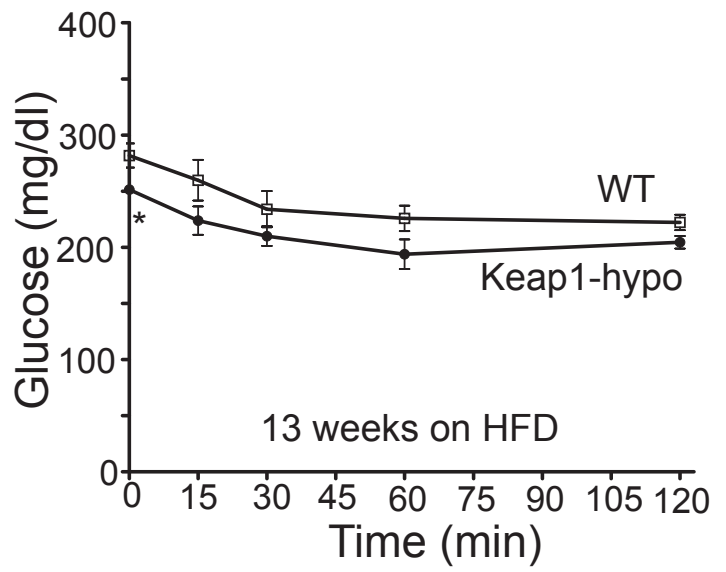
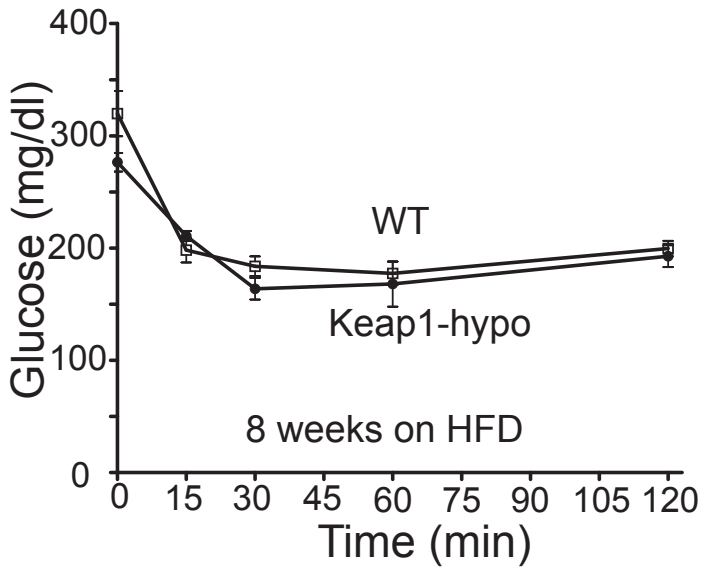
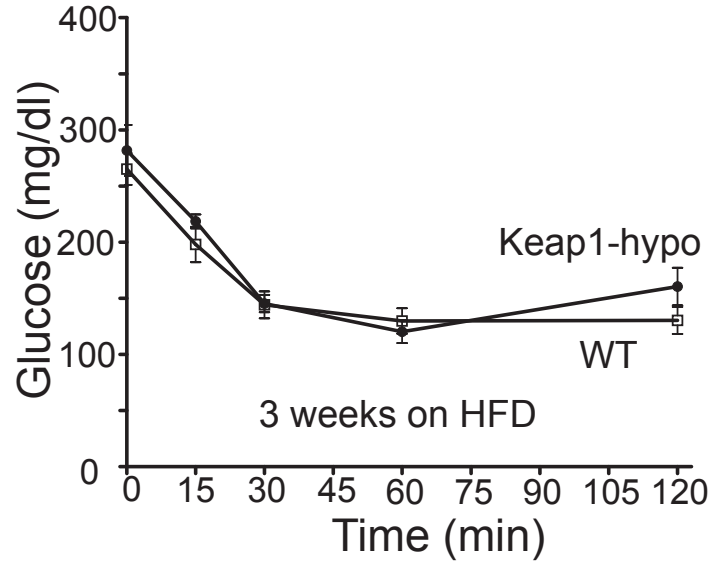
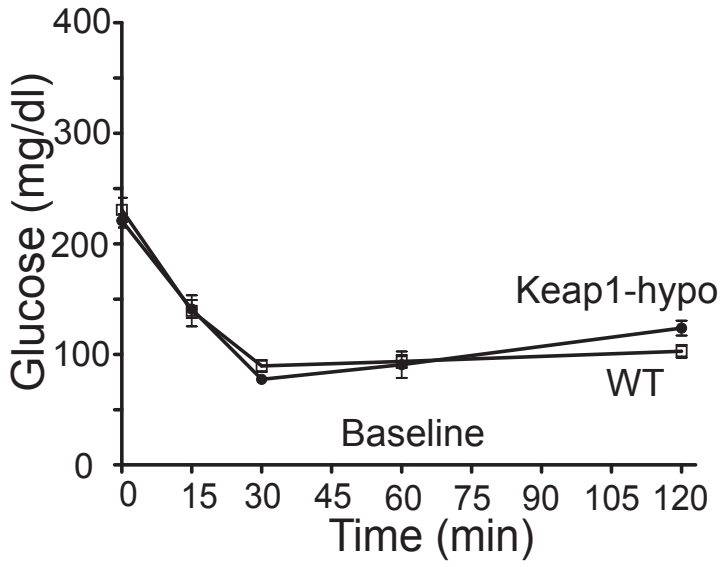
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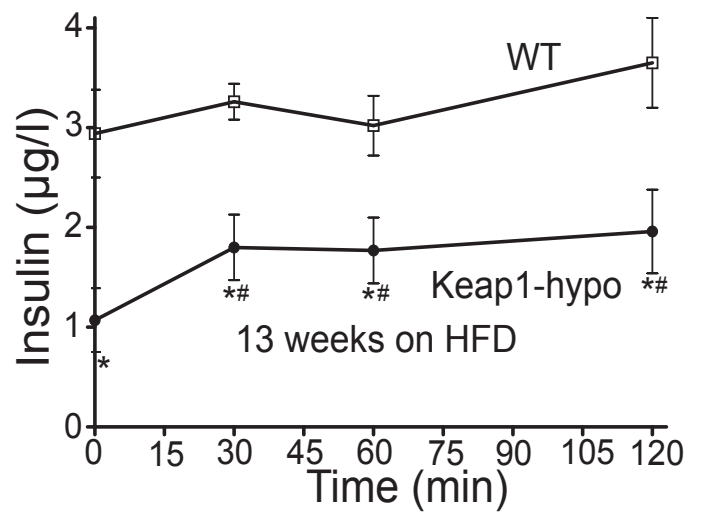
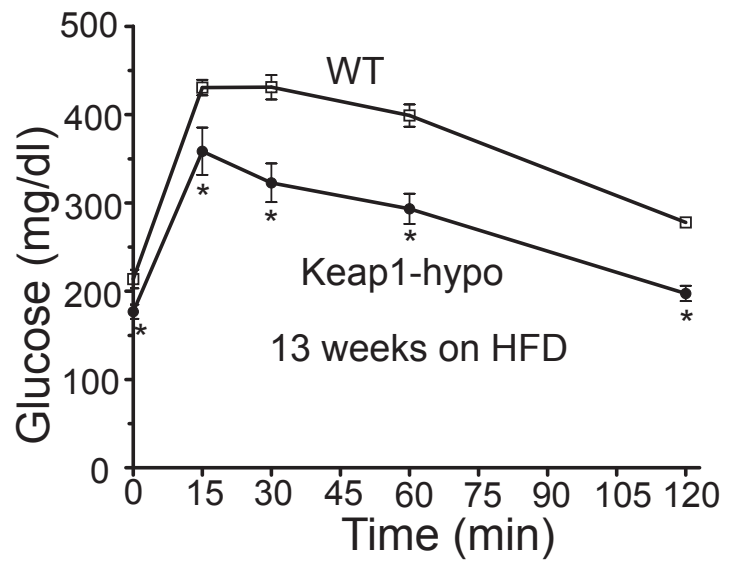
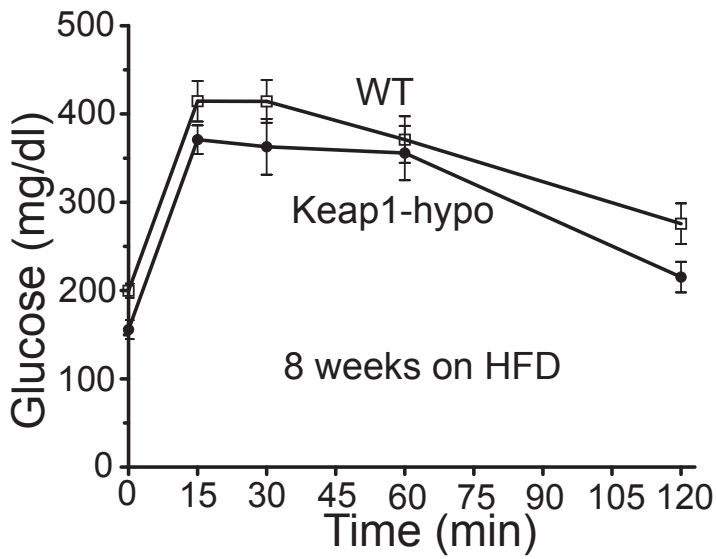
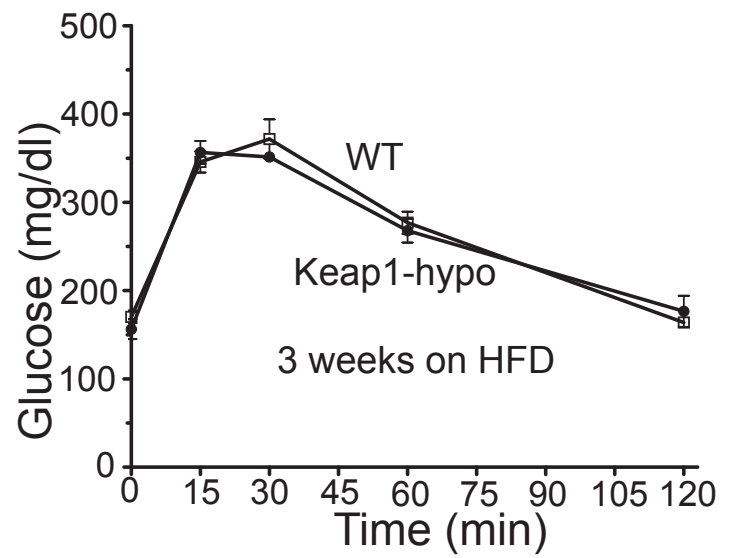
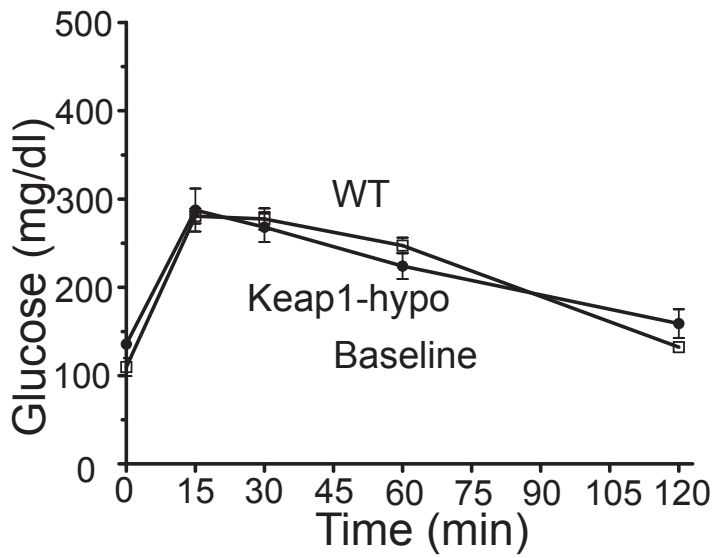
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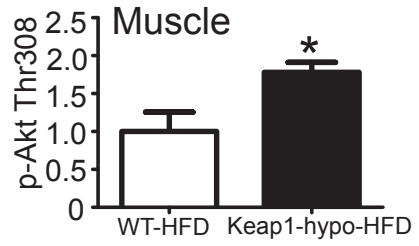
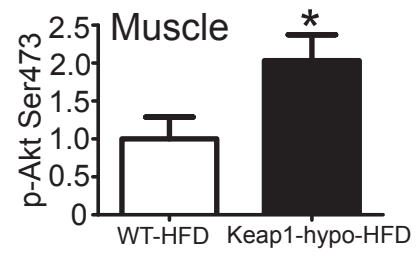
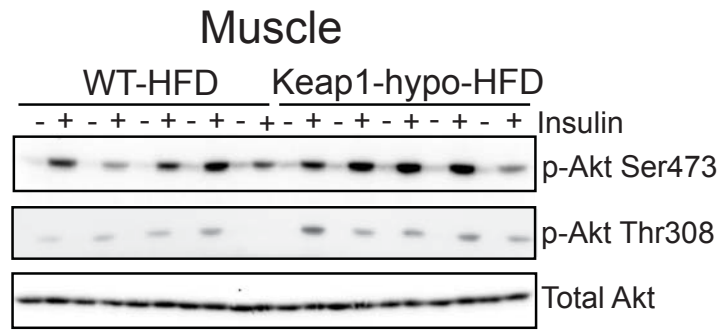
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4



Supplementary Figure 1.

Nqo1 and Nrf2 expression in livers of Keap1-hypo mice by immunoblotting.

A. Nqo1 expression in total liver extracts of 3 WT and 3 Keap1-hypo 2-month old male mice on standard diet. Gapdh expression and coomassie blue staining are shown for loading control purposes.

B. Nrf2 expression in nuclear liver extracts of 3 WT and 3 Keap1-hypo 2-month old male mice on standard diet. Coomassie blue staining is shown for loading control purposes. Note: this membrane was cut to increase exposure to the anti-Nrf2 antibody.

Supplementary Figure 2. Insulin action in Keap1-hypo mice. Intraperitoneal insulin tolerance test (IPITT) was performed at baseline and after 3, 8 and 13 weeks on HFD. n = 5 per genotype. *P<0.05 compared to WT-HFD

Supplementary Figure 3. Keap1-hypo mice are more glucose tolerant than WT mice after 13 weeks on HFD and preserve their glucose-stimulated insulin secretion. Results from intraperitoneal glucose tolerance tests (IPGTT) are shown. Tests were performed at baseline and after 3, 8 and 13 weeks on HFD. During the IPGTT at the 13 weeks, serum insulin concentration was also evaluated. n = 5 per genotype. *P<0.05 compared to WT-HFD; #P<0.05 compared to insulin value at time = 0 of the same genotype. Note that the panel of glucose tolerance of 13 weeks is the same as in Figure 2A in the main text. It is copied here so as to be combined with the insulin levels during this test.

Supplementary Figure 4. In vivo muscle insulin signaling and indirect calorimetry in Keap1-hypo mice. Mice that have been on high-fat diet for 90 days were fasted for 16h overnight and then injected intraperitoneally with 10 units/kg insulin. Muscle biopsies were obtained before and five minutes after the insulin injection. Immunoblots show phosphorylation of Akt at Ser473, Thr308 and total Akt in the livers of WT and Keap1-hypo mice before (-) and after (+) intraperitoneal insulin administration. The diagrams show relative protein amount of p-Akt Ser473 and p-Akt Thr308 after normalization to total Akt levels. n = 5 per genotype. *P<0.05 compared to WT-HFD.