Supplemental Figure Legends

- Fig. 1. Recombinant SH2B1 and R555E are specifically expressed in neurons in SH2B1 and R555E transgenic mice. (A) Tissue extracts were prepared from a SH2B1 transgenic male (2 month), immunoprecipitated with α SH2B1 and immunoblotted with α Myc. WAT: white adipose tissue; BAT: brown adipose tissue. (B) Tissue extracts were prepared from a KO/R555E male, immunoprecipitated with α SH2B1, and immunoblotted with α SH2B1.
- **Fig. 2.** Neuron-specific expression of the SH2 domain alone does not alter body weight or glucose metabolism in WT mice. (A) Growth curves for WT and ΔN503 male littermates. (B) Whole body fat content in WT and ΔN503 male mice (15-17 weeks of age). (C) Fasting (16 h) blood glucose in WT and ΔN503 male mice (17-18 weeks of age). (D) Glucose tolerance tests (GTT) performed on WT and ΔN503 male mice (18-19 weeks of age; 2 g/kg body weight). (E) Insulin tolerance tests (ITT) in male mice (18-19 weeks of age; 1 U/kg body weight). The number in parenthesis indicates the number of mice per group.

SH2B1 Transgenic Mice Muscle Brain _iver WAT BAT IP: αSH2B1 nonspecific IB: αMyc SH2B1 B KO/R555E Mice Muscle Brain WAT BAT IP: αSH2B1 **SH2B1** IB: αSH2B1 **IgG**

