

BODY WEIGHT


Supplemental Figure 1. Blood glucose and body weight. Time course changes in blood glucose and body weight during treatment beginning at 18 weeks and continuing until 24 weeks of age. Body weight and blood glucose levels are elevated in 24 weeks BTBR ob/ob control mice and remain elevated in all treatment groups except BTBR ob/ob mice with leptin replacement. Leptin replacement decreased body weight and blood glucose levels beginning the first week after starting treatment. *** $\mathrm{p}<0.001$ vs BTBR ob/ob control, BTBR ob/ob hydralazine, BTBR ob/ob losartan and BTBR ob/ob enalapril, +++ $p<0.001$ vs. BTBR ob/ob hydralazine, BTBR ob/ob losartan and BTBR ob/ob enalapril, \# p<0.05 vs. BTBR ob/ob control.

## Serum insulin



Supplemental Figure 2. Serum insulin levels are significantly elevated in BTBR ob/ob mice at 18 and 24 weeks compared to WT mice. Leptin replacement reduced serum insulin levels to levels seen in BTBR WT mice. ${ }^{* * *} \mathrm{p}<0.001$ vs 24 week BTBR WT, +++ $p<0.001$ vs 18 and 24 week BTBR ob/ob.

Serial Section 1



Serial Section 2


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Supplemental Figure 3


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Supplemental Figure 4

BTBR WT 20 week


BTBR ob/ob 20 week


BTBR ob/ob saline 28 week


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Supplemental Figure 5.


Supplemental Figure 6
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