In vivo, ERb activation protects against obesity and white adipose tissue (WAT) dysfunction. Mechanisms are unknown, but we hypothesize that it involves adipocyte-specific mitochondrial activity via induction of OXPHOS and UCP1– proteins that characterize WAT "browning," a process sufficient to rescue metabolic dysfunction. In cancer cells, increasing mitochondrial ERb increases OXPHOS transcription and mitochondrial activity via a mechanism requiring mitochondrial transporter, GRP75. We sought to determine whether this mechanism applies to adipocytes in vitro, and the potential in vivo implications. In wild type (WT) mice, the adipocyte-specific B3AR ligand, CL316,243 (CL) induced WAT UCP1 and ERb protein (Western blot), and GRP75 mRNA (qPCR) (all n=10/grp, $P<0.05$). In primary adipocytes from WT mice (n=3/treatment), CL increased UCP1 (~2-fold; $P<0.05$) and ERb protein (~4-fold; trend, $P=0.097$). In vivo, we show that adipocytes harvested from mutant mice missing ERb DNA binding domain (ERbDBDKO) display suppressed mitochondrial O2 consumption (via Oroboros; n=6-8/grp, $P<0.05$). We next tested whether ERbDBDKO mice would have impaired exercise-induced WAT browning. Remarkably, unlike WT (~3-fold UCP1 increase; $P<0.05$), ERbDBDKO mice were nonresponsive to exercise induction of UCP1 protein in WAT. Taken together, our data support a critical role for adipocyte ERb in mediating lipolysis driven mitochondrial responses. We hypothesize that the mechanism involves GRP75. Identifying the mechanism by which ERb enhances adipocyte mitochondrial activity has enormous potential to treat a spectrum of metabolic diseases