SUPPLEMENTARY DATA

Supplementary Figure S1. Schematic summary of the pathways involved in TRIB3 mediated-insulin resistance. In summary, the current study, in combination with our previous studies, demonstrated that: **1)** Multiple stress conditions such as nutrient (glucose/lipids) overload and hyperglycemia can lead to increased TRIB3 expression; **2)** Overactivity of TRIB3 mediates the development of insulin resistance in nutrition overload and glucose toxicity; **3)** Induction of TRIB3 by high glucose requires the Hexosamine biosynthetic pathway known to mediate glucose toxicity, which is part of the mechanisms of TRIB3-mediated glucose toxicity in diabetes; **4)** In addition to directly blocking AKT phosphorylation, additional mechanisms via which TRIB3 exacerbates insulin resistance under nutrient excess/hyperglycemia conditions involves increased ROS production, impaired anti-oxidation pathway, elevated inflammation, decreased adiponectin action and increased oxidative stress which can further cause mitochondrial dysfunction or directly interfere with insulin signaling pathway.