Transaldolase Inhibition Impairs Mitochondrial Response and Induces a Starvation-like Longevity Response in Caenorhabditis Elegans.

Mitochondrial dysfunction can increase oxidative stress and extend lifespan in *Caenorhabditis elegans*. Homeostatic mechanism exists to cope with disruptions to mitochondrial function that promote cellular health and organismal longevity. Previously, we determined that decreased expression of the cytosolic pentose phosphate pathway (PPP) enzyme transaldolase activates the mitochondrial unfolded protein response (UPR^{mt}) and extends lifespan. Here we report that transaldolase (*tald-1*) deficiency impairs mitochondrial function in vivo, as evidenced by altered mitochondrial morphology, decreased respiration, and increased cellular H_2O_2 levels. Lifespan extension from knockdown of *tald-1* is associated with an oxidative stress response involving p38 and c-Jun N-terminal kinase (JNK) MAPKs and a starvation-like response regulated by the transaction factor EB (TFEB) homolog HLH-30. The latter response promotes autophagy and increases expression of the flavin-containing monooxygenase 2 (*fmo-2*). We conclude that cytosolic redox established through the PPP is a key regulator of mitochondrial function and defines a new mechanism for mitochondrial regulation of longevity.