with a T-cell-specific Tfam deficiency (Tfam<sup>Lck<sup>−/−</sup> mice) and these animals also showed premature age-associated multi-morbidity. Why then does loss of mitochondrial function in T cells have this effect? Transcriptomics showed upregulation of senescence-associated markers (including p21) in various tissues of Tfam<sup>Lck<sup>−/−</sup> and Tfam<sup>Cd4<sup>−/−</sup> mice. Incubation of hepatocytes or pre-adipocytes with serum from Tfam<sup>Lck<sup>−/−</sup> mice or with TNF was sufficient to induce p21 expression, suggesting that the increased expression of pro-inflammatory cytokines in T cells with defective mitochondria may drive senescence and morbidity.

In support of this idea, TNF blockade prevented systemic senescence and multi-morbidity in Tfam<sup>Cd4<sup>−/−</sup> mice. Boosting levels of the metabolic cofactor NAD<sup>+</sup> (which is known to decline during ageing) also had a protective effect in Tfam<sup>Cd4<sup>−/−</sup> mice. The authors propose that these new mouse models could help to identify other beneficial therapeutics for patients with age-associated inflammatory diseases.

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