Faulty engines in T cells accelerate ageing and disease

A new report in Science has found that mice with T cell-specific mitochondrial defects show premature ageing and multi-system morbidity. The authors link this to an aberrant T helper 1 (T<sub>H</sub>1)-type response, which accelerates immunaging.

Previous studies have detailed age-related declines in mitochondrial function. To examine the impact of a T cell-specific loss of mitochondrial function, Desdin-Miço et al. generated T<sub>imtfam<sup>−/−</sup></sub>Cd4<sup>−/−</sup> mice. In these mice, both CD4<sup>+</sup> T cells and CD8<sup>+</sup> T cells lack mitochondrial transcription factor A (TFAM), which is important for the stabilization and replication of mitochondrial DNA. Tfm<sup>−/−</sup>Cd4<sup>−/−</sup> mice showed metabolic dys-function resembling that normally seen in aged (22-month-old) wild-type mice, and this was associated with increased expression of T-bet, IFNγ and tumour necrosis factor (TNF). Young T<sub>imtfam<sup>−/−</sup></sub>Cd4<sup>−/−</sup> mice were also immunocompromised; both old wild-type mice and young T<sub>imtfam<sup>−/−</sup></sub>Cd4<sup>−/−</sup> mice universally succumbed to acute infection with a highly virulent poxvirus, whereas young wild-type mice all survived this infection.

From the age of 7 months, T<sub>imtfam<sup>−/−</sup></sub>Cd4<sup>−/−</sup> mice had a prematurely aged appearance and progressively developed anaemia and curving of the spine and lost body weight. Metabolic cage experiments showed that T<sub>imtfam<sup>−/−</sup></sub>Cd4<sup>−/−</sup> mice were less active and slower than age-matched wild-type mice, despite expending more energy. The T<sub>imtfam<sup>−/−</sup></sub>Cd4<sup>−/−</sup> mice also showed premature loss of muscular, cardiovascular and cognitive function and, on average, only lived for half as long as controls. Importantly, the authors generated a distinct mouse.