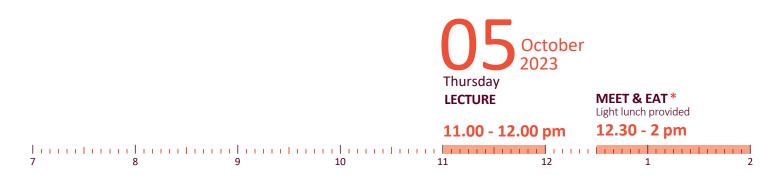
LECTURE SERIES 2023





Regulatory proteins of mitophagy restrict cell death for mounting memory CD8+ T cell formation

ABSTRACT

Mitophagy, a central process guarding mitochondrial guality, is commonly impaired in human diseases such as Parkinson's disease, but its impact in adaptive immunity remains unclear. The differentiation and survival of memory CD8+ T cells relies on oxidative metabolism, a process that requires robust mitochondrial quality control. Here, we found that Parkinson's disease patients have a reduced frequency of CD8+ memory T cells compared to healthy donors and failed to form memory T cells upon vaccination against COVID-19, highlighting the importance of mitochondrial quality control for memory CD8+ T cell formation. We further uncovered that regulators of mitophagy, including Parkin and NIX, were upregulated in response to interleukin-15 (IL-15) for supporting memory T cell formation. Mechanistically, Parkin suppressed VDAC1-dependent apoptosis in memory T cells. In contrast, NIX expression in T cells counteracted ferroptosis by preventing metabolic dysfunction resulted from impaired mitophagy. Together, our results indicate that the mitophagy machinery orchestrates survival and metabolic dynamics required for memory T cell formation, as well as highlight a deficit in T cell-mediated antiviral responses in Parkinson's disease patients.



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