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MITOCHONDRIAL SIRTUIN 3 (SIRT3) IN AGEING: EXPLORING CELLULAR RESPONSES TO ETOPOSIDE-INDUCED DNA DAMAGE IN MALE AND FEMALE MOUSE EMBRYONIC FIBROBLASTS

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Ageing is a complex process characterised by the gradual deterioration of physiological functions and increased susceptibility to various age-related diseases. Mitochondrial dysfunction is an important factor contributing to ageing. Sirtuin 3 (Sirt3), a mitochondrial protein essential for energy homeostasis, plays a critical role in maintaining mitochondrial function, as loss of Sirt3 reduces energy and impairs cellular repair, which accelerates ageing. The aim of this study was to investigate the role of Sirt3 in male and female mouse embryonic fibroblasts (MEF) exposed to etoposide-induced DNA damage. We employed state-of-the-art genetic, molecular, and imaging technologies as well as metabolomic analyses to provide insights into the molecular mechanisms underlying these responses. We found that the loss of Sirt3 affected metabolic responses differently depending on sex: while male MEF showed minimal damage, possibly due to earlier stress adaptation, female MEF lacking Sirt3 were more vulnerable, suggesting that Sirt3 plays a critical role in enhancing their ability to withstand such challenges. By focusing on Sirt3 and sex-specific signalling pathways it modulates, this study has a potential for developing new strategies to combat diseases associated with DNA damage – a cornerstone of the ageing process.