T-cell-restricted intracellular antigen-1 directs cellular senescence by regulating mitochondrial dynamics

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Mitochondrial homeostasis is critical for various cellular processes and mitochondrial dysfunction is involved in the pathophysiology of cells. Senescent cells exhibit a diverse spectrum of changes in their morphology, proliferative capacity, senescence-associated secretory phenotype (SASP) production, and mitochondrial homeostasis. These cells often manifest with elongated mitochondria, a hallmark of cellular senescence. However, the precise regulatory mechanisms orchestrating this phenomenon remain predominantly unexplored. In this study, we provide compelling evidence for decreases in the expression of T-cell-restricted intracellular antigen-1 (TIA-1), a pivotal regulator of mitochondrial dynamics, in models of both replicative senescence and ionizing radiation (IR)-induced senescence. The downregulation of TIA-1 was determined to trigger mitochondrial elongation and enhance the expression of senescence-associated β-galactosidase, a marker of cellular senescence, in human fibroblasts and keratinocytes. Conversely, the overexpression of TIA-1 mitigated IR-induced cellular senescence. Taken together, our findings underscore the significance of TIA-1 in governing mitochondrial dynamics and cellular senescence.