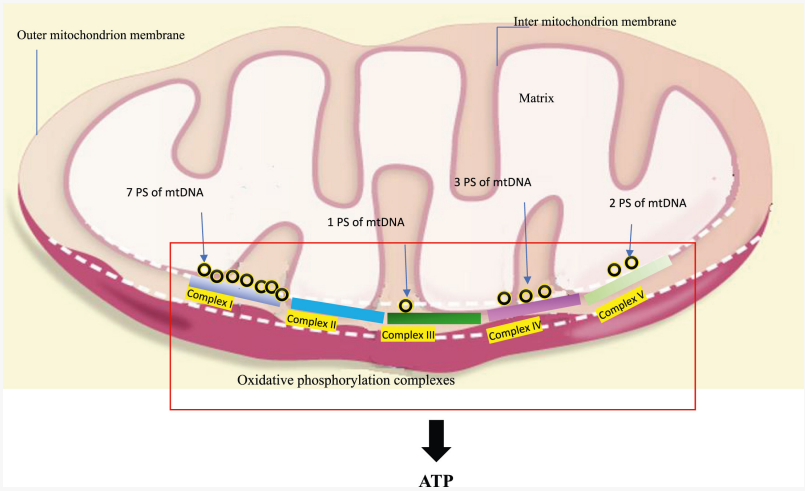
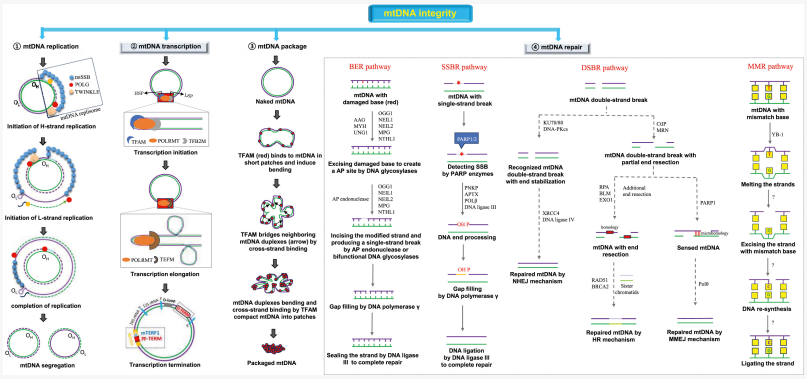
Unraveling the Role of Mitochondrial DNA Integrity in Cardiomyocyte Injury

SHANNON, CLARE, IRELAND, March 4, 2025 /EINPresswire.com/ -- Maintaining mitochondrial DNA (mtDNA) integrity is crucial for cardiomyocyte function, and its disruption plays a significant role in ischemia/reperfusion (I/R) injury. This review sheds light on the impact of mtDNA damage on cardiac health and highlights potential therapeutic strategies.



Summary of the effect of mammalian mtDNA on contributing 13 polypeptide subunits (PS) to five oxidative phosphorylation complexes (I–V) that make up the OXPHOS. The inner mitochondrial membrane containing five complexes is where ATP production takes place



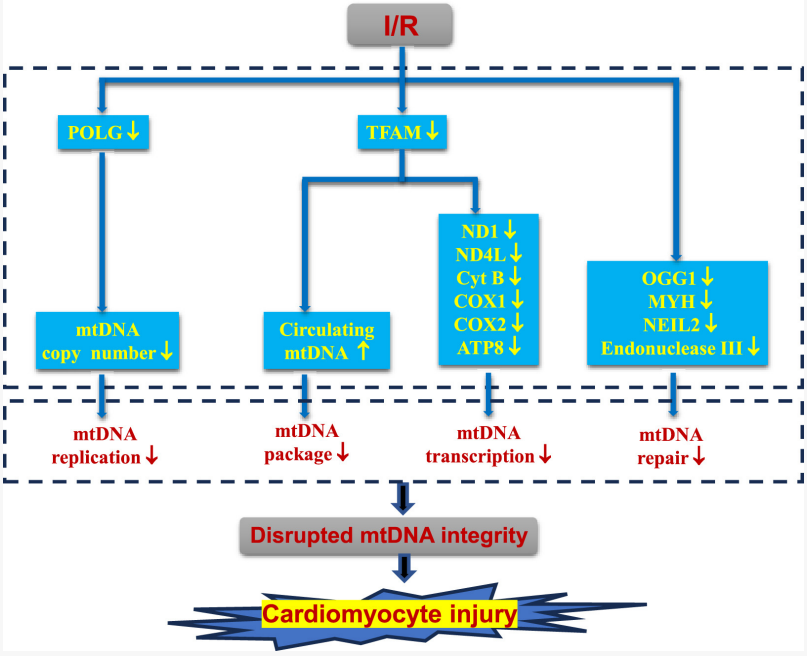
Overview of mtDNA integrity maintenance involving mtDNA replication, transcription, package, and repair.

Mitochondria, the powerhouses of the cell, rely on intact mtDNA to produce energy. Any impairment in mtDNA replication, transcription, packaging, or repair can trigger mitochondrial dysfunction, ultimately leading to cardiomyocyte injury. Emerging evidence underscores how I/R disrupts mtDNA integrity, contributing to oxidative stress, inflammation, and cell death.

Following an ischemic event, reperfusion therapy, while essential for restoring blood flow, paradoxically induces further damage by generating reactive oxygen species (ROS). These oxidative molecules attack mtDNA, causing strand breaks, mutations, and transcriptional suppression. As a result, the affected mitochondria fail to generate sufficient adenosine triphosphate (ATP), leading to cardiomyocyte dysfunction and myocardial infarction.

Studies have identified that key proteins such as transcription factor A, mitochondrial (TFAM) and

DNA polymerase gamma (POLG), both critical for mtDNA maintenance, are downregulated in I/R injury. Additionally, mtDNA fragments released into circulation further exacerbate inflammatory responses, amplifying cardiac damage.



Summary of the molecular mechanisms by which I/R disrupts mtDNA integrity, thereby inducing cardiomyocyte injury.

Restoring mtDNA integrity presents a promising avenue for cardioprotective strategies. Potential interventions include antioxidants, autophagy modulators, and epigenetic regulators, all of which help stabilize mtDNA and enhance mitochondrial biogenesis. Molecules such as 5-azacytidine, MitoQ, and fisetin have demonstrated efficacy in reducing oxidative damage, restoring mtDNA copy number, and improving cardiac function post-I/R. Additionally, novel therapeutic approaches like targeting DNA repair enzymes and preventing mtDNA release offer further avenues for mitigating myocardial injury. Emerging research supports the integration of mtDNA-targeted therapies into clinical practice to enhance outcomes for patients at risk of cardiac complications.

Understanding the intricate relationship between mtDNA integrity and cardiomyocyte survival opens new possibilities for therapeutic advancements. With growing recognition of mitochondrial dysfunction in I/R injury, interventions aimed at preserving mtDNA stability hold immense potential in revolutionizing cardiovascular treatment and recovery.

Funding Information:
National Natural Science Foundation of China 81970246
National Natural Science Foundation of China 81470437

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regenerative medicine.
Scopus CiteScore: 7.3
Impact Factor: 6.9

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Shengnan Hu, Xueying Tang, Fangrui Zhu, Chen Liang, Sa Wang, Hongjie Wang, Peifeng Li, Yuzhen Li, Disruption of mitochondrial DNA integrity in cardiomyocyte injury upon ischemia/reperfusion, Genes & Diseases, Volume 12, Issue 3, 2025, 101282, https://doi.org/10.1016/j.gendis.2024.101282

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