

# Mitochondrial Transplantation from Induced Pluripotent Stem Cells Reverses Cellular Bioenergetic Failure in Sepsis-Induced Acute Kidney Injury

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## Abstract

Sepsis-associated acute kidney injury (SA-AKI) is characterized by mitochondrial dysfunction and ATP depletion. This proof-of-concept study demonstrates that transplantation of healthy, respiration-competent mitochondria isolated from induced pluripotent stem cell-derived renal tubular cells restores bioenergetic capacity in injured kidneys. Intra-renal arterial injection of autologous platelet-derived mitochondria coated with Pep-1 cell-penetrating peptide in a murine cecal ligation and puncture model preserved tubular integrity, reduced oxidative stress markers, and improved renal function biomarkers (creatinine clearance  $\uparrow$  65%). Metabolic flux analysis confirmed restoration of oxidative phosphorylation and spare respiratory capacity. Mitochondrial transplantation emerges as a novel cytoprotective modality for septic organ failure.

**Keywords:** mitochondrial transplantation, sepsis, acute kidney injury, bioenergetics, iPSC-derived mitochondria, Pep-1 peptide



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