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Glucosylated albumin ameliorates kidney injury through improvement of mitochondrial function

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Objectives: Mitochondrial damage and dysfunction are important mechanisms of kidney injury, suggesting the possibility of treating kidney disease through improvement of mitochondrial homeostasis and function. An albumin-based nanoplatform (glucosylated albumin, Glc-Alb) that controls the half-life in the body, minimizes hepatic and renal toxicity, and increases the delivery rate to the target has been secured. Using this, we evaluated the renal targeting ability and its efficacy, and explored the mechanism in the acute kidney injury model.

Methods: Glc-Alb (40 μg/kg) was intravenously injected 1 hour before bilateral ischemia-reperfusion injury (bIRI) in mice, and kidneys were excised 48 hours later. An oxidative stress model was established by treating human primary cultured proximal tubular epithelial cells with hydrogen peroxide (1 mM) and treated with Glc-Alb (1000 nM). In each experiment, albumin alone was used as a control group.

Results: When Glc-Alb was administered to the bIRI group, renal function was improved, the expression of NGAL, cytochrome C, and p21 decreased, and the expression of Sod-1 and E-cadherin increased. In the MTS assay, there was no cytotoxicity even after administration of high concentrations of Glc-Alb. In the oxidative stress model, apoptosis/necrosis was significantly decreased in the Glc-Alb-administered group compared to the albumin-administered group, and the damaged mitochondrial morphology was remarkably recovered. In addition, intracellular expression of Glc-Alb was confirmed to prove its distribution and targeting ability in the kidney. Glc-Alb intake was validated by positron emission tomography, and the Glc-Alb administration group showed higher renal intake than the albumin alone group, proving that the target ability increases according to disease.

Conclusions: Glc-Alb was involved in improvement of renal function and histological findings, reduction of apoptosis/necrosis, restoration of mitochondrial morphology and improvement of function through high intake and distribution in the kidney in animal and cell models of acute kidney injury.

Figure 1.

Figure 1. Glucose-albumin administration improves renal function and restores renal damage and mitochondrial function.

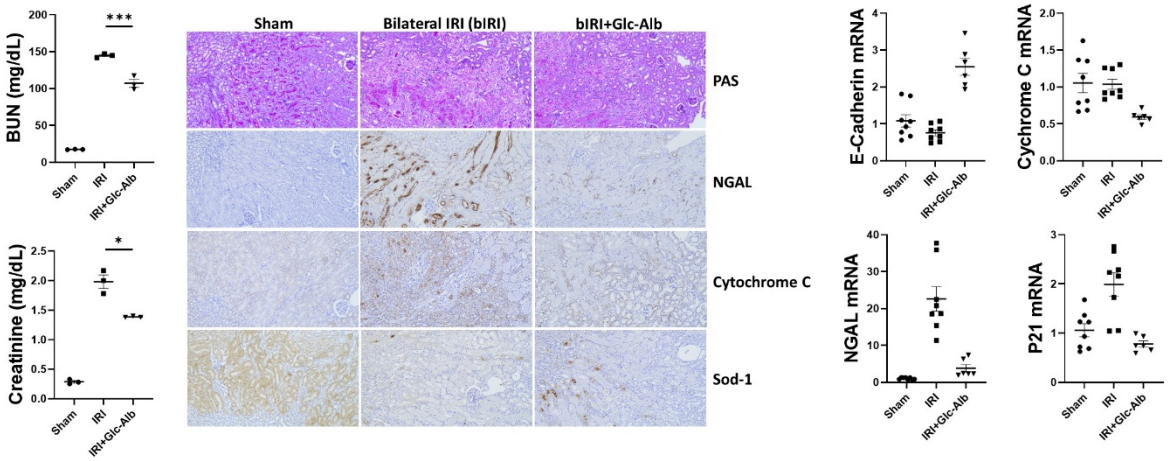

Figure 2.

Figure 2. Improvement of apoptosis/necrosis and restoration of mitochondrial morphology by glucose-albumin administration in an oxidative stress model