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Glucosylated albumin mitigates LPS-induced kidney injury by rescuing cells from G1/S cell cycle arrest

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Objectives : Acute kidney injury (AKI) arises from multiple pathological mechanisms, including inflammation, cell cycle arrest, and oxidative stress, all of which contribute to the progression of chronic kidney disease. We engineered a glucosylated albumin (Glc-alb) nanoplatform that regulates its half-life in the body while minimizing renal toxicity. In this study, we assessed the therapeutic efficacy of Glc-alb and its underlying mechanisms in an LPS-induced AKI model.
Methods : C57BL/6 mice were intravenously injected with Glc-alb (200μg/mouse) 1 hour before LPS administration, and kidneys were harvested after 24 hours. For in vitro validation, HK-2 and THP-1 cells were each treated with Glc-alb (30, 300nM) 1 hour before LPS stimulation for 24 hours, using albumin alone as the vehicle control.
Results : Glc-alb significantly improved renal function by lowering both BUN and creatinine levels in mice injected with LPS versus albumin alone. These therapeutic effects were further supported by Glc-alb reversing LPS-induced increases in NGAL, ICAM-1, pp65, and pSTAT3 expression, while restoring the G1/S cell cycle marker pCDK4 in the kidney. Glc-alb also reduced the frequency of circulating $CD11b^{+}F4/80^{+}$macrophages and $CD11b^{+}Gr\text{-}1^{+}$neutrophils induced by LPS in the spleen and downregulated pro-inflammatory markers in THP-1 cells. In HK-2 cells, Glc-alb suppressed LPS-induced reactive oxygen species (ROS) production and enhanced mitochondrial activity and wound healing ability even under hypoxic conditions. These findings suggest that Glc-alb exerts potent renoprotective effects, possibly by regulating ROS production and STAT3-mediated inflammation that impair the cell cycle.
Conclusions : Glc-alb exhibits potent therapeutic potential by reducing inflammation, preventing G1/S cell cycle arrest, and alleviating oxidative stress, ultimately protecting against LPS-induced kidney injury.