

## BASIC RESEARCH

**Kidney-specific antioxidant targeting for renal ischemic injury**

Antioxidant therapy has the potential to protect against renal ischemia–reperfusion injury; however the inability to selectively target the kidney necessitates the administration of excessively high doses of antioxidants, thereby increasing the risk of off-target and adverse effects. Researchers have now developed a way to target antioxidant therapy to the kidney and demonstrated the ability of this approach to reduce renal superoxide levels and protect kidney function in a mouse model of renal ischemia–reperfusion injury. “The model used induces a fairly

significant injury to the kidney and the results demonstrate considerable protection of renal function”, notes researcher W. Robert Taylor.

In order to specifically target an antioxidant to the kidney, the researchers coupled the membrane-permeable superoxide dismutase mimetic 4-hydroxy-Tempo (tempol) to folate. They hypothesized that the tempol–folate conjugate would target folate receptors, which are highly expressed in the renal proximal tubule. “The decision to use folate as a targeting strategy was driven by the relatively unique and localized uptake of folate in the proximal tubule of the kidney that results in concentration of the tempol–folate conjugate in the anatomic location of the kidney that is very susceptible to damage from oxidative stress during ischemia–reperfusion injury”, explains Taylor. “Our biodistribution studies confirmed that this was indeed the case.”

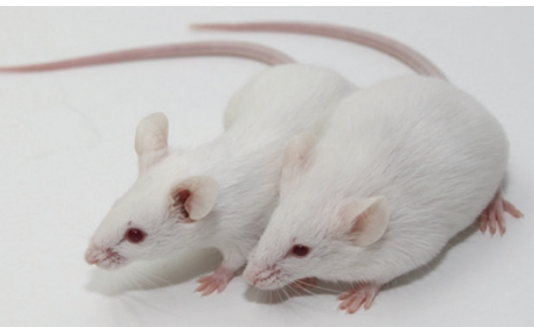
To investigate the ability of conjugated tempol–folate to prevent oxidative

damage, the researchers used a mouse model of renal ischemia–reperfusion injury. They found that tempol–folate reduced superoxide levels to a greater extent than tempol alone, and also reduced renal cell apoptosis. They also demonstrated that tempol–folate significantly reduced macrophage infiltration in the postischemic kidney and prevented increases in levels of blood urea nitrogen and plasma creatinine, indicative of preserved renal function.

The researchers hope to progress this research with a goal of moving towards clinical studies. They also say that using folate as a targeting strategy for the kidney has considerable potential and are considering exploiting this overall strategy for other therapeutics.

*Susan J. Allison*

**Original article** Knight, S. F. *et al.* Folate receptor–targeted antioxidant therapy ameliorates renal ischemia–reperfusion injury. *J. Am. Soc. Nephrol.* doi:10.1681/ASN.2011070711



© Dreamstime