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Muscles Protect the Kidneys

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Skeletal muscles protect our internal organs, such as the kidneys, from physical injury. But protecting renal function in chronic kidney disease (CKD) is an unanticipated role of muscles. Hanatani *et al.* describe the cross-talk between skeletal muscles and kidneys in mice, concluding that muscles regulate inflammation and fibrosis within kidneys to protect renal function.

Although previous studies showed renoprotective effect of muscle exercise, it remained unclear whether this protection was a function of muscles or of improvement in cardiovascular parameters. Exercise increases skeletal muscle Akt1, a kinase responsible for its growth; thus, the authors first generated a skeletal muscle–specific inducible Akt1 transgenic animal to emulate the effect of muscle exercise. Interestingly, the Akt1 transgenic animals exhibited reduced renal tubular atrophy, tubulointerstitial fibrosis, and apoptosis of epithelial cells and inflammatory cells within obstructed kidney (a model of CKD) despite normal cardiovascular parameters, suggesting that renoprotection was due to the muscles, not the cardiovascular system. In the obstructed kidneys of Akt1 transgenic animals, the authors also noted inhibition of transforming growth factor–β (TGF-β), a potent proinflammatory pathway. Furthermore, an increase in renoprotective cytokines in serum, such as interleukins 2 and 10, and a reduction in renal-damaging cytokines, such as tumor necrosis factor–α (TNF-α) and adiponectin, was noted in Akt1 animals. Inhibiting endothelial nitric oxide synthetase (eNOS) abolished the renoprotective effect of Akt1 in obstructed kidneys, strongly suggesting eNOS as a mediator of renoprotection.

Hanatani and colleagues demonstrated that skeletal muscles impart renal protection through several mechanisms, including altering the secreted cytokines in serum, collectively called “secretome,” increasing eNOS, and inhibiting TGF-β. Although several questions remain, including the role of skeletal muscle Akt1 in humans and the mechanisms of Akt1 in regulating secretome or eNOS, this study suggests that maintaining muscle mass through exercise could retard renal deterioration.

S. Hanatani *et al.*, Akt1-mediated fast/glycolytic skeletal muscle growth attenuates renal damage in experimental kidney disease. *J. Am. Soc. Nephrol.* **25**, 2800–2811 (2014). **[Abstract]**