中文題目：尿酸引朵乙酸抑制內皮前軀幹細胞生長，且可以用司坦汀改善

英文題目：In acute kidney injury, indoxyl sulfate impairs human endothelial progenitor cells – modulation by statin

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Background: Renal ischemia rapidly mobilizes endothelial progenitor cells (EPCs), which provides renoprotection in acute kidney injury (AKI). Indoxyl sulfate (IS) is a protein-binding uremic toxin with a potential role in endothelial injury.

Materials and Reuslts: In this study, we examined the effects and mechanisms of action of IS on EPCs in AKI. In forty-one consecutive patients (26 male; age, 70.1 ± 14.1 years) diagnosed with AKI according to the AKIN criteria were enrolled. The AKI patients had higher serum IS levels than patients with normal kidney function ($1.35\pm 0.94 \times 10^{-4}$M vs $0.02\pm 0.02 \times 10^{-4}$M, $p<0.01$). IS levels were negatively correlated to the number of double-labeled ($CD34^{+}KDR^{+}$) circulating EPCs ($p<0.001$). After IS stimulation, the cells decreased expression of p-eNOS, VCAM-1, increased reactive oxygen species, decreased proliferative capacity, increased senescence and autophagy, defects in migration, as well as decreased angiogenesis. In vitro, some of the effects of IS on EPCs were blunted by atorvastatin. Further, increased serum IS level significantly reduced EPC number and nitric oxide signaling in mouse arterial endothelium and injury kidney after ischemia-reperfusion injury, and this effect was reversed by statins.

Results : Our results are the first to demonstrate that the IS level is elevated in AKI and has direct effects on EPCs. Reduction of IS levels and/or targeting the pathways it activates by NO-releasing statins may preempt disordered vascular wall pathology and represent a novel EPC-assisted approach to the management of impaired neovascularization after AKI.

Key Words; indoxyl sulfate † statin † eNOs † endothelial progenitor cells† autophagy