



**EFFECT OF INDOXYL SULFATE ON ATORVASTATIN MEDIATED PRODUCTION  
OF ENDOTHELIAL NITRIC OXIDE SYNTHASE**

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Globally, it is estimated that about 5 million people have end stage renal disease (ESRD) [1]. Patients with ESRD require either a kidney transplant or dialysis. The median wait time for a kidney transplant is 4 years in the US [2]. Therefore, many patients need dialysis for renal replacement therapy. Hemodialysis requires functional vascular access to send blood to the dialysis machine from the patient and return blood to the patient from the dialysis machine [2]. It has been proposed that increasing vasodilation will help keep vessels open and usable for hemodialysis. The endothelial nitric oxide synthase (eNOS) produces nitric oxide, a vasodilator [3]. However, a uremic toxin called indoxyl sulfate (IS), which accumulates in ESRD patients, has been shown to decrease eNOS expression [4]. Atorvastatin (ATV), a common cardiovascular disease medication, has been shown to increase eNOS expression [5], but it is unknown how IS affects this vascular beneficial effect of ATV. An in vitro cell culture model with human umbilical vein endothelial cells (HUVECs) was used to investigate the combined effect ATV and IS on eNOS. Both Western blotting and immunofluorescence were used to quantify eNOS expression. This study found that IS inhibited the ability of ATV to increase eNOS expression. Thus, because of IS, ATV may not be able to increase nitric oxide mediated vessel dilation in ESRD patients as effectively as in patients with normal kidney function. Future research could consider if higher doses of ATV in the presence of IS could lead to the same effect on eNOS as lower doses without IS. Overall, this study demonstrates the importance of considering the effect of the accumulation of uremic toxins in ESRD patients on potential treatments.

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*Nat Commun.* vol. 9, no. 292, pp. 1-13, 2018.