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### **Nicotine Exacerbates Tacrolimus-Induced Renal Injury**

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**Objectives:** The progression of chronic kidney disease is accelerated by cigarette smoking. However, the role for cigarette smoking on transplantation is limited. This study examined whether nicotine (NIC), a major toxic component of cigarette smoking, would exacerbates tacrolimus (TAC)-induced renal injury in vivo and in vitro.

**Methods:** Male Sprague-Dawley rats were given vehicle (olive oil, 1mL/kg), NIC, TAC, or a combination of NIC and TAC for 4 weeks. Basic parameters, histopathology, analysis of cytokine expression, oxidative stress, and programmed cell death were examined. In addition, human kidney tubular epithelial cells (HK-2) and mouse mesangial cells (SV40 MES13) treated with TAC and NIC were also studied

**Results:** Both of NIC and TAC treatment significantly impaired renal function and histopathology, and combined treatment of NIC and TAC aggravated these parameters compared with giving each drug alone. Increased oxidative stress, expression of pro-inflammatory and pro-fibrotic cytokines, and programmed cell death by either NIC or TAC were further escalated by the combination of the two. In HK-2 and SV40 MES13 cells, NIC accelerated TAC-induced overproduction of reactive oxygen species and apoptotic cell death.

**Conclusions:** Our observations suggest that NIC exacerbates the severity of chronic TAC nephropathy, implying that smoking cessation may be beneficial to transplant smokers taking TAC.