P21 Effect of nitric oxide on the *cyp1a1* gene expression

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In order to study the effect of nitric oxide on the regulation of mouse *cyp1a1* expression, 5′ flanking DNA of mouse cytochrome P450 *1a1* was cloned into pGL3 basic vector encoding luciferase gene. p*cyp1a1*-Luc was transfected into Hepa I cells and various chemicals were treated. Luciferase activity was stimulated 1000 folds over that of control by TCDD (2,3,7,8-tetrachloro-*p*-dioxin) treatment and this stimulation was dose dependent. When SNP (sodium nitroprusside) which donates nitric oxide was administrated, this stimulatory effect of TCDD on luciferase activity was decreased. And LPS (lipopolysaccharide) which is an *i*NOS (inducible nitric oxide synthase) inducer also decreased the stimulatory effect of TCDD on luciferase. And *i*NOS inhibitor N^G-nitro-*l*-arginine + TCDD treatment increased the stimulation effect of TCDD and this effect was abolished when *l*-arginine was added to N^G-nitro-*l*-arginine + TCDD treatment. When N^G-nitro-*l*-arginine was concomitantly administrated with SNP or LPS to confirm the effect of nitric oxide, the inhibitory effect of SNP or LPS was abolished. These data strongly suggest that nitric oxide might be an inhibitory regulator on the cytochrome P450 *1a1* gene expression in Hepa cells.