hearts exhibited thick-walled and increased the heart to body weight ratio when compared with WT hearts, and the dilated left ventricle, thin wall and dysfunction of contraction were significantly ameliorated in the siRNA-CYP2E1×cTnT^{R141W} transgenic mice compared with the cTnT^{R141W} transgenic mice. Interstitial fibrosis, disarray of myofibrils and swollen mitochondria with loss of cristae were significantly improved in the myocardium of siRNA-CYP2E1×cTnT^{R141W} transgenic mice compared with the cTnT^{R141W} transgenic mice. The expression of caspase-3, caspase-9 and cytochrome c in the myocardium, and apoptosis were significantly decreased in the siRNA-CYP2E1×cTnT^{R141W} transgenic mice compared with the cTnT^{R141W} transgenic mice.

Conclusions Downregulation of CYP2E1 ameliorates DCM phenotype in the cTnT^{R141W} transgenic mice, and oxidative stress and apoptosis may be the mechanism of the regulation of CYP2E1 on DCM, which may have a positive therapeutic effect on the treatment of cardiomyopathy.

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DOWNREGULATION OF THE CYP2E1 AMELIORATES OXIDATIVE STRESS AND APOPTOSIS

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Objective Cytochrome P450 2E1 (CYP2E1) is an effective generator of reactive oxygen species, and it is known to be regulated in the course of progression of myocardial ischemia and cardiomyopathy. And this paper aims to analyse the regulation of CYP2E1 on the dilated cardiomyopathy (DCM) in the cTnT^{R141W} transgenic mice.

Methods The siRNA-CYP2E1 transgenic mice were created by the method of microinjection, and the siRNA-CYP2E1×cTnT^{R141W} transgenic mice were generated through mating of the siRNA-CYP2E1 with the α-MHC-cTnT^{R141W} transgenic mice. Pathological changes in the heart of transgenic mice were observed by echocardiographic, histologic, transmission electron microscope analyse. The levels of H_2O_2, malondialdehyde, glutathione and total antioxidant capability were measured. The expression of Col3α1, CYP2E1, caspase-3, caspase-9 and cytochrome c in the myocardium of transgenic mice were determined by Reverse transcription polymerase chain reaction (RT-PCR) or Western Blot. Apoptiotic cells were detected by the performed In situ terminal dUTP nick end-labeling (TUNEL) analyses.

Results The transgenic mice with cardiac-specific silence of CYP2E1 were established. To sum up, the siRNA-CYP2E1