

论著

昆明种小鼠细胞色素氧化酶CYP1A基因表达的昼夜节律变化

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摘要 目的 探究昆明种小鼠细胞色素氧化酶1A1 (CYP1A1)的昼夜节律、性别差异以及对肝毒物毒性变化的影响。方法 昆明小鼠在环境控制的SPF饲养室内适应性饲养2周后,于06:00, 10:00, 14:00, 18:00, 22:00和次日02:00处死取肝,用逆转录PCR方法检测24 h内核激素孤儿受体 α (*Rev-erba*), 时钟基因(*Per*)1, *Per*2和CYP1A1, CYP1A2及其调控核受体基因AhR的表达。另取小鼠于6:00和18:00 ip给予对乙酰氨基酚500 mg·kg⁻¹, 12 h后检测血清中丙氨酸转氨酶(ALT)和天冬氨酸转氨酶(AST)活性。结果 细胞色素氧化酶基因CYP1A1, CYP1A2及其调节基因AhR在18:00左右表达最高,且雌鼠的表达高于雄鼠,在6:00左右表达最低,表达峰谷差为4~7倍,其节律变化的差异与*Rev-erba*, *Per*1, *Per*2的节律差异大致相符。与此节律相对应,对乙酰氨基酚引起的肝毒性在18:00给药高于6:00给药。结论 昆明种小鼠细胞色素氧化酶CYP1A1基因表达存在昼夜节律及性别差异,该差异可影响肝毒物如对乙酰氨基酚的代谢和毒性。

关键词 [细胞色素P450 CYP1A1](#) [昼夜节律](#) [性别特性](#) [基因表达](#)

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Circadian rhythm variation of cytochrome CYP1A gene expression in liver of Kunming mice

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Abstract

OBJECTIVE To examine circadian rhythm and sex variation of cytochrome P-450 1A1(CYP1A1) and aryl hydrocarbon receptor (AhR) expression in the liver of Kunming (KM) mice. **METHODS** Adult KM mice were maintained in the SPF-grade animal facilities for 2 weeks, and livers were collected every 4 h during the 24 h period. Total RNA was isolated, purified, and subjected to reverse transcription (RT)-PCR analysis for expression of CYP1A1, AhR and clock genes.

Paracetamol 500 mg·kg⁻¹ was ip given another 20 mice at 6:00 and 18:00, and alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were determined. **RESULTS** The expressions of AhR and AhR-regulated CYP1A1 and CYP1A2 peaked about 18:00 pm and reached the nadir about 6:00 am. Sex-differences for AhR (6-fold for females and 7-fold for males), CYP1A1 (4-fold for females and 29-fold for males), and CYP1A2 (3-fold for females and 5-fold for males) were also evident. The circadian variation of CYP1A1 and AhR resembled the clock genes *Rev-erba*, *Per*1 and *Per*2.

Circadian rhythm of CYP1A1 expression influenced the hepatotoxicity of paracetamol, which is bioactivated by CYP1A1.

CONCLUSION Circadian rhythm and sex variation of CYP1A1 and AhR were evident in the liver of KM mice, which could impact the pharmacology and toxicology of drugs such as paracetamol.

Key words [cytochrome P-450 CYP1A1](#) [circadian rhythm](#) [gender identity](#) [gene expression](#)

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