## S39-5 Mechanism for circadian clock-controlled rhythm of drug metabolism and excretion

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Many biological processes in mammals are subject to daily oscillations, and some of these are controlled by self-sustained oscillation mechanism called circadian clock. This machinery operates at cellular levels and coordinates a wide variety of physiological processes and behavioral activities. Recent molecular dissection of the circadian biological clock system has revealed that oscillation in the transcription of specific clock genes plays a central role in the generation of circadian rhythms. Although mice deficient in the function of clock genes have shown to increase the toxicity of alkylating agents, the mechanism remains to be clarified. The circadian clock system regulates daily variations in output physiology through periodic activation/repression of clock-controlled output genes. Proline- and acid-rich (PAR) basic leucine zipper (bZIP) proteins, hepatic leukemia factor (HLF), thyrotroph embryonic factor (TEF), and D-site binding protein (DBP), are examples of such output mediators, because their expression is regulated by core oscillator components. The circadian-controlled output pathways include those that control the expression of many enzymes and regulators involved in xenobiotic detoxification, such as cytochrome P450 enzymes and efflux transporters. In this symposium, we would like to summarize our recent findings on the molecular mechanism regulating daily variations in drug metabolism and excretion, and to introduce the chronopharmacological strategy for xenobiotic detoxification.