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## Inhibitory Effect of PXR on Ammonia-induced Hepatocyte Autophagy via P53

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### Highlights

- PXR interferes with ammonia-induced hepatocyte autophagy.
- PXR inhibits ammonia-induced AMPK $\beta$ 1 accumulation and activation.
- P53 binds to the AMPK $\beta$ 1 promoter (–253 to –19) and transactivates its expression.
- Interaction of PXR and P53 affects AMPK $\beta$ 1 expression.

### Abstract

Pregnane X Receptor (PXR), a nuclear receptor transcription factor, participates in a wide range of physiological activities, but the regulation of ammonia-induced hepatocyte autophagy by PXR is not yet clear. In this study, the levels of down-regulated LC3B-II and up-regulated SQSTM1 were found in ammonia-induced PXR-overexpressing (PXR+) liver cells, but the opposite appeared in PXR-knockdown (PXR–) liver cells. Rifampicin, a PXR-activating agent, elicits a similar effect as PXR+ cells. The mechanism analysis reveals that the levels of the energy-sensitive molecule AMPK $\beta$ 1 and phosphorylated AMPK $\beta$ 1 (p-AMPK $\beta$ 1) in PXR– cells are higher than those in control cells, whereas the levels of this molecule in PXR+ cells are lower than those in control cells. Two active sites that bind to P53 exist in –253 to –19 at the promoter region of AMPK $\beta$ 1, and their mutation can reduce the transactivating effect of AMPK $\beta$ 1 that P53 relies on. A protein interaction also exists between PXR and P53. These findings indicate that PXR is a factor

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