

Optimizing combination of liver-enriched transcription factors and nuclear receptors simultaneously favors ammonia and drug metabolism in liver cells

Yongfa Su, Zhanfei Chen, Linlin Yan, Fen Lian, Jianhua You, Xiaoqian Wang, Nanhong Tang



PII: S0014-4827(17)30669-9
DOI: <https://doi.org/10.1016/j.yexcr.2017.12.015>
Reference: YEXCR10854

To appear in: *Experimental Cell Research*

Received date: 9 November 2017
Revised date: 12 December 2017
Accepted date: 14 December 2017

Cite this article as: Yongfa Su, Zhanfei Chen, Linlin Yan, Fen Lian, Jianhua You, Xiaoqian Wang and Nanhong Tang, Optimizing combination of liver-enriched transcription factors and nuclear receptors simultaneously favors ammonia and drug metabolism in liver cells, *Experimental Cell Research*, <https://doi.org/10.1016/j.yexcr.2017.12.015>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Optimizing combination of liver-enriched transcription factors and nuclear receptors simultaneously favors ammonia and drug metabolism in liver cells

Yongfa Su^a, Zhanfei Chen^a, Linlin Yan^a, Fen Lian^a, Jianhua You^a, Xiaoqian Wang^a, Nanhong Tang^{a,b,*}

^a*Fujian Institute of Hepatobiliary Surgery, Fujian Medical University Union Hospital, Fuzhou, China;*

^b*Key Laboratory of Ministry of Education for Gastrointestinal Cancer, Research Center for Molecular Medicine, Fujian Medical University, Fuzhou, China.*

*Corresponding author.

Email: fztnh@sina.com (N. Tang)

Abstract

The HepG2 cell line is widely used in studying liver diseases because of its immortalization, but its clinical application is limited by its low expression of the urea synthesis key enzymes and cytochromes P450 (CYPs). On the basis of our previous work, we investigated the transcriptional regulation of arginase 1 (Arg1) and ornithine transcarbamylase (OTC) in HepG2 cells. We also screened for the optimal combination of liver enrichment transcription factors (LETfs) and xenobiotic nuclear receptors that can promote the expression of key urea synthases and five major CYPs in HepG2 cells. Thus, recombinant HepG2 cells were established. Results showed that C/EBP β , not C/EBP α , could upregulate expression of Arg1 and PGC1 α and HNF4 α cooperatively regulate the expression of OTC. The two optimal combinations C/EBP β +HNF4 α +HNF6+PXR and C/EBP β +HNF4 α +HNF6+CAR were selected. Compared with the control cells, the recombinant HepG2 cells modified by the two optimal combinations exhibited enhanced ammonia metabolism and CYP enzyme activity. Moreover, the HepG2/(C/EBP β +HNF4 α +HNF6+PXR) cells more strongly reduced ammonia

Download English Version:

<https://daneshyari.com/en/article/8451750>

Download Persian Version:

<https://daneshyari.com/article/8451750>

[Daneshyari.com](https://daneshyari.com)