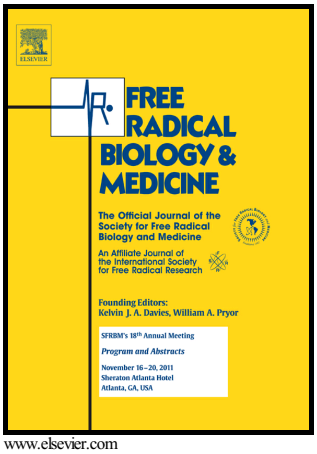

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ABSTRACT

Bile acid transporters and the nuclear factor erythroid 2-related factor (Nrf-2)-mediated adaptive response play important roles in the development of drug-induced liver injury (DILI). However, little is known about the contribution of the adaptive response to rifampicin (RFP)-induced cell injury. In this study, we found RFP decreased the survival rate of HepG2 cells and increased the levels of lactate dehydrogenase (LDH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (AKP), γ-glutamyl-transferase (γ-GT), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), total bile acid (TBA) and adenosine triphosphate (ATP) in the cell culture supernatants in both a concentration- and a time-dependent manner. RFP increased the expression levels of bile acid transporter proteins and mRNAs, such as bile salt export pump (BSEP), multidrug resistance protein 1 (MDR1), multidrug resistance-associated protein 2 (MRP2), Na^+/taurocholate cotransporter (NTCP), organic anion transporting protein 2 (OATP2), organic solute transporter β (OSTβ) and Nrf2. Following the transient knockdown of Nrf2 and treatment with RFP, the expression levels of the BSEP, MDR1, MRP2, NTCP, OATP2 and OSTβ proteins and