

ID	Description	RF		SVM		Known/ <i>plausible</i> in DILI?	Citation(s)
		GeneRatio	FDR	GeneRatio	FDR		
R-HSA-2142753	Arachidonic acid metabolism	5/32	0.025	6/57	0.039	Involvement in Acetaminophen and galactosamine/endotoxin induced liver injuries	Suciu, et al. (1); Xue-Jun, et al. (2)
R-HSA-8978868	Fatty acid metabolism	6/32	0.025	8/57	0.021	Involvement in Acetaminophen and divalproex sodium induced liver injuries	Suciu, et al. (1); Wang, et al. (3)
R-HSA-556833	Metabolism of lipids	12/32	0.025	-	-	Involvement in drug induced toxicity	Xu, et al. (4); Begriche, et al. (5)
R-HSA-6804756	Regulation of TP53 Activity through Phosphorylation	5/32	0.034	-	-	Involvement in Acetaminophen induced liver injuries	Huo, et al. (6)
R-HSA-2162123	Synthesis of Prostaglandins (PG) and Thromboxanes (TX)	3/32	0.034	-	-	Role in liver injuries	Nagai, et al. (7); Peltekian, et al. 1996(8)
R-HSA-8939243	RUNX1 interacts with co-factors whose precise effect on RUNX1 targets is not known	3/32	0.034	-	-	No involvement in DILI, but Increased expression in NASH patients	Kaur et al. (9)
R-HSA-1592230	Mitochondrial biogenesis	4/32	0.034	-	-	Central role in DILI	Pessayre, et al. (10); Ramachandran et al. (11); Mansouri, et al. (12)
R-HSA-5633007	Regulation of TP53 Activity	6/32	0.037	-	-	Involvement in Acetaminophen induced liver injuries	Huo, et al. (6)

R-HSA-211859	Biological oxidations	-	-	9/57	0.014	Oxidative reactions catalyzed by CYP enzymes potentially cause DILI	Corsini, et al. (13); (14)
R-HSA-211945	Phase I - Functionalization of compounds	-	-	8/57	0.014	Oxidative reactions catalyzed by CYP enzymes potentially cause DILI	Corsini, et al. (13); (14)

1. Suciu M, Gruia AT, Nica DV, Azghadi SM, Mic AA, Mic FA. Acetaminophen-induced liver injury: implications for temporal homeostasis of lipid metabolism and eicosanoid signaling pathway. *Chem Biol Interact.* 2015;242:335–44.
2. Xue-jun M, Jia-long W. Arachidonic acid metabolism in galactosamine/endotoxin induced acute liver injury in rats. *J Tongji Med Univ.* 1994;14(3):169–72.
3. Wang W, Lin R, Zhang J, Mao Y, Bu X, Ji Q, et al. Involvement of fatty acid metabolism in the hepatotoxicity induced by divalproex sodium. *Hum Exp Toxicol.* 2012;31(11):1092–101.
4. Xu S, Chen Y, Ma Y, Liu T, Zhao M, Wang Z, et al. Lipidomic Profiling Reveals Disruption of Lipid Metabolism in Valproic Acid-Induced Hepatotoxicity. *Front Pharmacol.* 2019 Jul 19;10:819.
5. Begriche K, Massart J, Robin M-A, Borgne-Sanchez A, Fromenty B. Drug-induced toxicity on mitochondria and lipid metabolism: Mechanistic diversity and deleterious consequences for the liver. *J Hepatol.* 2011 Apr;54(4):773–94.
6. Huo Y, Yin S, Yan M, Win S, Aung Than T, Aghajan M, et al. Protective role of p53 in acetaminophen hepatotoxicity. *Free Radic Biol Med.* 2017 May;106:111–7.
7. Nagai H, Shimazawa T, Yakuo I, Aoki M, Koda A, Kasahara M. The role of thromboxane A2 [TXA2] in liver injury in mice. *Prostaglandins.* 1989;38(4):439–46.
8. Peltekian KM, Makowka L, Williams R, Blendis LM, Levy GA, Prostaglandins in Liver Transplantation Research Group. Prostaglandins in liver failure and transplantation: Regeneration, immunomodulation, and cytoprotection. *Liver Transpl Surg.* 1996 May;2(3):171–84.
9. Kaur S, Rawal P, Siddiqui H, Rohilla S, Sharma S, Tripathi DM, et al. Increased Expression of RUNX1 in Liver Correlates with NASH Activity Score in Patients with Non-Alcoholic Steatohepatitis (NASH). *Cells.* 2019;8(10):1277.
10. Pessayre D, Fromenty B, Berson A, Robin M-A, Lettéron P, Moreau R, et al. Central role of mitochondria in drug-induced liver injury. *Drug Metab Rev.* 2012;44(1):34–87.
11. Ramachandran A, Duan L, Akakpo JY, Jaeschke H. Mitochondrial dysfunction as a mechanism of drug-induced hepatotoxicity: current understanding and future perspectives. *J Clin Transl Res.* 2018;4(1).
12. Mansouri A, Gattolliat C-H, Asselah T. Mitochondrial Dysfunction and Signaling in Chronic Liver Diseases. *Gastroenterology.* 2018 Sep;155(3):629–47.
13. Corsini A, Bortolini M. Drug-induced liver injury: The role of drug metabolism and transport. *J Clin Pharmacol.* 2013;53(5):463–74.

14. Ye H, Nelson LJ, del Moral MG, Martínez-Naves E, Cubero FJ. Dissecting the molecular pathophysiology of drug-induced liver injury. *World J Gastroenterol.* 2018;24(13):1373.