References

- ***Aithal PG, Day CP.*** 1999; The natural history of histologically proved drug induced liver disease. *Gut*. 44: 731-735.
- ***Alatalo , Heidi Koivisto, Katri Puukka .***2008. Effect of moderate alcohol consumption on liver enzymes increases with increasing body mass index. *Am. J. Clin. Nutr*. 88, 1097–1103.
- ***Anania FA, Rabin L***. 2002; Terbinafine hepatotoxicity resulting in chronic biliary ductopenia and portal fibrosis. *Am J Med*. 112: 741-742.
- ***Andersson U, Lindberg J, Wang S.,*** 2009 A systems biology approach to understanding elevated serum alanine transaminase levels in a clinical trial with ximelagatran. *Biomarkers* 14, 572–586.
- ***Andrade, RJ, MI Lucena, and MC Fernandez .,*** 2005, Drug-Induced Liver Injury: An Analysis of 461 Incidences Submitted to the Spanish Registry Over a 10-Year Period, *Gastroenterology*, 129(2):512-21.
- ***Antoine DJ, Williams DP, Park BK.,*** 2008 Understanding the role of reactive metabolites in drug-induced hepatotoxicity: state of the science. *Expert Opin Drug Metab Toxicol*;4(11): 1415–1427.
- ***Arteel GE.*** 2003; Oxidants and antioxidants in alcohol-induced liver disease. *Gastroenterology.* 124: 778-790.
- ***Bauduceau B. , Baigts F, Bordier L, Burnat P, Ceppa F, Dumenil V ;*** 2007. Should we have more definitions of metabolic syndrome or simply take waist measurement? *Diabetes Metab.* 33, 333–339.

- ***Beaune P, Dansette PM, Mansuy D;*** 1987 Human antiendoplasmic reticulum autoantibodies appearing in a druginduced hepatitis are directed against a human liver cytochrome P-450 that hydroxylates the drug. *Proc Natl Acad Sci U S A*;84(2):551–555.

- ***Beaune PH, Lecoeur S, Bourdi M;*** 1996 Anti-cytochrome P450 autoantibodies in drug-induced disease. *Eur J Haematol Suppl*;60:89–92.

- ***Beevers, D.G. & Stamler, J.***, 2003 Background to the INTERMAP study of nutrients and blood pressure. *J. Hum. Hypertens*. 17, 589–590.

- ***Bernini P, Bertini I, Luchinat C, Nepi S, Saccenti E, Schäfer H, Schütz B.,*** 2009 Individual human phenotypes in metabolic space and time. *J. Proteome Res*. 8, 4264–4271.

- ***Bienvenu L, Burel F, Hofman V, Itchai C, Amaro J, Hofman P.*** 2001; [A rare etiology of hepatic steatosis associated with lactic acidosis: the toxicity of antiviral nucleoside analogues] *Ann Pathol.* 21: 160-163.

- ***Björnsson, E and R Olsson,*** 2005, Outcome and Prognostic Markers in Severe Drug-Induced Liver Disease, *Hepatology,* 42(2):481-9.

- ***Blackstock WP, Weir MP***., 1999 Proteomics: quantitative and physical mapping of cellular proteins. *Trends Biotechnol*. 17 (3): 121–127.

- ***Blomme EA, Yang Y, Waring JF.***, 2009 Use of toxicogenomics to understand mechanisms of drug-induced hepatotoxicity during drug discovery and development. *Toxicol Lett;* 186(1):22–31.

- ***Bourdi M, Larrey D, Nataf J.***, 1990 Anti-liver endoplasmic reticulum autoantibodies are directed against human cytochrome P-450IA2. A specific marker of dihydralazine- induced hepatitis. *J Clin Invest*;85(6):1967–1973.

- ***Boyd MA, Srasuebkul P, Ruxrungtham K.,*** 2006 Relationship between hyperbilirubinaemia and UDP-glucuronosyltransferase 1A1 (UGT1A1) polymorphism in adult HIV-infected Thai patients treated with indinavir. *Pharmacogenet. Genomics* 16(5), 321–329.

- ***Brass EP.***1993; Hepatic toxicity of antirheumatic drugs. *Cleve Clin J Med* 60: 466-472.

- ***Bushel PR, Heinloth AN, Li J.***, 2007 Blood gene expression signatures predict exposure levels. *Proc Natl Acad Sci U S A* ;104(46):18211–18216.

- ***Castell JV.*** 1998; Allergic hepatitis: a drug-mediated organ-specific mmune reaction. *Clin Exp Allergy*. 28 Suppl 4: 13-19.

- ***Chan KA, Truman A, Gurwitz JH, Hurley JS, Martinson B, Platt R, Everhart JE, Moseley RH, Terrault N, Ackerson L, Selby JV. A*** 2003; cohort study of the incidence of serious acute liver injury in diabetic patients treated with hypoglycemic agents. *Arch Intern Med.* 163: 728-734.

- ***Chau.*** 2008; Drug Induced Liver Injury; an update *Medical Bulletin* .March 3 ;23-26 .

- ***Chen H, Paul WE.*** 1997; Cultured NK1.1+ CD4+ T cells produce large amounts of IL-4 and IFN-gamma upon activation by anti-CD3 or CD1. *J Immunol.* 159: 2240-2249.

- ***Chen Q, Cederbaum AI.*** 1998; Cytotoxicity and apoptosis produced by cytochrome P450 2E1 in Hep G2 cells. *Mol Pharmacol*. 53: 638-648.

- ***Chitturi S, George J***. 2002; Hepatotoxicity of commonly used drugs: nonsteroidal anti-inflammatory drugs, antihypertensives, antidiabetic agents, anticonvulsants, lipid-lowering agents, psychotropic drugs. *Semin Liver Dis.* 22: 169-183.

- ***Clark JM., Brancati FL, Diehl AM;*** 2003. The prevalence and etiology of elevated aminotransferase levels in the United States. *Am. J. Gastroenterol*. 98, 960–967.

- ***Clayton TA, Lindon JC, Cloarec O, Antti H, Charuel C, Hanton G .,*** 2006 Pharmaco-metabonomic phenotyping and personalized drug treatment. *Nature* 440, 1073–1077.

- ***Clayton, T.A., Baker, D., Lindon, J.C., Everett, J.R. & Nicholson, J.K.***, 2009 Pharmacometabonomic identification of a significant host-microbiome metabolic interaction affecting human drug metabolism. *Proc. Natl. Acad. Sci. U.S.A.* 106, 14728–14733.

- ***Cohen SD, Pumford NR, Khairallah EA;*** 1997 Selective protein covalent binding and target organ toxicity. *Toxicol Appl Pharmacol*;143(1):1–12.

- ***Connell TM O, Watkins PB.,*** 2010 The Application of Metabonomics to Predict Drug-Induced Liver Injury. *Clinical pharmacology & Therapeutics*;88(3):394-399.

- ***Critchley JA, Nimmo GR, Gregson CA, Woolhouse NM, Prescott LF.*** 1986; Inter-subject and ethnic differences in paracetamol metabolism. *Br J Clin Pharmacol.* 22: 649-657.

- ***Dai X, Fang X, Zhang C;*** 2007. Determination of serum uric acid using high-performance liquid chromatography (HPLC)/isotope dilution mass spectrometry (ID-MS) as a candidate reference method. *J. Chromatogr. B Analyt. Technol. Biomed. Life Sci.* 857, 287–295.

- ***Despres, J.P.,*** 2001. Health consequences of visceral obesity. *Ann. Med*. 33, 534–541

- ***De Valle MB, Av Klinteberg V, Alem N, Olsson R, Bjornsson E.*** 2006; Drug-induced liver injury in a Swedish University hospital out-patient hepatology clinic. *Aliment Pharmacol Ther*. 24: 1187-1195.

- ***Dixit V, Hariparsad N, Desai P, Unadkat JD***. 2007; In vitro LCMS cocktail assays to simultaneously determine human cytochrome P450 activities. *Biopharm Drug Dispos* 28: 257-262.

- ***Doherty DG, Norris S, Madrigal-Estebas L, McEntee G, Traynor O, Hegarty JE, O'Farrelly C***. 1999; The human liver contains multiple populations of NK cells, T cells, and CD3+CD56+ natural T cells with distinct cytotoxic activities and Th1, Th2, and Th0 cytokine secretion patterns. *J Immunol.* 163: 2314-2321**.**

- ***Dourakis SP, Sevastianos VA, Kaliopi P***. 2002; Acute severe steatohepatitis related to prednisolone therapy. *Am J Gastroenterol.* 97: 1074-1075.

- ***Eichelbaum M, Evert B***. 1996; Influence of pharmacogenetics on drug disposition and response. *Clin Exp Pharmacol Physiol*. 23: 983-985.

- ***Fannin RD, Russo M, O'Connell TM, Gerrish K, Winnike JH ,*** 2010; Acetaminophen dosing of humans results in blood transcriptome and metabolome changes consistent with impaired oxidativephosphorylation. *Hepatology* 51, 227–236.

- ***FDA***, Guidance for Industry: Drug-Induced Liver Injury: Premarketing Clinical Evaluation 2009.

- ***Ford E.S. Giles WH, Dietz WH;*** 2004. Increasing prevalence of the metabolic syndrome among U.S. Adults. *Diabetes Care* 27, 2444–2449.

- ***Friedman LS, Dienstag. JL, Watkins E;*** 1987. Evaluation of blood donors with elevated serum alanine aminotransferase levels. *Ann. Int. Med.* 107, 137–144.

- ***Fuhr U***. 2000; Induction of drug metabolising enzymes: pharmacokinetic and toxicological consequences in humans. *Clin Pharmacokinet.* 38: 493-504.

- ***Fujita K, Kamataki T.*** 2002; Genetically engineered bacterial cells co-expressing human cytochrome P450 with NADPHcytochrome P450 reductase: prediction of metabolism and toxicity of drugs in humans. *Drug Metab Pharmacokinet* . 17: 1-22.

- ***Garbino J, Henry JA, Mentha G, Romand JA.*** 2001; Ecstasy ingestion and fulminant hepatic failure: liver transplantation to be considered as a last therapeutic option. *Vet Hum Toxicol*. 43: 99-102.

- ***Garcia LA, Ruigomez A, Jick H.*** 1997; A review of epidemiologic research on drug-induced acute liver injury using the general practice research data base in the United Kingdom. *Pharmacotherapy* **.**17: 721-728.

- ***Geubel AP, De Galocsy C, Alves N, Rahier J, Dive C.*** 1991; Liver amage caused by therapeutic vitamin A administration: estimate of dose-related toxicity in 41 cases. *Gastroenterology*. 100: 1701-1709.

- ***Giovanni , Matteo Nicola Dario Di Minno, Domenico Capone.*** 2009; Drug-induced liver injury: Is it somehow foreseeable? *World J Gastroenterol* . June 21; 15(23): 2817-2833.

- ***Goldkind, L., Laine, L.,*** 2006. A systematic review of NSAIDs withdrawn from the market due to hepatotoxicity: lessons learned from the bromfenac experience.Pharmacoepidemiol. *Drug Saf.* 15, 213–220.

- ***Green RM, Flamm S.*** 2002. AGA technical review on the evaluation of liver chemistry tests. *Gastroenterology;* 123(4):1367–1384.

- ***Gunawan B, Kaplowitz N***. 2004. Clinical perspectives on xenobiotic-induced hepatotoxicity. *Drug Metab Rev*; 36: 301-312.

- ***Haouzi D, Lekehal M, Moreau A, Moulis C, Feldmann G, Robin MA, Letteron P, Fau D, Pessayre D.*** 2000; Cytochrome P450-generated reactive metabolites cause mitochondrial permeability transition, caspase activation, and apoptosis in rat hepatocytes. *Hepatology*. 32: 303-311**.**

- ***Hautekeete ML, Horsmans Y, Van Waeyenberge C.,*** 1999 HLA association of amoxicillin-clavulanate-induced hepatitis.*Gastroenterology* 117(5), 1181–1186.

- ***Hinson JA, Reid AB, McCullough SS, James LP***., 2004 Acetaminophen- induced hepatotoxicity: role of metabolic activation, reactive oxygen/nitrogen species, and mitochondrial permeability transition. *Drug Metab Rev*;36(3-4):805– 822.

- ***Holden A.,*** 2008 Detecting and Investigating Drug Induced Adverse Events . . . the International Serious Adverse Event Consortium's Experience to Date. Available at: http:// www.fda.gov/downloads/Drugs/ScienceResearch/Research Areas/ucm077482.pdf. Accessed July 10, 2009.

- ***Holmes E, Loo RL, Stamler J, Bictash M, Yap IK, Chan Q, Ebbels T, De Iorio M .,*** 2008 Human metabolic phenotype diversity and its association with diet and blood pressure. *Nature* 453, 396–400.

- ***Homberg JC, Andre C, Abuaf N.***, 1984 A new anti-liver-kidney microsome antibody (anti-LKM2) in tienilic acid-induced hepatitis. *Clin Exp Immunol*;55(3):561–570.

- ***Hoofnagle JH.***, 2004 Drug-induced liver injury network (DILIN). *Hepatology*;40(4):773.

- ***Hussaini SH, Farrington EA.*** 2007; Idiosyncratic drug-induced liver injury: an overview. *Expert Opin Drug Saf* . 6: 673-684.

- ***Ioannou GN, Boyko EJ, Lee SP.,*** 2006a. The prevalence and predictors of elevated serum aminotransferase activity in the United States in 1999–2002. *Am. J. Gastroenterol*. 101, 76–82.

- ***Ioannou GN, Weiss NS, Boyko EJ.,*** 2006b. Elevated serum alanine aminotransferase activity and calculated risk of coronary heart disease in the United States. *Hepatology* 43, 1145–1151.

- ***James***., 1997 Protein identification in the post-genome era: the rapid rise of proteomics. *Quarterly reviews of biophysics* 30 (4): 279–331.

- ***James LP, Letzig L, Simpson PM.***, 2009. Pharmacokinetics of acetaminophen-protein adducts in adults with acetaminophen overdose and acute liver failure. *Drug Metab Dispos* ;37(8):1779–1784.

- ***Jeong DH, Lee SJ, Lee JH, Bae IH, Jeong KS, Jang JJ, Lim IK, Kim MR, Lee MJ, Lee YS.*** 2001; Subcellular redistribution of protein kinase C isozymes is associated with rat liver cirrhotic changes induced by carbon tetrachloride or thioacetamide. *J Gastroenterol Hepatol.* 16: 34-40.

- ***Jia N, Liu X, Wen J, Qian L, Qian X, Wu Y, Fan G***. 2007; A proteomic method for analysis of CYP450s protein expression changes in carbon tetrachloride induced male rat liver microsomes. *Toxicology*. 237: 1-11.

- ***Jones JO, Diamond MI.*** 2007; Design and implementation of cellbased assays to model human disease. *ACS Chem Biol*. 2: 718-724.

- ***Josef S. Ozer, Chetty R, Kenna G.***,2010. Enhancing the utility of alanine aminotransferase as a reference standard biomarker for drug-induced liver injury *Regulatory Toxicology and Pharmacology* .56 , 237–246.

- ***Kang YH, Min HG, Kim IJ, Kim YK, Son SM.,*** 2008. Comparison of alanine aminotransferase, white blood cell count, and uric acid in their association with metabolic syndrome: a study of Korean adults. *Endocr. J*. 55, 1093–1102.

- ***Kariv R, Leshno M, Beth-Or A, Strul H, Blendis L,. Kokia E.,*** 2006. Re-evaluation of serum alanine aminotransferase upper normal limit and its modulating factors in a large-scale population study. *Liver Int*. 26, 445–450.

- ***Kaplowitz N.*** 2002; Biochemical and cellular mechanisms of toxic liver injury. *Semin Liver Dis.* 22: 137-144.

- ***Kazuto Tajiri,Yukihiro Shimizu;*** 2008 ; Practical guidelines for diagnosis and early management of drug-induced liver injury *; World J Gastroenterol*. 14(44): 6774–6785.

- ***Kechagias S, Ernersson A, Dahlqvist O.,*** 2008. Fast-food-based hyper-alimentation can induce rapid and profound elevation of serum alanine aminotransferase in healthy subjects. *Gut* . 57, 649–654.

- ***Klein, H.G.,*** 1990. Controversies in transfusion medicine. Alanine aminotransferase screening of blood donors: *pro. Transfusion* 30, 363–367.

- ***Klugewitz K, Blumenthal-Barby F, Schrage A, Knolle PA, Hamann A, Crispe IN.*** 2002; Immunomodulatory effects of the liver: deletion of activated CD4+ effector cells and suppression of IFN-gamma-producing cells after intravenous protein immunization. *J Immunol*. 169: 2407-2413**.**

- ***Kon K, Ikejima K, Okumura K, Aoyama T, Arai K, Takei Y, Lemasters JJ, Sato N***. 2007; Role of apoptosis in acetaminophen hepatotoxicity. *J Gastroenterol Hepatol.* 22 Suppl 1: S49-S52**.**

- ***Konstandi M, Marselos M, Radon-Camus AM, Johnson E, Lang MA.*** 1998; The role of stress in the regulation of drug metabolizing enzymes in mice. *Eur J Drug Metab Pharmacokinet*. 23: 483-490.

- ***Kundrotas, L.W., Clement, D.J.,*** 1993. Serum alanine aminotransferase (ALT) elevation in asymptomatic US Air Force basic trainee blood donors. *Dig. Dis. Sci*. 38, 2145–2150.

- ***Lammert C, Einarsson S, Saha C, Niklasson A, Bjornsson E, Chalasani N.*** 2008; Relationship between daily dose of oral medications and idiosyncratic drug-induced liver injury: search for signals. *Hepatology*. 47: 2003-2009.

- ***Larrey D.*** 2002; Epidemiology and individual susceptibility to adverse drug reactions affecting the liver. *Semin Liver Dis* . 22:145-155.

- ***Lee WM, Larrey D, Olsson R, Lewis JH, Keisu M, Auclert L, Sheth S.,*** 2005; Hepatic findings in long-term clinical trials of ximelagatran. *Drug Saf.* 28, 351–370.

- *Li H,* ***Ni Y, Su M.,*** 2007; Pharmacometabonomic phenotyping reveals different responses to xenobiotic intervention in rats. *J. Proteome Res*. 6, 1364–1370.

- ***Li J, Liu Y, Zhang JW, Wei H, Yang L.*** 2006; Characterization of hepatic drug-metabolizing activities of Bama miniature pigs (Sus scrofa domestica): comparison with human enzyme analogs. *Comp Med*. 56: 286-290.

- ***Li Z, Diehl AM***. Innate immunity in the liver. 2003; *Curr Opin Gastroenterol.* 19: 565-571.

- ***Limmer A, Ohl J, Kurts C, Ljunggren HG, Reiss Y, Groettrup M, Momburg F, Arnold B, Knolle PA***. 2000; Efficient presentation of exogenous antigen by liver endothelial cells to CD8+ T cells results in antigen-specific T-cell tolerance. *Nat Med.* 6: 1348-1354**.**

- ***Lindon, J.C., Keun, H.C., Ebbels, T.M., Pearce, J.M., Holmes, E. & Nicholson, J.K***., 2005; The Consortium for Metabonomic Toxicology (COMET): aims, activities and achievements. *Pharmacogenomics* 6, 691–699.

- ***Liu YT, Hao HP, Liu CX, Wang GJ, Xie HG***. 2007; Drugs as CYP3A probes, inducers, and inhibitors. *Drug Metab Rev*. 39: 699-721.

- **Marc R. Wilkins, Christian Pasquali, Ron D. Appel, Keli Ou, Olivier Golaz, Jean-Charles Sanchez, Jun X. Yan, Andrew. A. Gooley, Graham Hughes, Ian Humphery-Smith, Keith L. Williams & Denis F. Hochstrasser. 1996**; From Proteins to Proteomes: Large Scale Protein Identification by Two-Dimensional Electrophoresis and Arnino Acid Analysis. Nature Biotechnology 14 (1): 61–65.

- **Maria VA, Victorino RM., 1997;** Diagnostic value of specific T cell reactivity to drugs in 95 cases of drug induced liver injury. Gut;41(4):534–540.

- ***Marti L, Del Olmo JA, Tosca J, Ornia E, Garcia-Torres ML, Serra MA, Rodriguez F, Lluch P, Escudero A, Rodrigo JM.*** 2005; Clinical evaluation of drug-induced hepatitis. *Rev Esp Enferm Dig.* 97: 258-265.

- ***Masubuchi Y, Suda C, Horie T***. 2005; Involvement of mitochondrial permeability transition in acetaminophen-induced liver injury in mice. *J Hepatol* . 42: 110-116.

- ***Mehal WZ, Azzaroli F, Crispe IN.*** 2001; Immunology of the healthy liver: old questions and new insights. *Gastroenterology* 120: 250-260.

- ***Meier Y, Cavallaro M, Roos M, Pauli-Magnus C, Folkers G, Meier PJ, Fattinger K.*** 2005; Incidence of drug-induced liver injury in medical inpatients. *Eur J Clin Pharmacol* **.** 61: 135-143.

- ***Merk HF.***, 2005; Diagnosis of drug hypersensitivity: lymphocyte transformation test and cytokines. *Toxicology*;209(2): 217–220.

- ***Michael P. Holt and Cynthia Ju.*** 2006; Mechanisms of Drug-nduced Liver Injury, *The AAPS Journal.* 8; 48-54.

- ***Miyamoto M, Yanai M, Ookubo S, Awasaki N, Takami K, Imai R.***, 2008 ;Detection of cell-free, liver-specific mRNAs in peripheral blood from rats with hepatotoxicity: a potential toxicological biomarker for safety evaluation. *Toxicol Sci* ;106(2):538–545.

- ***Murray M.*** 2006; Altered CYP expression and function in response to dietary factors: potential roles in disease pathogenesis. *Curr Drug Metab.* **7**: 67-81.

- ***Mutlib A, Jiang P, Atherton J, Obert L, Kostrubsky S, Madore , Nelson S***. 2006; Identification of potential genomic biomarkers of hepatotoxicity caused by reactive metabolites of N-methylformamide: Application of stable isotope labeled compounds in toxicogenomic studies. *Chem Res Toxicol* .19: 1270-1283.

- ***Namias A, Bhalotra R, Donowitz M***. 1981; Reversible sulfasalazine- induced granulomatous hepatitis. *J Clin Gastroenterol* .3: 193-198.

- ***Nguyen C, Rose NR, Njoku DB.***, 2008; Trifluoroacetylated IgG4 antibodies in a child with idiosyncratic acute liver failure after first exposure to halothane. *J Pediatr Gastroenterol Nutr* ;47(2):199–202.

- ***Nicholson, J.K., Connelly, J., Lindon, J.C. & Holmes, E***., 2002 ;Metabonomics: a platform for studying drug toxicity and gene function. *Nat. Rev. Drug Discov*. 1, 153–161.

- ***Nolan CM, Goldberg SV, Buskin SE.***, 1999 ; Hepatotoxicity associated with isoniazid preventive therapy: a 7-year survey from a public health tuberculosis clinic. *JAMA*;281(11): 1014–1018.

- ***Nomura F, Ohnishi K, Satomura Y, Ohtsuki T, Fukunaga K, Honda M, Ema M, Tohyama T, Sugita S, Saito M.,*** 1986; Liver function in moderate obesity – study in 534 moderately obese subjects among 4613 male company employees. *Int. J. Obes.* 10, 349–354.

- ***Obermayer-Straub P, Strassburg CP, Manns MP.***, 2000; Target proteins in human autoimmunity: cytochromes P450 and UDP-glucuronosyltransferases. *Can J Gastroenterol*; 14(5):429–439.

- ***Odeh M, Oliven A***. 1998; [Verapamil-associated liver injury] *arefuah* 134: 36-37.

- ***Olsson, S.B.***, 2003; Stroke prevention with the oral direct thrombin inhibitor ximelagatran compared with warfarin in patients with non-valvular atrial fibrillation (SPORTIF III): randomised controlled trial. *Lancet* 362, 1691–1698.

- ***Onat A, Uyarel H, Hergenç G, Karabulut A, Albayrak S, Sari I.,*** 2006; Serum uric acid is a determinant of metabolic syndrome in a population-based study. *Am. J. Hypertens.* 19, 1055–1062.

- ***Pachkoria K, Lucena MI, Molokhia M.,*** 2007; Genetic and molecular factors in drug-induced liver injury: a review. *Curr Drug Saf;* 2(2):97–112.

- ***Papatheodoridis GV, Goulis J, Christodoulou D, Manolakopoulos S.,*** 2007; High prevalence of elevated liver enzymes in blood donors: associations with male gender and central adiposity. *Eur. J. Gastroenterol. Hepatol.* 19, 281–287.

- ***Parola M, Robino G.*** 2001; Oxidative stress-related molecules and liver fibrosis. *J Hepatol.* 35: 297-306.

- ***phapale PB, S Kim, HW Lee, M Lim, DD Kale, Y Kim, J Cho, D H wang and Y Yoon.,*** 2010; An integrative approach for identifying a metabolic phenotype predictive of individualized pharmacokinetics of tacrolimus. *Clin. Pharmacol. Ther.* 87, 426–436.

- ***Phillips, E., Mallal, S.,*** 2009; Successful translation of pharmacogenetics into the clinic: the abacavir example. *Mol. Diagn. Ther*. 13, 1–9.

- ***Pichler WJ, Tilch J.***, 2004; The lymphocyte transformation test in the diagnosis of drug hypersensitivity. *Allergy*;59(8): 809–820.

- ***Piton A, Poynard T, Imbert-Bismut F, Khalil L, Delattre J.,*** 1998; Factors associated with serum alanine transaminase activity in healthy subjects: consequences for the definition of normal values,

for selection of blood donors, and for patients with chronic hepatitis C. MULTIVIRC group. *Hepatology* 27, 1213–1219.

- ***Prandota J***. 2005; Important role of proinflammatory cytokines/ other endogenous substances in drug-induced hepatotoxicity: depression of drug metabolism during infections/inflammation states, and genetic polymorphisms of drugmetabolizing enzymes/cytokines may markedly contribute to this pathology. *Am J Ther* .12: 254-261.

- ***Ramesh V, Saraswat S, Choudhury N, Gupta RK.,*** 1995; Relationship of serum alanine aminotransferase (ALT) to body manss index (BMI) in blood donors: the need to correct ALT for BMI in blood donor screening. *Transfuse Med.* 5, 273–274.

- ***Ramaiah SK, Apte U, Mehendale HM.*** 2001; Cytochrome P4502E1 induction increases thioacetamide liver injury in diet-restricted rats. *Drug Metab Dispos.* 29: 1088-1095.

- ***Reuben A;*** 2004; Hy's Law, *Hepatology*, 39(2):574-578.

- ***Robinson, D., Whitehead, T.P.,*** 1989; Effect of body mass and other factors on serum liver enzyme levels in men attending for well population screening. *Ann. Clin. Biochem*. 26 (Pt 5), 393–400.

- ***Romeo S, Kozlitina J, Xing C, Pertsemlidis A, Pennacchio LA .,*** 2008; Genetic variation in PNPLA3 confers susceptibility to nonalcoholic fatty liver disease. *Nat. Genet*. 40, 1461–1465.

- ***Rosenzweig P, Miget N, Brohier S .,*** 1999; Transaminase elevation on placebo during phase I trials: prevalence and significance. *Br. J. Clin. Pharmacol*. 48, 19–23.

- ***Roy AK, Mahoney HC, Levine RA.*** 1993; Phenytoin-induced chronic hepatitis. *Dig Dis Sci.* 38: 740-743.

- ***Russo MW, Jacobson IM***. 2004; How to use statins in patients with chronic liver disease. *Cleve Clin J Med* .71: 58-62.

- ***Schreiber J, Zissel G, Greinert U, Schlaak M, Mu¨ ller- Quernheim J.***, 1999; Lymphocyte transformation test for the evaluation of adverse effects of antituberculous drugs. *Eur J Med Res*;4(2):67–71.

- ***Shakya R, Rao BS, Shrestha B.*** 2004; Incidence of hepatotoxicity due to antitubercular medicines and assessment of risk factors. *Ann Pharmacother*. 38: 1074-1079.

- ***Sheffield, L.J., Phillimore, H.E.,*** 2009; Clinical use of pharmacogenomic tests in 2009. Clin. *Biochem. Rev*. 30, 55–65.

- ***Schwab M, Schaeffeler E, Klotz U, Treiber G***. 2004; CYP2C19 polymorphism is a major predictor of treatment failure in white patients by use of lansoprazole-based quadruple therapy for eradication of Helicobacter pylori. *Clin Pharmacol Ther.* 76: 201-209.

- ***slupsky CM, Rankin KN, Wagner J, Fu H, Chang D.,*** 2007; Investigations of the effects of gender, diurnal variation, and age in human urinary metabolomic profiles. *Anal. Chem.* 79, 6995–7004.

- ***Smith, J.L., Wishnok, J.S. & Deen, W.M.***, 1994; Metabolism and excretion of methylamines in rats. *Toxicol. Appl. Pharmacol*. 125, 296–308.

- ***Somchit N, Wong CW, Zuraini A, Ahmad Bustamam A, Hasiah AH, Khairi HM, Sulaiman MR, Israf DA.*** 2006; Involvement of phenobarbital and SKF 525A in the hepatotoxicity of antifungal drugs itraconazole and fluconazole in rats. *Drug Chem Toxicol.* 29: 237-253**.**

- ***Stoevesandt O, Taussig MJ, He M***., 2009; Protein microarrays: high-throughput tools for proteomics. *Expert Rev Proteomics*;6(2):145–157.

- ***Sulis ML, Bessmertny O, Granowetter L, Weiner M, Kelly KM***. 2004; Veno-occlusive disease in pediatric patients receiving actinomycin D and vincristine only for the treatment of rhabdomyosarcoma. *Pediatr Hematol Oncol.* 26: 843-846.

- ***Sun, J., Schnackenberg, L.K. & Beger, R.D.,*** 2009; Studies of acetaminophen and metabolites in urine and their correlations with toxicity using metabolomics. *Drug Metab. Lett.* 3, 130–136.

- ***Tarantino G, Conca P, Basile V, Gentile A, Capone D, Polichetti G, Leo E.*** 2007; A prospective study of acute drug-induced liver injury in patients suffering from non-alcoholic fatty liver disease. *Hepatol Res.* 37: 410-415.

- ***Temple, R,*** 2001; Hepatotoxicity Through the Years: Impact on the FDA, presented 2/12/2001.

- ***Van Gijssel HE, Mullenders LH, van Oosterwijk MF, Meerman JH.*** 2003; Blockage of transcription as a trigger for p53 accumulation by 2-acetylaminofluorene DNA-adducts. *Life Sci* 73: 1759-1771**.**

- ***Vanderstigel M, Zafrani ES, Lejonc JL, Schaeffer A, Portos JL***. 1986; Allopurinol hypersensitivity syndrome as a cause of hepatic fibrin-ring granulomas. *Gastroenterology.* 90: 188-190**.**

- *Venkataramanan R,* ***Swaminathan*** *A,* ***Prasad T.,*** 1995; Clinical pharmacokinetics of tacrolimus. *Clin. Pharmacokinet*. 29, 404–430.

- ***Wang AG, Xia T, Yuan J, Yu RA, Yang KD, Chen XM, Qu W, Waalkes MP***. 2004; Effects of phenobarbital on metabolism and toxicity of diclofenac sodium in rat hepatocytes in vitro. *Food Chem Toxicol.* 42: 1647-1653**.**

- ***Wang H, LeCluyse EL***. 2003; Role of orphan nuclear receptors in the regulation of drug-metabolising enzymes. *Clin Pharmacokinet*. 42: 1331-1357.

- ***Wang K, Zhang S, Marzolf B.,*** 2009; Circulating microRNAs, potential biomarkers for drug-induced liver injury. *Proc Natl Acad Sci U S A*;106(11):4402–4407.

- ***Wang Z, Gerstein M, Snyder M.,*** 2009; RNA-Seq: a revolutionary tool for transcriptomics. *Nature Rev. Genetics* 10(1): 57-63.

- ***Waters, E., Wang, J.H., Redmond, H.P., Wu, Q.D., Kay, E. & Bouchier-Hayes, D.***, 2001; Role of taurine in preventing acetaminophen-induced hepatic injury in the rat. *Am. J. Physiol. Gastrointest. Liver Physiol.* 280, G1274–G1279.

- ***Watkins PB, Kaplowitz N, Slattery JT, Colonese CR, Colucci SV, Stewart PW, Harris SC.,*** 2006; Aminotransferase elevations in healthy adults receiving 4 grams of acetaminophen daily: a randomized controlled trial. *JAMA* 296, 87–93.

- ***Watkins PB, Zimmerman HJ, Knapp MJ, Gracon SI, Lewis KW .,*** 2008; Using controlled clinical trials to learn more about acute drug-induced liver injury. *Hepatology* 48, 1680–1689.

- ***Watkins, P.B.*** 2009; Biomarkers for the Diagnosis and Management of Drug-Induced Liver Injury; *Seminars in Liver Disease*; 4; 393-399.

- ***Weber LW, Boll M, Stampfl A***. 2003; Hepatotoxicity and mechanism of action of haloalkanes: carbon tetrachloride as a toxicological model. *Crit Rev Toxicol*. 33: 105-136.

- ***Winnike, J.H., Li, Z., Wright, F.A., Macdonald, J.M., O'Connell, T.M. & Watkins, P .B.***, 2010; Use of pharmaco-metabonomics for early prediction of acetaminopheninduced hepatotoxicity in humans. *Clin. Pharmacol. Ther*. 88, 45–51.

- ***Yuan X, Waterworth D, Perry JRB, Lim N, Song K, Chambers JC, Zhang W, Mooser V.,*** 2008; Population-based genome-wide association studies reveal six loci influencing plasma levels of liver enzymes. *Am. J. Hum. Genet.* 83, 520–528.

- ***Zimmerman, HJ,*** 1978; Drug-Induced Liver Disease, in: Hepatotoxicity, The Adverse Effects of Drugs and Other Chemicals on the Liver, 1st ed., pp. 351-3, Appleton-Century-Crofts, New York.

- ***Zimmerman, HJ,*** 1999; Drug-Induced Liver Disease, in: Hepatotoxicity, The Adverse Effects of Drugs and Other Chemicals on the Liver, 2nd ed., pp. 428-33, Lippincott Williams & Wilkins, Philadelphia.

- ***Zhang, K., Weinberg, J.M., Venkatachalam, M.A. & Dong, Z.***, 2003; Glycine protection of PC-12 cells against injury by ATP-depletion. *Neurochem. Res*. 28, 893–901.

- ***Zhu AX, Lauwers GY, Tanabe KK***. 2004; Cholangiocarcinoma in association with Thorotrast exposure. *J Hepatobiliary Pancreat Surg*. 11: 430-433.