

Supplemental Table 1: Only studies focusing on human liver disease have been included.

References in each section are listed in chronological order.

Search terms: M30 and serum; M65 and serum; (cyto)keratin 18 and liver and serum

Non-alcoholic fatty liver disease

- Wieckowska A, Zein NN, Yerian LM, Lopez AR, McCullough AJ, Feldstein AE. In vivo assessment of liver cell apoptosis as a novel biomarker of disease severity in nonalcoholic fatty liver disease. *Hepatology* 2006;44:27-33.
- Yilmaz Y, Dolar E, Ulukaya E, Akgoz S, Keskin M, Kiyici M, Aker S, et al. Soluble forms of extracellular cytokeratin 18 may differentiate simple steatosis from nonalcoholic steatohepatitis. *World J Gastroenterol* 2007;13:837-844.
- Diab DL, Yerian L, Schauer P, Kashyap SR, Lopez R, Hazen SL, Feldstein AE. Cytokeratin 18 fragment levels as a noninvasive biomarker for nonalcoholic steatohepatitis in bariatric surgery patients. *Clin Gastroenterol Hepatol* 2008;6:1249-1254.
- Vos MB, Barve S, Joshi-Barve S, Carew JD, Whittington PF, McClain CJ. Cytokeratin 18, a marker of cell death, is increased in children with suspected nonalcoholic fatty liver disease. *J Pediatr Gastroenterol Nutr* 2008;47:481-485.
- Mitry RR, De Bruyne R, Quaglia A, Hughes RD, Dhawan A. Noninvasive diagnosis of nonalcoholic fatty liver disease using serum biomarkers. *Hepatology* 2007;46:2047-2048; author reply 2048.
- Younossi ZM, Jarrar M, Nugent C, Randhawa M, Afendy M, Stepanova M, Rafiq N, et al. A novel diagnostic biomarker panel for obesity-related nonalcoholic steatohepatitis (NASH). *Obes Surg* 2008;18:1430-1437.
- Feldstein AE, Wieckowska A, Lopez AR, Liu YC, Zein NN, McCullough AJ. Cytokeratin-18 fragment levels as noninvasive biomarkers for nonalcoholic steatohepatitis: a multicenter validation study. *Hepatology* 2009;50:1072-1078.
- Yilmaz Y, Ulukaya E, Dolar E. Serum M30 levels: a potential biomarker of severe liver disease in nonalcoholic fatty liver disease and normal aminotransferase levels. *Hepatology* 2009;49:697; author reply 697.
- Musso G, Gambino R, Pacini G, De Michieli F, Cassader M. Prolonged saturated fat-induced, glucose-dependent insulinotropic polypeptide elevation is associated with adipokine imbalance and liver injury in nonalcoholic steatohepatitis: dysregulated enteroadipocyte axis as a novel feature of fatty liver. *Am J Clin Nutr* 2009;89:558-567.
- Musso G, Gambino R, Pacini G, Pagano G, Durazzo M, Cassader M. Transcription factor 7-like 2 polymorphism modulates glucose and lipid homeostasis, adipokine profile, and hepatocyte apoptosis in NASH. *Hepatology* 2009;49:426-435.
- Malik R, Chang M, Bhaskar K, Nasser I, Curry M, Schuppan D, Byrnes V, et al. The clinical utility of biomarkers and the nonalcoholic steatohepatitis CRN liver biopsy scoring system in patients with nonalcoholic fatty liver disease. *J Gastroenterol Hepatol* 2009;24:564-568.

- Balmer ML, Siegrist K, Zimmermann A, Dufour JF. Effects of ursodeoxycholic acid in combination with vitamin E on adipokines and apoptosis in patients with nonalcoholic steatohepatitis. *Liver Int* 2009;29:1184-1188.
- Tsutsui M, Tanaka N, Kawakubo M, Sheena Y, Horiuchi A, Komatsu M, Nagaya T, et al. Serum fragmented cytokeratin 18 levels reflect the histologic activity score of nonalcoholic fatty liver disease more accurately than serum alanine aminotransferase levels. *J Clin Gastroenterol* 2010;44:440-447.
- Bechmann LP, Gieseler RK, Sowa JP, Kahraman A, Erhard J, Wedemeyer I, Emons B, et al. Apoptosis is associated with CD36/fatty acid translocase upregulation in non-alcoholic steatohepatitis. *Liver Int* 2010;30:850-859.
- Younossi ZM, Page S, Rafiq N, Biredinc A, Stepanova M, Hossain N, Afendy A, et al. A biomarker panel for non-alcoholic steatohepatitis (NASH) and NASH-related fibrosis. *Obes Surg* 2011;21:431-439.
- Civera M, Urios A, Garcia-Torres ML, Ortega J, Martinez-Valls J, Cassinello N, del Olmo JA, et al. Relationship between insulin resistance, inflammation and liver cell apoptosis in patients with severe obesity. *Diabetes Metab Res Rev* 2010;26:187-192.
- Anty R, Iannelli A, Patouraux S, Bonnafous S, Lavallard VJ, Senni-Buratti M, Amor IB, et al. A new composite model including metabolic syndrome, alanine aminotransferase and cytokeratin-18 for the diagnosis of non-alcoholic steatohepatitis in morbidly obese patients. *Aliment Pharmacol Ther* 2010;32:1315-1322.
- Wong VW, Wong GL, Choi PC, Chan AW, Li MK, Chan HY, Chim AM, et al. Disease progression of non-alcoholic fatty liver disease: a prospective study with paired liver biopsies at 3 years. *Gut* 2010;59:969-974.
- Fitzpatrick E, Mitry RR, Quaglia A, Hussain MJ, DeBruyne R, Dhawan A. Serum levels of CK18 M30 and leptin are useful predictors of steatohepatitis and fibrosis in paediatric NAFLD. *J Pediatr Gastroenterol Nutr* 2010;51:500-506.
- Tamimi TI, Elgouhari HM, Alkhouri N, Yerian LM, Berk MP, Lopez R, Schauer PR, et al. An apoptosis panel for nonalcoholic steatohepatitis diagnosis. *J Hepatol* 2011;54:1224-1229.
- Williams CD, Stengel J, Asike MI, Torres DM, Shaw J, Contreras M, Landt CL, et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. *Gastroenterology* 2011;140:124-131.
- Tabuchi M, Tomioka K, Kawakami T, Murakami Y, Hiramatsu M, Itoshima T, Sugawara S, et al. Serum cytokeratin 18 M30 antigen level and its correlation with nutritional parameters in middle-aged Japanese males with nonalcoholic fatty liver disease (NAFLD). *J Nutr Sci Vitaminol (Tokyo)* 2010;56:271-278.
- Musso G, Cassader M, De Michieli F, Saba F, Bo S, Gambino R. Effect of lectin-like oxidized LDL receptor-1 polymorphism on liver disease, glucose homeostasis, and postprandial lipoprotein metabolism in nonalcoholic steatohepatitis. *Am J Clin Nutr* 2011;94:1033-1042.
- Lebensztejn DM, Wierzbicka A, Socha P, Pronicki M, Skiba E, Werpachowska I, Kaczmarek M. Cytokeratin-18 and hyaluronic acid levels predict liver fibrosis in children with non-alcoholic fatty liver disease. *Acta Biochim Pol* 2011;58:563-566.
- Pirvulescu I, Gheorghe L, Csiki I, Becheanu G, Dumbrava M, Fica S, Martin S, et al. Noninvasive clinical model for the diagnosis of nonalcoholic steatohepatitis in

- overweight and morbidly obese patients undergoing bariatric surgery. *Chirurgia (Bucur)* 2012;107:772-779.
- Fealy CE, Haus JM, Solomon TP, Pagadala M, Flask CA, McCullough AJ, Kirwan JP. Short-term exercise reduces markers of hepatocyte apoptosis in nonalcoholic fatty liver disease. *J Appl Physiol* (1985) 2012;113:1-6.
- Koehler E, Swain J, Sanderson S, Krishnan A, Watt K, Charlton M. Growth hormone, dehydroepiandrosterone and adiponectin levels in non-alcoholic steatohepatitis: an endocrine signature for advanced fibrosis in obese patients. *Liver Int* 2012;32:279-286.
- Musso G, Cassader M, De Michieli F, Rosina F, Orlandi F, Gambino R. Nonalcoholic steatohepatitis versus steatosis: adipose tissue insulin resistance and dysfunctional response to fat ingestion predict liver injury and altered glucose and lipoprotein metabolism. *Hepatology* 2012;56:933-942.
- Grigorescu M, Crisan D, Radu C, Grigorescu MD, Sparchez Z, Serban A. A novel pathophysiological-based panel of biomarkers for the diagnosis of nonalcoholic steatohepatitis. *J Physiol Pharmacol* 2012;63:347-353.
- Yilmaz Y, Eren F. Identification of a support vector machine-based biomarker panel with high sensitivity and specificity for nonalcoholic steatohepatitis. *Clin Chim Acta* 2012;414:154-157.
- Shen J, Chan HL, Wong GL, Chan AW, Choi PC, Chan HY, Chim AM, et al. Assessment of non-alcoholic fatty liver disease using serum total cell death and apoptosis markers. *Aliment Pharmacol Ther* 2012;36:1057-1066.
- Shen J, Chan HL, Wong GL, Choi PC, Chan AW, Chan HY, Chim AM, et al. Non-invasive diagnosis of non-alcoholic steatohepatitis by combined serum biomarkers. *J Hepatol* 2012;56:1363-1370.
- Harrold LR, Saag KG, Yood RA, Mikuls TR, Andrade SE, Fouayzi H, Davis J, et al. Validity of gout diagnoses in administrative data. *Arthritis Rheum* 2007;57:103-108.
- Bechmann LP, Kocabayoglu P, Sowa JP, Sydor S, Best J, Schlattjan M, Beilfuss A, et al. Free fatty acids repress small heterodimer partner (SHP) activation and adiponectin counteracts bile acid-induced liver injury in superobese patients with nonalcoholic steatohepatitis. *Hepatology* 2013;57:1394-1406.
- Kalsch J, Bechmann LP, Manka P, Kahraman A, Schlattjan M, Marth T, Rehbehn K, et al. Non-alcoholic steatohepatitis occurs in celiac disease and is associated with cellular stress. *Z Gastroenterol* 2013;51:26-31.
- Maliken BD, Nelson JE, Klintworth HM, Beauchamp M, Yeh MM, Kowdley KV. Hepatic reticuloendothelial system cell iron deposition is associated with increased apoptosis in nonalcoholic fatty liver disease. *Hepatology* 2013;57:1806-1813.
- Ghaemi A, Taleban FA, Hekmatdoost A, Rafiei A, Hosseini V, Amiri Z, Homayounfar R, et al. How Much Weight Loss is Effective on Nonalcoholic Fatty Liver Disease? *Hepat Mon* 2013;13:e15227.
- Cao W, Zhao C, Shen C, Wang Y. Cytokeratin 18, alanine aminotransferase, platelets and triglycerides predict the presence of nonalcoholic steatohepatitis. *PLoS One* 2013;8:e82092.
- Polyzos SA, Kountouras J, Papatheodorou A, Katsiki E, Patsiaoura K, Zafeiriadou E, Papadopoulou E, et al. Adipocytokines and cytokeratin-18 in patients with nonalcoholic fatty liver disease: Introduction of CHA index. *Ann Hepatol* 2013;12:749-757.

- Musso G, Bo S, Cassader M, De Michieli F, Gambino R. Impact of sterol regulatory element-binding factor-1c polymorphism on incidence of nonalcoholic fatty liver disease and on the severity of liver disease and of glucose and lipid dysmetabolism. *Am J Clin Nutr* 2013;98:895-906.
- de Jonge C, Rensen SS, Koek GH, Joosten MF, Buurman WA, Bouvy ND, Greve JW. Endoscopic duodenal-jejunal bypass liner rapidly improves plasma parameters of nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol* 2013;11:1517-1520.
- Kahraman A, Sowa JP, Schlattjan M, Sydor S, Pronadl M, Wree A, Beilfuss A, et al. Fetuin-A mRNA expression is elevated in NASH compared with NAFL patients. *Clin Sci (Lond)* 2013;125:391-400.
- Sowa JP, Heider D, Bechmann LP, Gerken G, Hoffmann D, Canbay A. Novel algorithm for non-invasive assessment of fibrosis in NAFLD. *PLoS One* 2013;8:e62439.
- Musso G, Cassader M, Bo S, De Michieli F, Gambino R. Sterol regulatory element-binding factor 2 (SREBF-2) predicts 7-year NAFLD incidence and severity of liver disease and lipoprotein and glucose dysmetabolism. *Diabetes* 2013;62:1109-1120.
- Baranova A, Tran TP, Afendy A, Wang L, Shamsaddini A, Mehta R, Chandhoke V, et al. Molecular signature of adipose tissue in patients with both non-alcoholic fatty liver disease (NAFLD) and polycystic ovarian syndrome (PCOS). *J Transl Med* 2013;11:133.
- Feldstein AE, Alkhouri N, De Vito R, Alisi A, Lopez R, Nobili V. Serum cytokeratin-18 fragment levels are useful biomarkers for nonalcoholic steatohepatitis in children. *Am J Gastroenterol* 2013;108:1526-1531.
- Kim YS, Jung ES, Hur W, Bae SH, Choi JY, Song MJ, Kim CW, et al. Noninvasive predictors of nonalcoholic steatohepatitis in Korean patients with histologically proven nonalcoholic fatty liver disease. *Clin Mol Hepatol* 2013;19:120-130.
- Miyasato M, Murase-Mishiba Y, Bessho M, Miyawaki M, Imbe H, Tsutsumi C, Tanimoto K, et al. The cytokeratin-18 fragment level as a biomarker of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus. *Clin Chim Acta* 2014;433:184-189.
- Bantel H, John K, Schulze-Osthoff K. Robust detection of liver steatosis and staging of NAFLD by an improved ELISA for serum cytokeratin-18 fragments. *Am J Gastroenterol* 2014;109:140-141.
- Caner S, Altinbas A, Sayki M, Buyukcam F, Yilmaz B, Cakal E, Coban S, et al. M30 does not predict the severity of hepatosteatosis, whereas adiponectin level declined with increase of ALT and the severity of hepatic steatosis. *J Clin Lab Anal* 2014;28:381-385.
- Morling JR, Fallowfield JA, Williamson RM, Nee LD, Jackson AP, Glancy S, Reynolds RM, et al. Non-invasive hepatic biomarkers (ELF and CK18) in people with type 2 diabetes: the Edinburgh type 2 diabetes study. *Liver Int* 2014;34:1267-1277.
- Cusi K, Chang Z, Harrison S, Lomonaco R, Bril F, Orsak B, Ortiz-Lopez C, et al. Limited value of plasma cytokeratin-18 as a biomarker for NASH and fibrosis in patients with non-alcoholic fatty liver disease. *J Hepatol* 2014;60:167-174.
- Del Ben M, Polimeni L, Baratta F, Bartimoccia S, Carnevale R, Loffredo L, Pignatelli P, et al. Serum Cytokeratin-18 Is Associated with NOX2-Generated Oxidative Stress in Patients with Nonalcoholic Fatty Liver. *Int J Hepatol* 2014;2014:784985.
- Del Ben M, Polimeni L, Carnevale R, Bartimoccia S, Nocella C, Baratta F, Loffredo L, et al. NOX2-generated oxidative stress is associated with severity of ultrasound liver steatosis in patients with non-alcoholic fatty liver disease. *BMC Gastroenterol* 2014;14:81.

- Chan WK, Sthaneshwar P, Nik Mustapha NR, Mahadeva S. Limited utility of plasma M30 in discriminating non-alcoholic steatohepatitis from steatosis--a comparison with routine biochemical markers. *PLoS One* 2014;9:e105903.
- Hyysalo J, Mannisto VT, Zhou Y, Arola J, Karja V, Leivonen M, Juuti A, et al. A population-based study on the prevalence of NASH using scores validated against liver histology. *J Hepatol* 2014;60:839-846.
- Yilmaz Y, Eren F. A Bayesian approach to an integrated multimodal noninvasive diagnosis of definitive nonalcoholic steatohepatitis in the spectrum of nonalcoholic fatty liver disease. *Eur J Gastroenterol Hepatol* 2014;26:1292-1295.
- Sanyal AJ, Abdelmalek MF, Suzuki A, Cummings OW, Chojkier M, Group E-AS. No significant effects of ethyl-eicosapentanoic acid on histologic features of nonalcoholic steatohepatitis in a phase 2 trial. *Gastroenterology* 2014;147:377-384 e371.
- Vuppalanchi R, Jain AK, Deppe R, Yates K, Comerford M, Masuoka HC, Neuschwander-Tetri BA, et al. Relationship between changes in serum levels of keratin 18 and changes in liver histology in children and adults with nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol* 2014;12:2121-2130 e2121-2122.
- El Bassat H, Ziada DH, Hasby EA, Nagy H, Abo Ryia MH. Apoptotic and anti-apoptotic seromarkers for assessment of disease severity of non-alcoholic steatohepatitis. *Arab J Gastroenterol* 2014;15:6-11.
- Dvorak K, Stritesky J, Petrtyl J, Vitek L, Sroubkova R, Lenicek M, Smid V, et al. Use of non-invasive parameters of non-alcoholic steatohepatitis and liver fibrosis in daily practice--an exploratory case-control study. *PLoS One* 2014;9:e111551.
- Ergelen R, Akyuz U, Aydin Y, Eren F, Yilmaz Y. Measurements of serum procollagen-III peptide and M30 do not improve the diagnostic accuracy of transient elastography for the detection of hepatic fibrosis in patients with nonalcoholic fatty liver disease. *Eur J Gastroenterol Hepatol* 2015;27:667-671.
- Yang M, Xu D, Liu Y, Guo X, Li W, Guo C, Zhang H, et al. Combined Serum Biomarkers in Non-Invasive Diagnosis of Non-Alcoholic Steatohepatitis. *PLoS One* 2015;10:e0131664.
- Faghihzadeh F, Adibi P, Rafiei R, Hekmatdoost A. Resveratrol supplementation improves inflammatory biomarkers in patients with nonalcoholic fatty liver disease. *Nutr Res* 2014;34:837-843.
- Adams LA, Crawford DH, Stuart K, House MJ, St Pierre TG, Webb M, Ching HL, et al. The impact of phlebotomy in nonalcoholic fatty liver disease: A prospective, randomized, controlled trial. *Hepatology* 2015;61:1555-1564.
- Aida Y, Abe H, Tomita Y, Nagano T, Seki N, Sugita T, Itagaki M, et al. Serum cytokeratin 18 fragment level as a noninvasive biomarker for non-alcoholic fatty liver disease. *Int J Clin Exp Med* 2014;7:4191-4198.
- Chen S, Zhao X, Ran L, Wan J, Wang X, Qin Y, Shu F, et al. Resveratrol improves insulin resistance, glucose and lipid metabolism in patients with non-alcoholic fatty liver disease: a randomized controlled trial. *Dig Liver Dis* 2015;47:226-232.
- Nagpal SJ, Lopez R, Feldstein AE, Alkhoury N. Serum cytokeratin-18 fragment levels predict development of type 2 diabetes mellitus in adult patients with NAFLD. *Liver Int* 2015:In press.
- Chen S, Zhao X, Wan J, Ran L, Qin Y, Wang X, Gao Y, et al. Dihydromyricetin improves glucose and lipid metabolism and exerts anti-inflammatory effects in nonalcoholic fatty liver disease: A randomized controlled trial. *Pharmacol Res* 2015;99:74-81.

Wong VW, Wong GL, Chan HY, Yeung DK, Chan RS, Chim AM, Chan CK, et al. Bacterial endotoxin and non-alcoholic fatty liver disease in the general population: a prospective cohort study. *Aliment Pharmacol Ther* 2015;42:731-740.

Viral hepatitis

- Bantel H, Luger A, Heidemann J, Volkmann X, Poremba C, Strassburg CP, Manns MP, et al. Detection of apoptotic caspase activation in sera from patients with chronic HCV infection is associated with fibrotic liver injury. *Hepatology* 2004;40:1078-1087.
- Seidel N, Volkmann X, Langer F, Flemming P, Manns MP, Schulze-Osthoff K, Bantel H. The extent of liver steatosis in chronic hepatitis C virus infection is mirrored by caspase activity in serum. *Hepatology* 2005;42:113-120.
- Kronenberger B, Wagner M, Herrmann E, Mihm U, Piiper A, Sarrazin C, Zeuzem S. Apoptotic cytokeratin 18 neopeptides in serum of patients with chronic hepatitis C. *J Viral Hepat* 2005;12:307-314.
- Macias J, Japon MA, Saez C, Palacios RB, Mira JA, Garcia-Garcia JA, Merchante N, et al. Increased hepatocyte fas expression and apoptosis in HIV and hepatitis C virus coinfection. *J Infect Dis* 2005;192:1566-1576.
- Volkmann X, Cornberg M, Wedemeyer H, Lehner F, Manns MP, Schulze-Osthoff K, Bantel H. Caspase activation is required for antiviral treatment response in chronic hepatitis C virus infection. *Hepatology* 2006;43:1311-1316.
- Papatheodoridis GV, Hadziyannis E, Tsochatzis E, Chrysanthos N, Georgiou A, Kafiri G, Manolakopoulos S, et al. Serum apoptotic caspase activity as a marker of severity in HBeAg-negative chronic hepatitis B virus infection. *Gut* 2008;57:500-506.
- Wedemeyer I, Bechmann LP, Odenthal M, Jochum C, Marquitan G, Drebber U, Gerken G, et al. Adiponectin inhibits steatotic CD95/Fas up-regulation by hepatocytes: therapeutic implications for hepatitis C. *J Hepatol* 2009;50:140-149.
- Jochum C, Gieseler RK, Gawlista I, Fiedler A, Manka P, Saner FH, Roggendorf M, et al. Hepatitis B-associated acute liver failure: immediate treatment with entecavir inhibits hepatitis B virus replication and potentially its sequelae. *Digestion* 2009;80:235-240.
- Valva P, De Matteo E, Galoppo MC, Gismondi MI, Preciado MV. Apoptosis markers related to pathogenesis of pediatric chronic hepatitis C virus infection: M30 mirrors the severity of steatosis. *J Med Virol* 2010;82:949-957.
- Sgier C, Mullhaupt B, Gerlach T, Moradpour D, Negro F, Male PJ, Heim MH, et al. Effect of antiviral therapy on circulating cytokeratin-18 fragments in patients with chronic hepatitis C. *J Viral Hepat* 2010;17:845-850.
- Eren F, Yilmaz Y, Kose S, Ozdemir FT, Yonal O, Kurt R, Ozdogan O, et al. Caspase-cleaved fragments of cytokeratin 18 in patients with chronic hepatitis B. *Clin Chim Acta* 2010;411:2029-2032.
- Connoy A, Turner J, Nunez M. Levels of serum markers of liver inflammation and fibrosis in patients with chronic hepatitis C virus infection according to HIV status and antiretroviral use. *AIDS Res Hum Retroviruses* 2011;27:719-725.
- Giannousis IP, Manolakopoulos SG, Hadziyannis E, Georgiou A, Papatheodoridis GV. Changes of serum levels of keratin-18 fragments in hepatitis B e antigen-negative chronic hepatitis B patients under oral antiviral therapy. *Antivir Ther* 2011;16:505-514.

- Cheong JY, Kim DJ, Hwang SG, Yang JM, Kim YB, Park YN, Cho SW. Serum markers for necroinflammatory activity in patients with chronic viral hepatitis and normal or mildly elevated aminotransferase levels. *Liver Int* 2011;31:1352-1358.
- Farnik H, Lange CM, Hofmann WP, Berger A, Allwinn R, Welker MW, Trojan J, et al. Nucleos(t)ide analogue treatment reduces apoptotic activity in patients with chronic hepatitis B. *J Clin Virol* 2011;52:204-209.
- Koo JH, Lee MH, Kim SS, Kim DH, Kim IS, Lee KM, Yoo BM, et al. Changes in serum histologic surrogate markers and procollagen III N-terminal peptide as independent predictors of HBeAg loss in patients with chronic hepatitis B during entecavir therapy. *Clin Biochem* 2012;45:31-36.
- Jazwinski AB, Thompson AJ, Clark PJ, Naggie S, Tillmann HL, Patel K. Elevated serum CK18 levels in chronic hepatitis C patients are associated with advanced fibrosis but not steatosis. *J Viral Hepat* 2012;19:278-282.
- Khattab MA, Eslam M, Aly MM, Shatat M, Hussen A, Moussa YI, Elsaghir G, et al. Association of serum adipocytokines with insulin resistance and liver injury in patients with chronic hepatitis C genotype 4. *J Clin Gastroenterol* 2012;46:871-879.
- Valva P, Casciato P, Lezama C, Galoppo M, Gadano A, Galdame O, Galoppo MC, et al. Serum apoptosis markers related to liver damage in chronic hepatitis C: sFas as a marker of advanced fibrosis in children and adults while M30 of severe steatosis only in children. *PLoS One* 2013;8:e53519.
- Abdel Haleem H, Zayed N, Abdel Hafez H, Fouad A, Akl M, Hassan M, Hammam O, et al. Evaluation of the diagnostic value of serum and tissue apoptotic cytokeratin-18 in patients with chronic hepatitis C. *Arab J Gastroenterol* 2013;14:68-72.
- Parfieniuk-Kowerda A, Lapinski TW, Rogalska-Plonska M, Swiderska M, Panasiuk A, Jaroszewicz J, Flisiak R. Serum cytochrome c and m30-neoepitope of cytokeratin-18 in chronic hepatitis C. *Liver Int* 2014;34:544-550.
- Sumer S, Aktug Demir N, Kolgelier S, Cagkan Inkaya A, Arpaci A, Saltuk Demir L, Ural O. The Clinical Significance of Serum Apoptotic Cytokeratin 18 Neoepitope M30 (CK-18 M30) and Matrix Metalloproteinase 2 (MMP-2) Levels in Chronic Hepatitis B Patients with Cirrhosis. *Hepat Mon* 2013;13:e10106.
- Bae CB, Kim SS, Ahn SJ, Cho HJ, Kim SR, Park SY, Song GW, et al. Caspase-cleaved fragments of cytokeratin-18 as a marker of inflammatory activity in chronic hepatitis B virus infection. *J Clin Virol* 2013;58:641-646.
- Zheng SJ, Liu S, Liu M, McCrae MA, Li JF, Han YP, Xu CH, et al. Prognostic value of M30/M65 for outcome of hepatitis B virus-related acute-on-chronic liver failure. *World J Gastroenterol* 2014;20:2403-2411.
- Rohrbach J, Stickel F, Schmid P, Thormann W, Kovari H, Scherrer A, Gunthard HF, et al. Changes in biomarkers of liver disease during successful combination antiretroviral therapy in HIV-HCV-coinfected individuals. *Antivir Ther* 2014;19:149-159.
- Caviglia GP, Ciancio A, Rosso C, Abate ML, Olivero A, Pellicano R, Touscoz GA, et al. Non-invasive methods for the assessment of hepatic fibrosis: transient elastography, hyaluronic acid, ¹³C-aminopyrine breath test and cytokeratin 18 fragment. *Ann Hepatol* 2013;13:91-97.
- Ding G, Li Z, Zhang L, Ma H, Li H. Circulating full-length cytokeratin 18 for predicting prognosis of hepatitis B virus-related acute-on-chronic liver failure patients with lamivudine treatment. *Hepatol Res* 2015:In press.

Acute liver failure

- Rutherford AE, Hynan LS, Borges CB, Forcione DG, Blackard JT, Lin W, Gorman AR, et al. Serum apoptosis markers in acute liver failure: a pilot study. *Clin Gastroenterol Hepatol* 2007;5:1477-1483.
- Volkman X, Anstaett M, Hadem J, Stiefel P, Bahr MJ, Lehner F, Manns MP, et al. Caspase activation is associated with spontaneous recovery from acute liver failure. *Hepatology* 2008;47:1624-1633.
- Bechmann LP, Jochum C, Kocabayoglu P, Sowa JP, Kassalik M, Gieseler RK, Saner F, et al. Cytokeratin 18-based modification of the MELD score improves prediction of spontaneous survival after acute liver injury. *J Hepatol* 2010;53:639-647.
- Dechene A, Sowa JP, Gieseler RK, Jochum C, Bechmann LP, El Fouly A, Schlattjan M, et al. Acute liver failure is associated with elevated liver stiffness and hepatic stellate cell activation. *Hepatology* 2010;52:1008-1016.
- Rutherford A, King LY, Hynan LS, Vedvyas C, Lin W, Lee WM, Chung RT, et al. Development of an accurate index for predicting outcomes of patients with acute liver failure. *Gastroenterology* 2012;143:1237-1243.
- Antoine DJ, Jenkins RE, Dear JW, Williams DP, McGill MR, Sharpe MR, Craig DG, et al. Molecular forms of HMGB1 and keratin-18 as mechanistic biomarkers for mode of cell death and prognosis during clinical acetaminophen hepatotoxicity. *J Hepatol* 2012;56:1070-1079.
- Possamai LA, McPhail MJ, Quaglia A, Zingarelli V, Abeles RD, Tidswell R, Puthuchery Z, et al. Character and temporal evolution of apoptosis in acetaminophen-induced acute liver failure*. *Crit Care Med* 2013;41:2543-2550.

Alcoholic liver disease

- Ramskogler K, Brunner M, Hertling I, Dvorak A, Kapusta N, Krenn C, Moser B, et al. CDT values are not influenced by epithelial cell apoptosis in chronic alcoholic patients-preliminary results. *Alcohol Clin Exp Res* 2004;28:1396-1398.
- Lavallard VJ, Bonnafous S, Patouraux S, Saint-Paul MC, Rousseau D, Anty R, Le Marchand-Brustel Y, et al. Serum markers of hepatocyte death and apoptosis are non invasive biomarkers of severe fibrosis in patients with alcoholic liver disease. *PLoS One* 2011;6:e17599.
- Patouraux S, Bonnafous S, Voican CS, Anty R, Saint-Paul MC, Rosenthal-Allieri MA, Agostini H, et al. The osteopontin level in liver, adipose tissue and serum is correlated with fibrosis in patients with alcoholic liver disease. *PLoS One* 2012;7:e35612.

Hepatocellular carcinoma

- Fingas CD, Altinbas A, Schlattjan M, Beilfuss A, Sowa JP, Sydor S, Bechmann LP, et al. Expression of apoptosis- and vitamin D pathway-related genes in hepatocellular carcinoma. *Digestion* 2013;87:176-181.
- Waidmann O, Koberle V, Bettinger D, Trojan J, Zeuzem S, Schultheiss M, Kronenberger B, et al. Diagnostic and prognostic significance of cell death and macrophage activation markers in patients with hepatocellular carcinoma. *J Hepatol* 2013;59:769-779.
- Morris KL, Tugwood JD, Khoja L, Lancashire M, Sloane R, Burt D, Shenjere P, et al. Circulating biomarkers in hepatocellular carcinoma. *Cancer Chemother Pharmacol* 2014;74:323-332.
- Godin C, Louandre C, Bodeau S, Diouf M, Saidak Z, Conte MA, Chauffert B, et al. Biomarkers of apoptosis and necrosis in patients with hepatocellular carcinoma treated with sorafenib. *Anticancer Res* 2015;35:1803-1808.

Others

- Baskin-Bey ES, Washburn K, Feng S, Oltersdorf T, Shapiro D, Huyghe M, Burgart L, et al. Clinical Trial of the Pan-Caspase Inhibitor, IDN-6556, in Human Liver Preservation Injury. *Am J Transplant* 2007;7:218-225.
- Yagmur E, Trautwein C, Leers MP, Gressner AM, Tacke F. Elevated apoptosis-associated cytokeratin 18 fragments (CK18Asp386) in serum of patients with chronic liver diseases indicate hepatic and biliary inflammation. *Clin Biochem* 2007;40:651-655.
- Luft T, Conzelmann M, Benner A, Rieger M, Hess M, Strohmaecker U, Gorner M, et al. Serum cytokeratin-18 fragments as quantitative markers of epithelial apoptosis in liver and intestinal graft-versus-host disease. *Blood* 2007;110:4535-4542.
- Hetz H, Hoetzenecker K, Hacker S, Faybik P, Pollreisz A, Moser B, Roth G, et al. Caspase-cleaved cytokeratin 18 and 20 S proteasome in liver degeneration. *J Clin Lab Anal* 2007;21:277-281.
- Simopoulos C, Tsaroucha AK, Asimakopoulos B, Giatromanolaki A, Gavriilidis P, Polychronidis A, Karayiannakis A. Total and caspase-cleaved cytokeratin 18 in chronic cholecystitis: a prospective study. *BMC Gastroenterol* 2008;8:14.
- Feldstein A, Kleiner D, Kravetz D, Buck M. Severe hepatocellular injury with apoptosis induced by a hepatitis C polymerase inhibitor. *J Clin Gastroenterol* 2009;43:374-381.
- Yilmaz Y, Dolar E, Ulukaya E, Akgoz S, Keskin M, Kiyici M, Yerci O, et al. Elevated serum levels of caspase-cleaved cytokeratin 18 (CK18-Asp396) in patients with nonalcoholic steatohepatitis and chronic hepatitis C. *Med Sci Monit* 2009;15:CR189-193.
- Hofer S, Brenner T, Bopp C, Stepan J, Lichtenstern C, Weitz J, Bruckner T, et al. Cell death serum biomarkers are early predictors for survival in severe septic patients with hepatic dysfunction. *Crit Care* 2009;13:R93.
- Tan S, Bechmann LP, Benson S, Dietz T, Eichner S, Hahn S, Janssen OE, et al. Apoptotic markers indicate nonalcoholic steatohepatitis in polycystic ovary syndrome. *J Clin Endocrinol Metab* 2010;95:343-348.
- Li X, Zhang Y, Wu K, Fan D. Serum cytokeratin-18 fragment level: a noninvasive biomarker for not only nonalcoholic steatohepatitis, but also alcoholic steatohepatitis. *Hepatology* 2010;51:1865-1866.

- Cave M, Falkner KC, Ray M, Joshi-Barve S, Brock G, Khan R, Bon Homme M, et al. Toxicant-associated steatohepatitis in vinyl chloride workers. *Hepatology* 2010;51:474-481.
- Papathodoridis GV, Hadziyannis E, Tsochatzis E, Georgiou A, Kafiri G, Tiniakos DG, Margariti K, et al. Serum apoptotic caspase activity in chronic hepatitis C and nonalcoholic Fatty liver disease. *J Clin Gastroenterol* 2010;44:e87-95.
- Herzer K, Kneiseler G, Bechmann LP, Post F, Schlattjan M, Sowa JP, Neumann T, et al. Onset of heart failure determines the hepatic cell death pattern. *Ann Hepatol* 2011;10:174-179.
- Craig DG, Lee P, Pryde EA, Masterton GS, Hayes PC, Simpson KJ. Circulating apoptotic and necrotic cell death markers in patients with acute liver injury. *Liver Int* 2011;31:1127-1136.
- Cave M, Falkner KC, Henry L, Costello B, Gregory B, McClain CJ. Serum cytokeratin 18 and cytokine elevations suggest a high prevalence of occupational liver disease in highly exposed elastomer/polymer workers. *J Occup Environ Med* 2011;53:1128-1133.
- Grattagliano I, Palmieri VO, Portincasa P, Minerva F, Palasciano G. Long-term ursodeoxycholate improves circulating redox changes in primary biliary cirrhotic patients. *Clin Biochem* 2011;44:1400-1404.
- Harrill AH, Roach J, Fier I, Eaddy JS, Kurtz CL, Antoine DJ, Spencer DM, et al. The effects of heparins on the liver: application of mechanistic serum biomarkers in a randomized study in healthy volunteers. *Clin Pharmacol Ther* 2012;92:214-220.
- Joka D, Wahl K, Moeller S, Schlue J, Vaske B, Bahr MJ, Manns MP, et al. Prospective biopsy-controlled evaluation of cell death biomarkers for prediction of liver fibrosis and nonalcoholic steatohepatitis. *Hepatology* 2012;55:455-464.
- Liu H, Han T, Tian J, Zhu ZY, Liu Y, Li Y, Xiao SX, et al. Monitoring oxidative stress in acute-on-chronic liver failure by advanced oxidation protein products. *Hepatol Res* 2012;42:171-180.
- Puls F, Goldschmidt I, Bantel H, Agne C, Brocker V, Dammrich M, Lehmann U, et al. Autophagy-enhancing drug carbamazepine diminishes hepatocellular death in fibrinogen storage disease. *J Hepatol* 2013;59:626-630.
- Singhal R, Harrill AH, Menguy-Vacheron F, Jayyosi Z, Benzerdjeb H, Watkins PB. Benign elevations in serum aminotransferases and biomarkers of hepatotoxicity in healthy volunteers treated with cholestyramine. *BMC Pharmacol Toxicol* 2014;15:42.
- Thulin P, Nordahl G, Gry M, Yimer G, Aklillu E, Makonnen E, Aderaye G, et al. Keratin-18 and microRNA-122 complement alanine aminotransferase as novel safety biomarkers for drug-induced liver injury in two human cohorts. *Liver Int* 2014;34:367-378.
- Denk G, Omary AJ, Reiter FP, Hohenester S, Wimmer R, Holdenrieder S, Rust C. Soluble intracellular adhesion molecule, M30 and M65 as serum markers of disease activity and prognosis in cholestatic liver diseases. *Hepatol Res* 2014;44:1286-1298.
- Reis H, Wohlschlagel J, Hagemann S, Wenzel P, Bechmann LP, Suttorp AC, Schlattjan MJ, et al. (Cleaved) CK18 serum and tissue expression levels differentiate acute HCV reinfection from acute rejection in liver allografts. *Liver Int* 2015;35:905-913.
- Ersoy AO, Kirbas A, Ozler S, Ersoy E, Ozgu-Erdinc AS, Ergin M, Erkaya S, et al. Maternal and fetal serum levels of caspase-cleaved fragments of cytokeratin-18 in intrahepatic cholestasis of pregnancy. *J Matern Fetal Neonatal Med* 2015:1-5.
- Tan S, Vollmar N, Benson S, Sowa JP, Bechmann LP, Gerken G, Fuhrer D, et al. Liver Injury Indicating Fatty Liver but Not Serologic NASH Marker Improves under Metformin Treatment in Polycystic Ovary Syndrome. *Int J Endocrinol* 2015;2015:254169.

- Sekiguchi T, Umemura T, Fujimori N, Shibata S, Ichikawa Y, Kimura T, Joshita S, et al. Serum cell death biomarkers for prediction of liver fibrosis and poor prognosis in primary biliary cirrhosis. *PLoS One* 2015;10:e0131658.
- Karakus S, Bozoklu Akkar O, Yildiz C, Sancakdar E, Cetin M, Cetin A. Serum levels of ET-1, M30, and angiopoietins-1 and -2 in HELLP syndrome and preeclampsia compared to controls. *Arch Gynecol Obstet* 2015:In press.
- Singhal R, Harrill AH, Menguy-Vacheron F, Jayyosi Z, Benzerdjeb H, Watkins PB. Benign elevations in serum aminotransferases and biomarkers of hepatotoxicity in healthy volunteers treated with cholestyramine. *BMC Pharmacol Toxicol* 2014;15:42.
- Woolbright BL, Dorko K, Antoine DJ, Clarke JI, Gholami P, Li F, Kumer SC, et al. Bile acid-induced necrosis in primary human hepatocytes and in patients with obstructive cholestasis. *Toxicol Appl Pharmacol* 2015;283:168-177.
- Masuoka HC VR, Deppe R, Bybee P, Comerford M, Liangpunsakul S, Ghabril M, Chalasani N. Individuals with Primary Sclerosing Cholangitis Have Elevated Levels of Biomarkers for Apoptosis but Not Necrosis. *Dig Dis Sci.* 2015:In press.
- Sadeghi M, Lahdou I, Oweira H, Daniel V, Terness P, Schmidt J, Weiss KH, et al. Serum levels of chemokines CCL4 and CCL5 in cirrhotic patients indicate the presence of hepatocellular carcinoma. *Br J Cancer* 2015;113:756-762.