

BIOGRAPHICAL SKETCH

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NAME Diehl, Anna Mae	POSITION TITLE Florence McAlister Professor of Medicine Chief, Division of Gastroenterology		
eRA COMMONS USER NAME ADIEHL			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Georgetown University	B.S./M.D.	1978	Biology/Medicine
Johns Hopkins University	Intern	1979	Medicine
Johns Hopkins University	Resident	1981	Medicine
Johns Hopkins University	GI Fellow	1984	Gastroenterology

A. Positions and Honors.**Employment and Professional Experience**

7/84-6/87	Assistant Professor, The Uniformed Services University School of Medicine, Bethesda, MD
7/87-6/90	Assistant Professor, Georgetown University, Washington, DC
7/90-3/97	Associate Professor, Gastroenterology Division, Johns Hopkins University, Baltimore, MD
4/97-4/04	Professor, Gastroenterology Division, Johns Hopkins University, Baltimore, MD
4/04-present	Professor, Chief, Gastroenterology Division /Director, Duke Liver Center, Duke University, Durham, NC

Honors

Undergraduate: Phi Beta Kappa, Cum Laude Graduate; Medical School: Alpha Omega Alpha (President), Kober Medal for Academic Excellence, Lange Book Award, Outstanding Performance in Medicine, Outstanding Performance in Surgery, Janet M. Glasgow Award, Summa Cum Laude Graduate; Postgraduate: Editorial Board for Hepatology, NIAAA & VA Study sections; NIH Consensus Panels; NIDDK Scientific Safety Advisory Panel; AASLD/AGA Education Committee (Chair); Board of Directors, American Liver Foundation; Advisory Council, Alcoholic Beverage Medical Research Foundation; American Society for Clinical Investigation; Interurban Clinical Club; Gastroenterology Research Group(President); AASLD Research Committee (Chair), ADHF Policy Committee, NIAAA Advisory Council, Leon Schiff Award for Excellence in Clinical Research (2001), Hans Popper Award for Excellence in Basic Liver Research (2002), Co-Director AGA Post-Graduate Course (2002), Elected Co-Chair of FASEB Summer Conference, Liver Injury and Repair (2002), Moses and Helen Golden Paulson Professorship of Gastroenterology, Johns Hopkins University (2003), Florence McAlister Professor of Medicine, Duke University (2005)

B. Selected peer-reviewed publications (in chronological order from 2000).

1. Lin HZ, Yang SQ, Chuckaree C, Kuhajda F, Ronnet G, **Diehl AM**. Metformin reverses fatty liver disease in obese, leptin-deficient mice. Nat Med 6(9):998-1003, 2000.
2. Cope K, Risby T, **Diehl AM**. Increased gastrointestinal ethanol production in obese mice: implications for fatty liver disease pathogenesis. Gastroenterology 119(5):1340-7, 2000.
3. Guebre-Xabier M, Yang S, Lin HZ, Schwenk R, Krzych U, **Diehl AM**. Altered hepatic lymphocyte subpopulations in obesity-related murine fatty livers: potential mechanism for sensitization to liver damage. Hepatology. 31(3):633-40, 2000.
4. Tilg H, **Diehl AM**. Cytokines in alcoholic and nonalcoholic steatohepatitis. N Engl J Med 343(20):1467-76, 2000.
5. Yang SQ, Lin HZ, Huang J, Chacko VP, **Diehl AM**. Hepatic hyperplasia in noncirrhotic fatty livers: Is obesity-related hepatic steatosis a pre-malignant condition? Cancer Res 61(13):5016-5023, 2001.
6. Yang SQ, Lin HZ, **Diehl AM**. Fatty liver vulnerability to endotoxin-induced damage despite NF-kappaB induction and inhibited caspase 3 activation. Am J Physiol Gastrointest Liver Physiol 28(2): G382-92, 2001.
7. Yang SQ, Lin HZ, Mandal AK, Huang J, **Diehl AM**. Disrupted signaling and inhibited regeneration in obese mice with fatty livers: implications for nonalcoholic fatty liver disease pathophysiology. Hepatology 34(4 Pt 1):694-706, 2001.
8. Koteish A, Yang SQ, Lin HZ, Huang X, **Diehl AM**. Chronic ethanol exposure potentiates lipopolysaccharide liver injury despite inhibiting Jun N-terminal kinase and caspase 3 activation. J Biol Chem 277(15):13037-13044, 2002.

9. Torbenson M, Yang SQ, Lin HZ, Huang J, Gage W, **Diehl AM**. STAT-3 overexpression and p21 up-regulation accompany impaired regeneration of fatty livers. *Am J Pathol* 161(1):155-161, 2002
10. Li Z, Lin H, Yang S, **Diehl AM**. Murine leptin deficiency alters Kupffer cell production of cytokines that regulate the innate immune system. *Gastroenterology* 123:1304-10, 2002.
11. Koteish A, Yang S, Lin H, Huang J, **Diehl AM**. Ethanol induces redox-sensitive cell-cycle inhibitors and inhibits liver regeneration after partial hepatectomy. *Alcohol Clin Exp Res* 26(11):1710-1718, 2002.
12. Oben JA, Yang S, Lin H, Ono M, **Diehl AM**. Acetylcholine promotes the proliferation and collagen gene expression of myofibroblastic hepatic stellate cells. *Biochem Biophys Res Commun* 300(1):172-77, 2003.
13. Li Z, Yang S, Lin H, Huang J, Watkins PA, Moser AB, Desimone C, Song XY, **Diehl AM**. Probiotics and antibodies to TNF inhibit inflammatory activity and improve nonalcoholic fatty liver disease. *Hepatology* 37(2):343-50, 2003.
14. Nair S, P Chacko V, Arnold C, **Diehl AM**. Hepatic ATP reserve and efficiency of replenishing: comparison between obese and nonobese normal individuals. *Am J Gastroenterology* 98(2):466-70, 2003.
15. Oben JA, Yang S, Lin H, Ono M, **Diehl AM**. Norepinephrine and neuropeptide Y promote proliferation and collagen gene expression of hepatic myofibroblastic stellate cells. *Biochem Biophys Res Commun* 302(4):685-90, 2003.
16. Sun Z, Wada T, Maemura K, Uchikura K, Hoshino S, **Diehl AM**, Klein AS. Hepatic allograft-derived Kupffer cells regulate T cell response in rats. *Liver Transpl* 9(5):489-97, 2003.
17. Hughes DE, Stolz DB, Yu S, Tan Y, Reddy JK, Watkins SC, **Diehl AM**, Costa RH. Elevated hepatocyte levels of the Forkhead box A2 (HNF-3beta) transcription factor cause postnatal steatosis and mitochondrial damage. *Hepatology* 37(6):1414-24, 2003.
18. Ogedegbe AE, Thomas DL, **Diehl AM**. Hyperlactataemia syndromes associated with HIV therapy. *Lancet Infect Dis* 3(6):329-37, 2003.
19. Clark JM, **Diehl AM**. Nonalcoholic fatty liver disease: an underrecognized cause of cryptogenic cirrhosis. *JAMA* 289(22):3000-4, 2003.
20. Clark JM, Brancati FL, **Diehl AM**. The prevalence and etiology of elevated aminotransferase levels in the United States. *Am J Gastroenterol* 98(5):960-67, 2003.
21. Sun Z, Klein AS, Radaeva S, Hong F, El-Assal O, Pan HN, Jaruga B, Batkai S, Hoshino S, Tian Z, Kunos G, **Diehl AM**, Gao B. In vitro interleukin-6 treatment prevents mortality associated with fatty liver transplants in rats. *Gastroenterology* 125(1):202-15, 2003.
22. Oben JA, Roskams T, Yang S, Lin H, Sinelli N, Li Z, Torbenson M, Thomas SA, **Diehl AM**. Norepinephrine induces hepatic fibrogenesis in leptin deficient ob/ob mice. *Biochem Biophys Res Commun* 308(2):284-92, 2003.
23. Oben JA, Roskams T, Yang S, Lin H, Sinelli N, Li Z, Torbenson M, Huang J, Guarino P, Kafrouni M, **Diehl AM**. Sympathetic nervous system inhibition increases hepatic progenitors and reduces liver injury. *Hepatology* 38(3):664-73, 2003.
24. Li Z, **Diehl AM**. Innate immunity in the liver. *Curr Opin Gastroenterol.* 19(6):565-71, 2003.
25. Roskams T, Yang SQ, Koteish A, Durnez A, DeVos R, Huang X, Achteng R, Verslype C, **Diehl AM**. Oxidative stress and oval cell accumulation in mice and humans with alcoholic and nonalcoholic fatty liver disease. *Am J Pathol* 163(4):1301-11, 2003.
26. **Diehl AM**, Clarke J, Brancati F. Insulin resistance syndrome and nonalcoholic fatty liver disease. *Endocr Pract* 9(Suppl 2):93-6, 2003.
27. Yang S, Koteish A, Lin H, Huang J, Roskams T, Dawson V, **Diehl AM**. Oval cells compensate for damage and replicative senescence of mature hepatocytes in mice with fatty liver disease. *Hepatology* 39(2):403-11, 2004.
28. Oben JA, Roskams T, Yang S, Lin H, Sinelli N, Torbenson M, Smedh U, Moran TH, Li Z, Huang J, Thomas SA, **Diehl AM**. Hepatic fibrogenesis requires sympathetic neurotransmitters. *Gut* 53(3):438-45, 2004.
29. Persad R, Liu C, Wu TT, Houlihan PS, Hamilton SR, **Diehl AM**, Rashid A. Overexpression of caspase-3 in hepatocellular carcinomas. *Mod Pathol* 17(7):861-7, 2004.
30. Solga, SF, **Diehl AM**. Gut flora-based therapy in liver disease? The liver cares about the gut. *Hepatology* 39(5):1197-200, 2004.
31. Jang YY, Collector MI, Baylin SB, **Diehl AM**, Sharkis SJ. Hematopoietic stem cells convert into liver cells within days without fusion. *Nat Cell Biol* 6(6):532-9, 2004.
32. **Diehl AM**. Fatty liver, hypertension, and the metabolic syndrome. *Gut* 53(7):923-4, 2004.

33. Nair S, **Diehl AM**, Wiseman M, Farr GH Jr, Perrillo RP. Metformin in the treatment of non-alcoholic steatohepatitis: a pilot open laboratory trial. *Aliment Pharmacol Ther* 20(1):23-8, 2004.
34. Gao D, Wei C, Chen L, Huang J, Yang S, **Diehl AM**. Oxidative DNA Damage and DNA Repair Enzyme Expression are Inversely Related in Murine Models of Fatty Liver Disease. *Am J Physiol Gastrointest Liver Physiol* 287(5):G1070-7, 2004.
35. Li A, Oben JA, Yang S, Lin H, Stafford EA, Soloski MJ, Thomas SA, **Diehl AM**. Norepinephrine regulates hepatic innate immune system in leptin-deficient mice with nonalcoholic steatohepatitis. *Hepatology* 40(2):434-41, 2004.
36. Solga S, Alkhuraishe AR, Clark JM, Torbenson M, Greenwald A, **Diehl AM**, Magnuson T. Dietary composition and nonalcoholic fatty liver disease. *Dig Dis Sci* 49(10):1578-83, 2004.
37. **Diehl AM**, Li ZP, Lin HZ, Yang SQ. Cytokines and the pathogenesis of non-alcoholic steatohepatitis. *Gut*. 54(2):303-6, 2005.
38. Kannangai R, **Diehl AM**, Sicklick J, Rojkind M, Thomas D, Torbenson M. Hepatic angiomyolipoma and hepatic stellate cells share a similar gene expression profile. *Hum Pathol*. 36(4):341-7, 2005.
39. Solga SF, Horska A, Clark JM, **Diehl AM**. Hepatic 31P magnetic resonance spectroscopy: a hepatologist's user guide. *Liver Int*. 25(3):490-500, 2005.
40. Clark JM, Alkhuraishe AR, Solga SF, Alli P, **Diehl AM**, Magnuson TH. Roux-en-Y gastric bypass improves liver histology in patients with non-alcoholic fatty liver disease. *Obes Res* 13(7):1180-6, 2005.
41. Sicklick JK, Li YX, Choi SS, Qi Y, Chen W, Bustamante M, Huang J, Zdanowicz M, Camp T, Torbenson MS, Rojkind M, **Diehl AM**. Role for Hedgehog signaling in hepatic stellate cell activation and viability. *Lab Invest*. 85(11):1368-80, 2005.
42. Li Z, Soloski MJ, **Diehl AM**. Dietary factors alter hepatic innate immune system in mice with nonalcoholic fatty liver disease. *Hepatology* 42(4):880-5, 2005.
43. Sicklick JK, Li YX, Melhem A, Schmelzer E, Zdanowicz M, Huang J, Caballero M, Fair JH, Ludlow JW, McClelland RE, Reid LM, **Diehl AM**. Hedgehog signaling maintains resident hepatic progenitors throughout life. *Am J Physiol Gastrointest Liver Physiol* 290(5): G859-70, 2006.
44. Sicklick JK, Li YX, Jayaraman A, Kannangai R, Qi Y, Vivekanandan P, Ludlow JW, Owzar K, Chen W, Torbenson MS, **Diehl AM**. Dysregulation of the Hedgehog pathway in human hepatocarcinogenesis. *Carcinogenesis* 27(4): 748-57, 2006.
45. Sicklick JK, Choi SS, Bustamante M, McCall SJ, Hernandez Perez E, Huang J, Li YX, Rojkind M, **Diehl AM**. Evidence for Epithelial-Mesenchymal Transitions in Adult Liver Cells. *Am J Physiol Gastrointest Liver Physiol* 291(4):G575-83, 2006.
46. Suzuki A, McCall S, Choi SS, Sicklick JK, Huang J, Qi Y, Zdanowicz M, Camp T, Li YX and **Diehl AM**. Interleukin-15 increases hepatic regenerative activity. *J Hepatol*. 45(3): 410-8, 2006.
47. Zhao C, Chen W, Yang L, Chen L, Stimpson SA, **Diehl AM**. PPARgamma agonists prevent TGFbeta1/Smad3-signaling in human hepatic stellate cells. *Biochem Biophys Res Commun*. 350(2):385-91, 2006.
48. Choi SS, Sicklick JK, Ma Q, Yang L, Huang J, Qi Y, Chen W, Li YX, Goldschmidt-Clermont PJ, **Diehl AM**. Sustained activation of Rac1 in hepatic stellate cells promotes liver injury and fibrosis in mice. *J Hepatol*. 44(5):1267-77, 2006.
49. Li YX, Yang HT, Danowicz M, Sicklick JK, Qi Y, Camp T and **Diehl AM**. Fetal Alcohol Exposure Impairs Hedgehog Cholesterol Modification and Signaling. *Laboratory Investigation*, 87(3):231-40, 2007.
50. Omenetti A, Yang L, Li YX, McCall SJ, Sicklick JK, Huang J, Choi S, Suzuki A and **Diehl AM**. Hedgehog mediated mesenchymal-epithelial interactions modulate hepatic response to bile duct ligation. *Laboratory Investigation*. 87(5):499-514, 2007.
51. Jung Y, McCall SS, Li YX, **Diehl AM**. Bile ductules and stromal cells express hedgehog ligands and/or hedgehog target genes in primary biliary cirrhosis. *Hepatology*. 45(5):1091-6, 2007.
52. Abdelmalek MF, **Diehl AM**. De Novo nonalcoholic fatty liver disease after liver transplantation. *Liver Transpl*. 13(6):788-790, 2007.
53. Yamaguchi K, Yang L, McCall S, Huang J, Yu XX, Pandey SK, Bhanot S, Monia BP, Li YX, **Diehl AM**. Inhibiting Triglyceride Synthesis Improves Hepatic Steatosis but Exacerbates Liver Damage and Fibrosis in Obese Mice with Nonalcoholic Steatohepatitis. *J Hepatol*. 45(6):1366-1374, 2007.
54. Yang L, Jhaveri R, Huang J, Qi Y, **Diehl AM**. Endoplasmic reticulum stress, hepatocyte CD1d and NKT cell abnormalities in murine fatty livers. *Lab Invest*. 87(9):927-37, 2007.
55. Fleig SV, Choi SS, Yang L, Jung Y, Omenetti A, Vandongen HM, Huang J, Sicklick JK, Diehl AM. Hepatic

accumulation of Hedgehog-reactive progenitors increases with severity of fatty liver damage in mice. Lab Invest. 2007 Oct 22; [Epub ahead of print].

C. Research Support

Active

Role of TNF alpha in Recovery from Alcoholic Liver Injury

Principal Investigator: Anna Mae Diehl

Agency: NIMH/NIDA/NIAAA

Type: RO1 AA10154

Period: 08/01/1994 - 07/31/09

Aim: To determine mechanisms that regulates TNF alpha induction and the hepatic responses to this cytokine during liver regeneration in normal and alcohol-fed mice.

Liver Disease in Obesity

Agency: NIDDK/NIH

Principal Investigator: Anna Mae Diehl

Type: RO1 DK53792

Period: 09/30/99 - 03/31/09

Aim: To determine the immunologic mechanisms for nonalcoholic fatty liver disease.

Metabolic Profiling to Identify Alcohol Biomarker Signature

Principal Investigator: Yin-Xiong Li (Anna Mae Diehl: Co-Investigator)

Agency: NIAAA/NIH

Type: R21 AA016144-01

Period: 06/01/06-05/30/08

The aim of this project is to determine whether alcohol disturbs the homeostasis of lipid metabolism and generates a molecular-metabolic fingerprint.

NASH Clinical Research Network

Principal Investigator: Anna Mae Diehl

Agency: NIH/NIDDK

Type: U01 DK61713

Period: 05/01/02 - 03/31/09

Aim: This is a multi-institutional clinical center grant to study NAFLD in patients.

Duke University High-throughput Screening Center

Principal Investigator: Marc Caron (Anna Mae Diehl: Collaborator)

Agency: NIH/NIDA

Type: U01-DA022950-01

Period: 09/30/06 – 06/30/09

To identify small molecules that modulate G-protein coupled receptors that is of interest in drug abuse.

Quantifying Liver Fibrosis with Acoustic Radiation Force

Principal Investigator: Katherine Nightingale (Anna Mae Diehl: Co-Investigator)

Agency: NIH/NIBIB

Type: R01 EB-002132

Period: 06/01/07 – 03/31/11

The goal of this project is to develop radiation force based methods for quantification of tissue shear modulus for the purpose of staging liver fibrosis.

Cholesterol, Hedgehog Signaling & Fetal Alcohol Syndrome

Principal Investigator: Yin-Xiong Li (Anna Mae Diehl: Co-Investigator)

Agency: NIAAA/NIH

Type: R21 AA-016001-01

Period: 09/28/07 – 08/31/09

To establish a model of defective cholesterol biosynthesis, to evaluate the influence of alcohol exposure on the cholesterol homeostasis and cholesterol modification of Hh ligand, and to determine whether activating Hh signaling or administering exogenous free cholesterol can rescue alcohol-induced embryonic developmental defects.

Completed

Fatty Liver Disease and Hepatic Energy Homeostasis in SHOW (Look AHEAD)

Ancillary Study to Look AHEAD Trial

Principal Investigator: Jeanne Clark (Anna Mae Diehl: collaborator, subcontract Duke/JHU -- Effective 4/04 Dr. Diehl reduced her effort and re-assigned the PI role to Dr. Jeanne Clark, at JHU).

Agency: NIDDK/NIH

Type: RO1 DK60427-03

Period: 07/01/01 – 6/30/06

Aim: To evaluate hepatic ATP stores in humans with different stages of nonalcoholic fatty liver disease

Bioenergetics and Alcoholic Liver Disease Pathogenesis

Principal Investigator: Anna Mae Diehl

Agency: NIAAA/NIH

Type: RO1 AA12059

Period: 05/01/00 – 04/30/06

Aim: To evaluate the role of uncoupling proteins in alcoholic liver injury in mice.

Environmental regulation of liver progenitors in zebrafish model of hepatocarcinogenesis

Principal Investigator: Yin-Xiong Li (Anna Mae Diehl: co-investigator)

Agency: Duke DCCC/NSOE

Type: Stanback Award

Period: 12/01/05 -11/30/06

To develop a progenitor cell model of HCC in zebrafish, and, to manipulate the activities of signaling pathways that promote progenitor cell viability, proliferation, and assess the impact on hepatocarcinogenesis.