



### References related to NAFLD, NASH and liver fibrosis

van den Hoek AM, Pieterman EJ, van der Hoorn JW, Iruarrizaga-Lejarreta M, Alonso C, Verschuren L, Skjæret T, Princen HMG, Fraser DA. Icosabutate exerts beneficial effects upon insulin sensitivity, hepatic inflammation, lipotoxicity and fibrosis in mice. **Hepatol Comm** 2020; 4: 193-207. doi:10.1002/hep4.1453 \*

Salic K, Gart E, Seidel F, Verschuren L, Caspers M, van Duyvenvoorde W, Wong KE, Keijer J, Bobeldijk-Pastorova I, Wielinga PY, Kleemann R. Combined treatment with L-carnitine and nicotinamide riboside improves hepatic metabolism and attenuates obesity and liver steatosis. **Int J Mol Sci** 2019; 20(18). pii: E4359. doi: 10.3390/ijms20184359.

Salic K, Kleemann R, Wilkins-Port C, McNulty J, Verschuren L, Palmer M. Apical sodium-dependent bile acid transporter inhibition with volixibat improves metabolic aspects and components of nonalcoholic steatohepatitis in Ldlr<sup>-/-</sup>.Leiden mice. **PLoS One** 2019; 14(6): e0218459. doi.org/10.1371/journal.pone.0218459. eCollection 2019. \*

Jacobs SAH, Gart E, Vreeken D, Franx BAA, Wekking L, Verweij VGM, Worms N, Schoemaker MH, Gross G, Morrison MC, Kleemann R, Arnoldussen IAC, Kiliaan AJ. Sex-specific differences in fat storage, development of non-alcoholic fatty liver disease and brain structure in juvenile HFD-induced obese Ldlr<sup>-/-</sup>.Leiden mice. **Nutrients** 2019; 11: 1861; doi:10.3390/nu11081861.

Abe N, Kato S, Tsuchida T, Sugimoto K, Saito R, Verschuren L, Kleemann R, Oka K. Longitudinal characterization of diet-induced genetic murine models of non-alcoholic steatohepatitis with metabolic, histological, and transcriptomic hallmarks of human patients. **Biol Open** 2019; 1; 8(5). pii: bio041251. doi: 10.1242/bio.041251. \*

Gart E, Souto Lima E, Schuren F, de Ruiter CGF, Attema J, Verschuren L, Keijer J, Salic K, Morrison MC, Kleemann R. Diet-independent correlations between bacteria and dysfunction of gut, adipose tissue, and liver: A comprehensive microbiota analysis in feces and mucosa of the ileum and colon in obese mice with NAFLD. **Int J Mol Sci** 2019; 20: 1. doi:10.3390/ijms200100.

Pouwer MG, Heinonen SE, Behrendt M, Andréasson AC, van Koppen A, Menke AL, Pieterman EJ, van den Hoek AM, Jukema JWJ, Leighton B, Jönsson- Rylander AC, Princen HMG. The APOE\*3-Leiden.heterozygous glucokinase knockout mouse as novel translational disease model for type 2 diabetes, dyslipidemia and diabetic atherosclerosis. **J Diab Res** 2019; Article ID 9727952. doi.org/10.1155/2019/9727952 \*

Morrison MC, Verschuren L, Salic K, Verheij J, Menke A, Wielinga PY, Iruarrizaga-Lejarreta M, Gole L, Yu WM, Turner S, Caspers MPM, Martínez-Arranz I, Pieterman E, Stoop R, van Koppen A, van den Hoek AM, Mato JM, Hanemaaijer R, Alonso C, Kleemann R. Obeticholic acid modulates serum metabolites and gene signatures characteristic of human NASH and attenuates inflammation and fibrosis progression in Ldlr<sup>-/-</sup>.Leiden mice. **Hepatol Commun** 2018. DOI 10.1002/hep4.1270. eCollection 2018 Sept.

Morrison MC, Kleemann R, van Koppen A, Hanemaaijer R, Verschuren L. Key inflammatory processes in human NASH are reflected in Ldlr<sup>-/-</sup>.Leiden mice: a translational gene profiling study. **Front Physiol** 2018 Feb 23;9:132. doi: 10.3389/fphys.2018.00132. eCollection 2018.

van Koppen A, Verschuren L, van den Hoek AM, Verheij J, Morrison MC, Li K, Nagabukuro H, Costessi A, Caspers MPM, van den Broek TJ, Sagartz J, Kluft C, Beysen C, Emson C, van Gool AJ, Goldschmeding R, Stoop R, Bobeldijk-Pastorova I, Turner SM, Hanauer G, Hanemaaijer R. Uncovering a Predictive Molecular Signature for the Onset of NASH-Related Fibrosis in a Translational NASH Mouse Model. **Cell Mol Gastroenterol Hepatol** 2017 Oct 14;5(1):83-98.e10. doi: 10.1016/j.jcmgh.2017.10.001. eCollection 2018.

Schoemaker MH, Kleemann R, Morrison MC, Verheij J, Salic K, van Tol EAF, Kooistra T, Wielinga PY. A casein hydrolysate based formulation attenuates obesity and associated non-alcoholic fatty liver disease and atherosclerosis in LDLr<sup>-/-</sup>.Leiden mice. **PLoS One** 2017; 12: e0180648. doi: 10.1371/journal.pone.0180648. \*

Zimmer M, Bista P, Benson EL, Lee DY, Liu F, Picarella D, Vega RB, Vu CB, Yeager M, Ding M, Liang G, Horton JD, Kleemann R, Kooistra T, Morrison MC, Wielinga PY, Milne JC, Jirousek MR, Nichols AJ. CAT-2003: A novel sterol regulatory element-binding protein inhibitor that reduces steatohepatitis, plasma lipids, and atherosclerosis in apolipoprotein E\*3-Leiden mice. **Hepatol Commun** 2017 May 12;1(4):311-325. doi: 10.1002/hep4.1042. eCollection 2017 Jun. \*



Mulder P, van den Hoek AM, Kleemann R. The CCR2 inhibitor propagermanium attenuates diet-induced insulin resistance, adipose tissue inflammation and non-alcoholic steatohepatitis. **PLoS One** 2017; 12: e0169740. doi: 10.1371/journal.pone.0169740.

Mulder P, Morrison MC, Verschuren L, Liang W, van Bockel JH, Kooistra T, Wielinga PY, Kleemann R. Reduction of obesity-associated white adipose tissue inflammation by rosiglitazone is associated with reduced non-alcoholic fatty liver disease in LDLr-deficient mice. **Sci Rep** 2016; 6: 31542. doi: 10.1038/srep31542

Morrison MC, Mulder P, Salic K, Verheij J, Liang W, van Duyvenvoorde W, Menke A, Kooistra T, Kleemann R, Wielinga PY. Intervention with a caspase-1 inhibitor reduces obesity-associated hyperinsulinemia, non-alcoholic steatohepatitis (NASH) and hepatic fibrosis in LDLR-/-Leiden mice. **Int J Obes (Lond)** 2016; 40: 1416-1423. doi: 10.1038/ijo.2016.74.

Mulder P, Morrison MC, Wielinga PY, van Duyvenvoorde W, Kooistra T, Kleemann R. Surgical removal of inflamed epididymal white adipose tissue attenuates the development of non-alcoholic steatohepatitis in obesity. **Int J Obes (Lond)** 2016 Apr;40(4):675-84. doi: 10.1038/ijo.2015.226. Epub 2015 Oct 26.

Liang W, Verschuren L, Mulder P, van der Hoorn JW, Verheij J, van Dam AD, Boon MR, Princen HM, Havekes LM, Kleemann R, van den Hoek AM. Salsalate attenuates diet induced non-alcoholic steatohepatitis in mice by decreasing lipogenic and inflammatory processes. **Br J Pharmacol** 2015; 172: 5293-5305. doi: 10.1111/bph.13315.

Morrison MC, Mulder P, Stavro PM, Suárez M, Arola-Arnal A, van Duyvenvoorde W, Kooistra T, Wielinga PY, Kleemann R. Replacement of dietary saturated fat by PUFA-rich pumpkin seed oil attenuates non-alcoholic fatty liver disease and atherosclerosis development, with additional health effects of virgin over refined oil. **PLoS One** 2015;10:e0139196. doi: 10.1371/journal.pone.0139196. \*

Morrison M, Liang W, Mulder P, Toet K, Heeringa P, Wielinga P, Kooistra T, Kleemann R. Mirtoselect, an anthocyanin-rich bilberry extract, attenuates non-alcoholic steatohepatitis and associated fibrosis in ApoE\*3Leiden mice. **J Hepatol** 2015; 62: 1180-1186. doi: 10.1016/j.jhep.2014.12.011.

Morrison MC, Kleemann R. Role of macrophage migration inhibitory factor in obesity, insulin resistance, type 2 diabetes, and associated hepatic co-morbidities: a comprehensive review of human and rodent studies. **Front Immunol** 2015; 15: 308. doi: 10.3389/fimmu.2015.00308

van der Heijden RA, Sheedfar F, Morrison MC, Hommelberg PP, Kor D, Kloosterhuis NJ, Gruben N, Youssef SA, de Bruin A, Hofker MH, Kleemann R, Koonen DP, Heeringa P. High-fat diet induced obesity primes inflammation in adipose tissue prior to liver in C57BL/6j mice. **Aging (Albany NY)** 2015;7:256-68.

Liang W, Menke AL, Driessen A, Koek GH, Lindeman JH, Stoop R, Havekes LM, Kleemann R, van den Hoek AM. Establishment of a general NAFLD scoring system for rodent models and comparison to human liver pathology. **PLoS ONE** 2014; 9: e115922. doi: 10.1371/journal.pone.0115922.

Liang W, Lindeman JH, Menke AL, Koonen DP, Morrison M, Havekes LM, van den Hoek AM, Kleemann R. Metabolically induced liver inflammation leads to NASH and differs from LPS- or IL-1b-induced chronic inflammation. **Lab Invest** 2014; 94: 491-502. doi:10.1038/labinvest.2014.11.

Van den Hoek AM, van der Hoorn JWA, Maas AC, van den Hoogen RM, van Nieuwkoop A, Droog S, Offerman EH, Pieterman EJ, Havekes LM, Princen HMG. APOE\*3Leiden.CETP transgenic mice as model for pharmaceutical treatment of the Metabolic Syndrome. **Diabet Obes Metab** 2014; 16: 537-544.

Wang Y, Parlevliet ET, Geerling JJ, van der Tuin SJ, Zhang H, Bieghs V, Jawad AH, Shiri-Sverdlov R, Bot I, de Jager SC, Havekes LM, Romijn JA, Willems van Dijk K, Rensen PC. Exendin-4 decreases liver inflammation and atherosclerosis development simultaneously by reducing macrophage infiltration. **Br J Pharmacol** 2014; 171: 723-34. doi: 10.1111/bph.12490.

Nachabé R, van der Hoorn JW, van de Molengraaf R, Lamerichs R, Pikkemaat J, Sio CF, Hendriks BH, Sterenborg HJ. Validation of interventional fiber optic spectroscopy with MR spectroscopy, MAS-NMR spectroscopy, high-performance thin-layer chromatography, and histopathology for accurate hepatic fat quantification. **Invest Radiol** 2012 Apr;47(4):209-16. \*

Van Ginneken V, Verhey E, Poelmann R, Ramakers R, van Dijk KW, Ham L, Voshol P, Havekes L, Van Eck M, van der Greef J. Metabolomics (liver and blood profiling) in a mouse model in response to fasting: a study of hepatic



steatosis. **Biochim Biophys Acta** 2007; 1771: 1263-1270.

den Boer M, Voshol PJ, Kuipers F, Havekes LM, Romijn JA. Hepatic steatosis: a mediator of the metabolic syndrome. Lessons from animal models. **Arterioscler Thromb Vasc Biol** 2004; 24: 644-649.