

## PERSONAL INFORMATION

Hendrikx Tim, PhD

Email: tim.hendrikx@meduniwien.ac.at

ORCID: <https://orcid.org/0000-0002-3381-2107>

Date and place of birth: March 25, 1986; Bree, Belgium

## CURRENT POSITION

Principal Investigator 4/2019 – present

Medical University Vienna, Dep. Laboratory Medicine, Vienna, AT

- Investigate mechanisms of steatotic liver disease in mice and human
- Assess gut humoral immunity in metabolic disease and atherosclerosis

## PREVIOUS POSITIONS

Postdoctoral fellow (*Erwin-Schrodinger Fellowship*) 2/2017 – 4/2019

Prof. B. Schnabl, University of California San Diego, Dep. Of Medicine, Division of

Gastroenterology, San Diego, USA

- Study host-microbiome crosstalk and the gut-liver axis during alcoholic liver disease
- Decipher the role of fungi in NASH development

Postdoctoral fellow (*Kootstra Fellowship*) 2/2015 – 12/2016

Prof. C. Binder, MUW, Dep. of Medical and Chemical Laboratory Diagnostics, Vienna, AT

- Identify natural antibodies as biomarkers for NAFLD
- Study oxidized lipids and humoral immunity in metabolic inflammation

PhD fellow 9/2010 – 2/2015

Maastricht University, Dep. Of Molecular Genetics, Maastricht, NL

Supervisor: Prof. R. Shiri-Sverdlov

Title PhD thesis: 'Intracellular traffic jam: cholesterol accumulation as cause for chronic inflammatory diseases'

- Study molecular mechanisms underlying lipid-induced NASH and atherosclerosis
- Explore intracellular pathways triggering inflammation in isolated macrophages

## EDUCATION

Master Biomedical Sciences, Clinical Molecular Life Sciences, 2008 – 2010

Hasselt University, Diepenbeek, Belgium

## GRANTS/ FELLOWSHIPS

WEAVE Project, FWF, AT;	398.128 €	01/2024 – 01/2028
Stand Alone Project, FWF, AT;	404.222 €	03/2023 – 03/2026
Zukunftkollegs, FWF, AT;	463.000 € (2.351.000 €)	11/2020 – 05/2025
'Right-On-Time' grant, MLDS, NL;	185.000 €	11/2020 – 11/2022
VENI grant, NWO, NL;	250.000 €	4/2019 – 4/2022
Erwin Schrödinger Fellowship, FWF, AT;	175.000 €	4/2017 – 4/2020
Andrew K. Burroughs Short Term Fellowship, EASL;	6.000 €	7/2016 – 10/2016
Kootstra Postdoc Fellow, NWO, NL;	55.000 €	2/2015 – 2/2016
EMBO Short Term Fellow;	5.000 €	5/2014 – 9/2014
Boehringer Ingelheim Fonds Travel Grant;	3.000 €	12/2013 – 4/2014

## SCIENTIFIC AWARDS

Helmut-Sinzinger Preis, Gesellschaft der Ärzte Wien, AT	2023
Researcher of the Month, MUW Vienna, AT	2023
Dora Brücke-Teleky Award, MUW Vienna, AT	2023
Abstract Award, EGIR-NAFLD Study groups Webinar	2022
Abstract Award, Center for ALPD and Cirrhosis, Los Angeles, USA	2018
Basic Science YI Travel Award, AASLD meeting, San Francisco, USA	2018
Abstract Award, Keystone meeting, Banff, CA	2018
Young Investigator Bursary, Monothematic NASH, EASL, Riga, LV	2016
Young Investigator Bursary, EASL meeting, Barcelona, ES	2016
Young Investigator Bursary, EASL meeting, Vienna, AT	2015
Dr. Jan Huynen Award for top 5 PhD thesis, NL	2015
Poster Award NVH Symposium, NL	2014
Proposal "So you think you can heal the liver", Dutch Liver Retreat, NL	2013
Poster Award, NUTRIM Symposium, NL	2012
Poster Award, Plenary meeting Genetics and Cell Biology, NL	2012
Dr. Jan Huynen Award for best Master thesis in Life Sciences, NL	2011

## ADDITIONAL COURSES AND CERTIFICATES

Managing teams and engaging in successful collaborations, UC San Diego, USA	2018
Strategic planning and academic time management, UC San Diego, USA	2017
Becoming a successful and effective science writer, UC San Diego, USA	2017
Tutor teaching course, Maastricht University, NL	2012
Article 9, Working with animals, Maastricht University, NL	2010
Radiation protection, University Hasselt, BE	2009
Working with animals, FELASA "C" module 1, University Hasselt, BE	2008

## REVIEWING ACTIVITIES

*Ad hoc* reviewer for multiple international peer-reviewed journals including *Frontiers of Immunology*, *Gut*, *Hepatology* and *Journal of Hepatology*.

## SUPERVISION OF GRADUATE STUDENTS AND FELLOWS

Supervisor of 3 PhD students and Co-supervisor of 1 PhD & 2 Diploma students, MU Vienna, Vienna, AT	2019 – present
Co-supervisor of 1 Diploma student, UC San Diego, San Diego, USA	2018 – 2019
Co-supervisor of 2 PhD & 1 Diploma student, MU Vienna, Vienna, AT	2014 – 2016
Co-supervisor of 3 PhD students, 2 research assistants & 6 Diploma students, Maastricht University, Maastricht, NL	2011 – 2014

## TEACHING ACTIVITIES

Lecturer – Endocrinology/Vascular Biology PhD program Topic: Dietary effects on microbiome in health and disease, MU Vienna, AT	2019 – present
Practical basic science seminar – Endocrinology PhD program MU Vienna, AT	2019 – present
Tutor – Master and Bachelor students Molecular Life Sciences at Maastricht University, NL	2012 – 2014

## PUBLICATION LIST

1. C Hoebinger, D Rajcic, **T Hendriks**. Chronic-binge ethanol feeding aggravates systemic dyslipidemia in Ldlr<sup>-/-</sup> mice, thereby accelerating hepatic fibrosis. *Front. Endocrinol., Sec. Cellular Endocrinology* Volume 14 – 2023. doi.org/10.3389/fendo.2023.1148827
2. MG Kiss, N Papac-Miličević, F Porsch, D Tsiantoulas, **T Hendriks**, M Takaoka, HQ Dinh, MS Narzt, L Göderle, M Ozsvár-Kozma, M Schuster, N Fortelny, A Hladik, S Knapp, F Gruber, MC Pickering, C Bock, FK Swirski, K Ley, A Zerneck, C Cochain, C Kemper, Z Mallat, CJ Binder. Cell-autonomous regulation of complement C3 by factor H limits macrophage efferocytosis and exacerbates atherosclerosis. *Immunity*. 2023 Jul 18;S1074-7613(23)00283-2. doi: 10.1016/j.immuni.2023.06.026.
3. **T Hendriks**, S Lang, D Rajcic, Y Wang, S McArdle, K Kim, Z Mikulski, B Schnabl. Hepatic plgR-mediated secretion of IgA limits bacterial translocation and prevents ethanol-induced liver disease in mice. *Gut* 2023 Jan 23;gutjnl-2022-328265. doi: 10.1136/gutjnl-2022-328265
4. **T Hendriks\***, F Porsch\*, MG Kiss, D Rajcic, N Papac-Miličević, C Hoebinger, L Göderle, A Hladik, LE Shaw, H Horstmann, S Knapp, S Derdak, M Bilban, L Heintz, M Krawczyk, R Paternostro, M Trauner, M Farlik, D Wolf, CJ Binder. Soluble TREM2 levels reflect the recruitment and expansion of TREM2<sup>+</sup> macrophages that localize to fibrotic areas and limit NASH. *J of Hepatology* 2022 Nov;77(5):1373-1385. doi: 10.1016/j.jhep.2022.06.004.
5. CD Fuchs, ED Dixon, **T Hendriks**, V Mlitz, A Wahlström, M Ståhlman, H Scharnagl, T Stojakovic, CJ Binder, H-U Marschall, M Trauner. Tetrahydroxylated bile acids improve cholestatic liver and bile duct injury in the Mdr2<sup>-/-</sup> mouse model of sclerosing cholangitis via immunomodulatory effects. *Hepatol Commun*. 2022 Sep;6(9):2368-2378. doi: 10.1002/hep4.1998.
6. C Hoebinger, D Rajcic, **T Hendriks**. Oxidized Lipids: Common Immunogenic Drivers of Non-Alcoholic Fatty Liver Disease and Atherosclerosis. *Front Cardiovasc Med*. 2022 Jan 10;8:824481. doi: 10.3389/fcvm.2021.824481.
7. Y Duan, H Chu, K Brandl, L Jiang, S Zeng, N Meshgin, E Papachristoforou, J Argemi, B Mendes, Y Wang, H Su, W Sun, C Llorente, **T Hendriks**, X Liu, M Hosseini, T Kisseleva, D Brenner, R Bataller, P Ramachandran, M Karin, W Fu, B Schnabl. CRlg on liver macrophages clears pathobionts and protects against alcoholic liver disease. *Nat Commun* 2021 Dec 9;12(1):7172. doi: 10.1038/s41467-021-27385-3.
8. D Tsiantoulas, M Eslami, G Obermayer, M Clement, D Smeets, FJ Mayer, MG Kiss, L Enders, J Weißer, L Göderle, J Lambert, F Frommlet, A Mueller, **T Hendriks**, M Ozsvár-Kozma, F Porsch, L Willen, T Afonyushkin, JE Murphy, P Fogelstrand, O Donzé, G Pasterkamp, M Hoke, S Kubicek, HF Jørgensen, N Danchin, T Simon, H Scharnagl, W März, J Borén, H Hess, Z Mallat, P Schneider, CJ Binder. APRIL limits atherosclerosis by binding to heparan sulfate proteoglycans. *Nature*. 2021 Sep;597(7874):92-96. doi: 10.1038/s41586-021-03818-3.
9. R Shiri-Sverdlov, IM Dos Reis, Y Oligschläger, **T Hendriks**, DM Meesters, A Vanclooster, N Vanhoutvin, GH Koek, M Westerterp, CJ Binder, D Cassiman, T Houben. The Influence of a Conjugated Pneumococcal Vaccination on Plasma Antibody Levels against Oxidized Low-Density Lipoprotein in Metabolic Disease Patients: A Single-Arm Pilot Clinical Trial. *Antioxidants (Basel)*. 2021 Jan 18;10(1):129. doi: 10.3390/antiox10010129.
10. **T Hendriks**, CJ Binder. Oxidation-specific epitopes in non-alcoholic fatty liver disease. *Front. Endocrinol*. 2020 December. doi.org/10.3389/fendo.2020.607011.

11. **T Hendriks**, Y Duan, Y Wang, JH Oh, LM Alexander, W Huang, P Stärkel, SB Ho, B Gao, O Fiehn, P Emond, H Sokol, JP van Pijkeren, B Schnabl. Bacteria engineered to produce IL-22 in intestine induce expression of REG3G to reduce ethanol-induced liver disease in mice. *Gut*. 2019 Aug;68(8):1504-1515. doi: 10.1136/gutjnl-2018-317232.
12. **T Hendriks**, B Schnabl. Antimicrobial proteins: intestinal guards to protect against liver disease. *J Gastroenterol*. 2019 Mar;54(3):209-217. doi: 10.1007/s00535-018-1521-8.
13. **T Hendriks**, B Schnabl. Indoles: metabolites produced by intestinal bacteria capable of controlling liver disease. *J Intern Med*. 2019 Mar 14. doi: 10.1111/joim.12892.
14. T Houben, I Magro dos Reis, H Steinbusch, M JJ Gijbels, **T Hendriks**, C J Binder, D Cassiman, J Prickaerts, R Shiri-Sverdlov. Pneumococcal immunization reduces neurological and systemic symptoms in a mouse model for Niemann-Pick type C1. *Front Immunol*. 2019 Jan 7;9:3089. doi: 10.3389/fimmu.2018.03089.
15. K Reesink, **T Hendriks**, P J van Gorp, A Hoeks, R Shiri-Sverdlov. Ultrasonic perfluorohexane-loaded monocyte imaging: Towards a minimally invasive technique for selective detection of liver inflammation in fatty liver disease. *J Ultrasound Med*. 2018 Apr;37(4):921-933. doi: 10.1002/jum.14432.
16. **T Hendriks**, B Schnabl. Lamin deficiency in the liver sets the stage for NASH development in men. *Clinical Gastroenterol Hepatol*, 2017 Sep 18;4(3):441-442. doi: 10.1016/j.cmg.2017.09.002.
17. T Houben, Y Oligschläger, A Bitorina, **T Hendriks**, S Walenbergh, M-H Lenders, M Gijbels, F Verheyen, D Lütjohann, M Hofker, C Binder, R Shiri-Sverdlov. Blood-derived macrophages prone to accumulate lysosomal lipids trigger oxLDL-dependent murine hepatic inflammation. *Sci Rep*. 2017 Oct 2;7(1):12550. doi: 10.1038/s41598-017-13058-z.
18. S Jäckel, M Lillich, K Kiouptsi, E Wilms, **T Hendriks**, A Khandagale, N Hörmann, C Reiss, S Subramaniam, B Kollar, K Ebner, B Lämmle, M von Brühl, P Rausch, S Haberichter, J F Baines, C J Binder, K Jurk, Z M Ruggeri, S Massberg, U Walter, W Ruf, and C Reinhardt. Gut microbiota regulate hepatic von Willebrand Factor synthesis and arterial thrombus formation via Toll-like receptor-2. *Blood*. 2017 Jul 27;130(4):542-553. doi: 10.1182/blood-2016-11-754416.
19. T Houben, Y Oligschlaeger, **T Hendriks**, A Bitorina, S MA Walenbergh, P J van Gorp, M Gijbels, S Friedrichs, J Plat, F Schaap, D Luetjohann, R Shiri-Sverdlov. Cathepsin D regulates lipid metabolism in murine steatohepatitis. *Sci Rep*, 2017 Jun 14;7(1):3494. doi: 10.1038/s41598-017-03796-5.
20. C JL Busch\*, **T Hendriks**\*, D Weismann, S Jackel, S MA Walenbergh, A F Rendeiro, J Weisser, F Puhm, A Hladik, L Goderle, N Papac-Milicevic, G Haas, V Millischer, S Subramaniam, S Knapp, K L Bennett, C Bock, C Reinhardt, R Shiri-Sverdlov, C J Binder. Malondialdehyde epitopes are sterile mediators of hepatic inflammation in hypercholesterolemic mice. *Hepatology*, 2016 Dec 16. doi: 10.1002/hep.28970.
21. S MA Walenbergh, T Houben, S Rensen, V Bieghs, **T Hendriks**, P J van Gorp, Y Oligschlaeger, M LJ Jeurissen, M Gijbels, W A Buurman A Vreugdenhil, JW Greve, J Plat, M H Hofker, S Kalhan, J Pihlajamaki, P J Lindsey, G H Koek, R Shiri-Sverdlov. Plasma cathepsin D correlates with histological classifications of fatty liver disease in adults and responds to intervention. *Sci Rep*. 2016 Dec 6;6:38278. doi: 10.1038/srep38278.
22. ML Jeurissen, SM Walenbergh, T Houben, **T Hendriks**, J Li, Y Oligschlaeger, PJ van Gorp, MJ Gijbels, A Bitorina, I Nessel, F Radtke, M Vooijs, J Theys, R Shiri-Sverdlov. Myeloid DLL4 Does Not Contribute to the Pathogenesis of Non-Alcoholic

- Steatohepatitis in *Ldlr*<sup>-/-</sup> Mice. *PLoS One*. 2016 Nov 29;11(11):e0167199. doi: 10.1371/journal.pone.0167199.
23. M LJ Jeurissen, S MA Walenbergh, T Houben, M Gijbels, J Li, **T Hendriks**, Y Oligschlaeger, P J van Gorp, C J Binder, M Donners, R Shiri-Sverdlov. Prevention of oxLDL uptake leads to decreased atherosclerosis in hematopoietic NPC1-deficient *Ldlr*<sup>-/-</sup> mice. *Atherosclerosis*. 2016 Dec;255:59-65. doi: 10.1016/j.atherosclerosis.2016.10.038.
  24. **T Hendriks**, M L Watzenböck, S MA Walenbergh, S Amir, S Gruber, M Ozsvar Kozma, H I Grabsch, G H Koek, M J Pierik, K Stauffer, M Trauner, S Kalhan, D Jonkers, M H Hofker, C J Binder, R Shiri-Sverdlov. Low levels of IgM antibodies recognizing oxidation-specific epitopes are associated with human non-alcoholic fatty liver disease. *BMC Med*. 2016 Jul 22;14(1):107 doi: 10.1186/s12916-016-0652-0.
  25. S Gruber, **T Hendriks**, D Tsiantoulas, M Ozsvar Kozma, L Göderle, JL Witztum, Z Mallat, R Shiri-Sverdlov, L Nitschke, CJ Binder. Sialic acid-binding immunoglobulin-like lectin G promotes atherosclerosis and liver inflammation by suppressing the protective functions of B-1 cells. *Cell Rep*. 2016 Mar 15;14(10):2348-61. doi: 10.1016/j.celrep.2016.02.027.
  26. **T Hendriks**, S MA Walenbergh, M LJ Jeurissen, T Houben, P J van Gorp, P J Lindsey, G H Koek, S Kalhan, J Pihlajamaki, M H Hofker, R Shiri-Sverdlov. Plasma interleukin 1 receptor antagonist levels correlate with the development of non-alcoholic steatohepatitis. *Biomark Med*. 2015;9(12):1301-9. doi: 10.2217/bmm.15.71.
  27. S MA Walenbergh, T Houben, **T Hendriks**, M LJ Jeurissen, P J van Gorp, N Vaes, S WM Olde Damink, F Verheyen, G H Koek, D Lütjohann, A Grebe, E Latz, R Shiri-Sverdlov. Weekly Treatment of 2-Hydroxypropyl- $\beta$ -cyclodextrin Improves Intracellular Cholesterol Levels in LDL Receptor Knockout Mice. *Int J Mol Sci*. 2015 Sep 2;16(9):21056-69. doi: 10.3390/ijms160921056.
  28. Y Wang, S van der Tuin, N Tjeerdema, A D van Dam, S S Rensen, **T Hendriks**, J F Berbée, B Atanasovska, J Fu, M Hoekstra, S Bekkering, N P Riksen, W A Buurman, JW Greve, M H Hofker, R Shiri-Sverdlov, C O Meijer, J W Smit, L M Havekes, K W van Dijk, P C Rensen. Plasma cholesteryl ester transfer protein is predominantly derived from Kupffer cells. *Hepatology*. 2015 Dec;62(6):1710-22. doi: 10.1002/hep.27985.
  29. **T Hendriks**, C Piersma, DK Dhar, L Mpabanzi, JJ Schreurs, M Malagó, R Shiri-Sverdlov, SWM Olde Damink. Anti-inflammatory pre-treatment to reduce mobilization-induced liver inflammation in mice: novel model to study liver injury. *MRI 2015*, Vol.4 No.1.
  30. **T Hendriks**, M LJ Jeurissen, P J van Gorp, M J Gijbels, S MA Walenbergh, T Houben, R van Gorp, C C Pöttgens, R Stienstra, M G Netea, M H Hofker, M M Donners, R Shiri-Sverdlov. Bone marrow specific caspase-1/11 deficiency inhibits atherosclerosis development in *Ldlr*<sup>-/-</sup> mice. *FEBS J*. 2015 Jun;282(12):2327-38. doi: 10.1111/febs.13279.
  31. S MA Walenbergh, T Houben, **T Hendriks**, M LJ Jeurissen, P J van Gorp, A CE Vreugdenhil, M P Adriaanse, W A Buurman, M H Hofker, A Mosca, P J Lindsey, A Alisi, D Liccardo, N Panera, G H Koek, V Nobili and R Shiri-Sverdlov. Plasma cathepsin D levels: a novel tool to predict pediatric hepatic inflammation. *Am J Gastroenterol*. 2015 Mar;110(3):462-70. doi: 10.1038/ajg.2015.29.
  32. **T Hendriks**, M LJ Jeurissen, V Bieghs, S MA Walenbergh, P J van Gorp, F Verheyen, Y D Guichot, M J Gijbels, E Leitersdorf, M H Hofker, D Lütjohann, R Shiri-Sverdlov. Kupffer cell specific *Cyp27a1* overexpression reduces hepatic inflammation in

hyperlipidemic Ldlr<sup>-/-</sup> mice. *J Hepatol.* 2015 Feb;62(2):430-6. doi: 10.1016/j.jhep.2014.09.027.

33. Plat J, **Hendriks T**, Bieghs V, Jeurissen ML, Walenbergh SM, van Gorp PJ, De Smet E, Konings M, Vreugdenhil AC, Guichot YD, Rensen SS, Buurman WA, Greve JW, Lütjohann D, Mensink RP, Shiri-Sverdlov R. Protective role of plant sterol and stanol esters in liver inflammation: insights from mice and humans. *PLoS One.* 2014 Oct 30;9(10):e110758. doi: 10.1371/journal.pone.0110758.
34. **T Hendriks**, S MA Walenbergh, M H Hofker and R Shiri-Sverdlov. Lysosomal cholesterol accumulation: driver on the road to inflammation during atherosclerosis and non-alcoholic steatohepatitis. *Obes Rev.* 2014 May;15(5):424-33. doi: 10.1111/obr.12159.
35. Bieghs V, Walenbergh SM, **Hendriks T**, van Gorp PJ, Verheyen F, Olde Damink SW, Masclee AA, Koek GH, Hofker MH, Binder CJ, Shiri-Sverdlov R. Trapping of oxidized LDL in lysosomes of Kupffer cells is a trigger for hepatic inflammation. *Liver Int.* 2013 Aug;33(7):1056-61. doi: 10.1111/liv.12170.
36. **Hendriks T**, Bieghs V, Walenbergh SM, van Gorp PJ, Verheyen F, Jeurissen ML, Steinbusch MM, Vaes N, Binder CJ, Koek GH, Stienstra R, Netea MG, Hofker MH, Shiri-Sverdlov R. Macrophage specific caspase-1/11 deficiency protects against cholesterol crystallization and hepatic inflammation in hyperlipidemic mice. 2013 Dec 2;8(12):e78792. doi: 10.1371/journal.pone.0078792.
37. Bieghs V, **Hendriks T**, van Gorp PJ, Verheyen F, Guichot YD, Walenbergh SM, Jeurissen ML, Gijbels M, Rensen SS, Bast A, Plat J, Kalhan SC, Koek GH, Leitersdorf E, Hofker MH, Lütjohann D, Shiri-Sverdlov R. The cholesterol derivative 27-hydroxycholesterol reduces steatohepatitis in mice. *Gastroenterology.* 2013 Jan;144(1):167-178.e1. doi: 10.1053/j.gastro.2012.09.062.
38. Bieghs V, Verheyen F, van Gorp PJ, **Hendriks T**, Wouters K, Lütjohann D, Gijbels MJ, Febbraio M, Binder CJ, Hofker MH, Shiri-Sverdlov R. Internalization of modified lipids by CD36 and SR-A leads to hepatic inflammation and lysosomal cholesterol storage in Kupffer cells. *PLoS One.* 2012;7(3):e34378. doi: 10.1371/journal.pone.0034378.
39. Bieghs V, Van Gorp PJ, Wouters K, **Hendriks T**, Gijbels MJ, van Bilsen M, Bakker J, Binder CJ, Lütjohann D, Staelens B, Hofker MH, Shiri-Sverdlov R. LDL receptor knock-out mice are a physiological model particularly vulnerable to study the onset of inflammation in non-alcoholic fatty liver disease. *PLoS One.* 2012;7(1):e30668. doi: 10.1371/journal.pone.0030668.