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## General information

### *Personal details*

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Male/female	Female
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### Academic education and degrees

What, When and Where

Ph.D. (1998) Cardiovascular Physiology  
Faculty of Medicine  
University of Amsterdam  
Amsterdam

MSc. (1994) in Medical Biology  
Faculty of Medicine  
University of Utrecht  
Utrecht

Doctorate

PhD

University

University of Amsterdam

Date

30-09-1998

Supervisor(s)

Prof JAE Spaan, Prof F Kajiya

Title of thesis

Determinants of Coronary Blood Flow at Low Coronary Arterial Pressure

*Work experience and appointments since graduation (dates, full or part-time (fte) and permanent or fixed-term position)*

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## Research

My research aims to delineate a key role for microvascular dysfunction in development and progression of cardiovascular disease with a focus on heart failure and pulmonary hypertension. The microcirculation is not only critical for perfusion of organs, but also exerts direct paracrine effects on the surrounding tissue and forms the entrypoint of inflammatory cells. Conditions like diabetes and chronic kidney disease cause systemic low grade inflammation, thereby causing microvascular dysfunction, and aggravating organ dysfunction. Such systemic diseases can only be studied using an integrated in vivo/ in vitro approach in relevant models. I have developed several large animal models, with diabetes, chronic kidney disease and/or pulmonary hypertension. I study microvascular function as well as its impact

on cardiac function and remodelling using an integrative approach. I combine studies of isolated blood vessels, isolated cardiomyocytes with studies in chronically instrumented awake animals with or without cardiovascular disease as well as histological, molecular and biochemical analyses of tissues obtained from these animals to get a more complete picture of the process of regulation of microvascular and cardiac function and vascular remodelling and to be able to identify biomarkers of disease severity.

In addition, I value and enjoy collaboration with people from different fields, including pulmonary diseases, neonatology, pediatric cardiology, nephrology and clinical chemistry.

*Thesis supervised since 2021 (Doktoranden, 4 years Thesis supervision)*

Jens van de Wouw (2021)

Siyu Tian (2022)

Michelle Broekhuizen (2023)

Lakshme Kottu (2024)

Hengliang Zhang (2024)

Jarno Steenhorst (2026)

Jules Hamers (2026)

Current in the Netherlands:

Rahi Alipour Symakani (research focus: Adaptation of the Right Ventricle in Tetralogy of Fallot), 2026

Ruben van Drie (research focus: potential side effects of CGRP antagonists for migraine in patients with microvascular disease) 2026

Nicoleta Cius (research focus: exercise preconditioning: in vitro models), 2028

Myrthe van de Ven (research focus: exercise preconditioning for cardiac surgery), 2028

Current in Munich:

Theresa Sittig (research focus: Effect of Diabetes on Coronary Microvascular Dysfunction), 2027

Laura d'Ambrosio (research focus: Effect of Stat1 in the heart), 2028

Irem Ornek (research focus: molecular mechanisms of heart failure), 2028

Lili Wang (research focus: Klotho connecting chronic kidney disease and heart failure), 2027

Dual Affiliation

Lotte Zandbergen (research focus: Molecular mechanisms of Chronic kidney disease induced myocardial remodeling) 2026

*Grant allocation*

Period (from – to)	Funding source and project code	Own share of grant (€)	Total grant (€)	Project title	Role of PI*
2026-2030	DZHK	648.000,-	648.000,-	Microvascular disease in heart failure	PI
2024-2028	NWO SEP-HELPS	320.000,-	750.000,-	Short term exercise protection: exploring how, why and in whom exercise leads to immediate protection against cardiovascular injury	Co-PI
2023-2026	TKI-NAPH	59.000,-	266.000,-	<b>Novel animal-free production and pharmaceutical characterisation of heparin (NAPH)</b>	
2024-2026	DZHK- external collaboration	24.000,-	48.000,-	Mitochondrial dysfunction as a key factor in CKD induced HFpEF	PI
2023	DZHK	30.000,-	30.000,-	Myocardial transcriptomic changes in chronic kidney disease: Focus on klotho and diabetes (ARTERIOLE)	PI
2021-2025	DZHK81Z0600207	579.919,-	579.919,-	Coronary microvascular disease: Linking Chronic Kidney Disease, Heart Failure, and Atrial Fibrillation	PI
2021-2025	DCVA-RECONNEXT	150.000,-	3.000.000,-	Renal connection to microvascular disease and heart failure with preserved ejection fraction; the next phase	WP-leader

\* examples: principal investigator, project leader, project manager, coordinator, work package leader, etc.

*Active main (inter)national collaborations (collaborator, topic, institute)*

Sebastian Clauss, Arrhythmogenesis in Diabetes and Chronic Kidney Disease, LMU- Munich, Germany

Andreas Dendorfer, Cardiac slices: a novel s biomimetic research tool, LMU-Munich, Germany

Christian Schulz, Clonal Hematopoiesis and atherosclerosis, LMU-Munich Germany

Thomas Frohlich, Proteomics in swine, LMU-Munich Germany

Eckhard Wolf/ Elisabeth Kemter, transgenic swine in cardiovascular disease, LMU-Munich Germany

Christophe Guignabert, tryptophan metabolites in pulmonary hypertension, Hôpital Marie Lannelongue, Le Plessis-Robinson, France

T Dylan Olver, Heart-brain connection, University of Saskatchewan, Canada

Shawn B Bender, Swine models of cardiac disease, University of Missouri, USA

**Commissions of trust**

**Editorial board**

Physiological Reports (associate editor, 2024-present)

Cardiovascular Research (Editor 2016-2018, editorial board member 2016-present)

Journal of Applied Physiology (2016-2020)

Americal Journal of Physiology, Heart and Circulatory Physiology (2023)

Scientific Reports (2023)

**Review panel member**

European Commission, 2025

British Heart Foundation, 2018-present

National Science Center Poland, 2019- present

**Memberships**

**Board membership**

NVF, member since 1996, board member 2012-2020

MiVaB, Member since 2000, board member 2008-2012

ESC Working group of Group of Coronary Pathophysiology and Microcirculation, board member 2022-present

**Membership**

PVRi (member and Fellow since 2013)

American Physiological Society (since 2002, Fellow of CV section since 2010)

ESC (member since 2017), member of working group on Coronary Pathophysiology and Microcirculation as well as Pulmonary Hypertension

DZHK (member since 2019)

DZL (member since 2024)

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**Teaching**

I am currently actively involved in teaching at all levels of Medical Education. Thus, I teach first and second year Medical students (Exercise Physiology in the first year, Coordinator Keuzeonderwij second year), I organize and teach courses for PhD students, and give lectures and practical courses about exercise Physiology in the Cardiovascular Research Master at the VU. Moreover, I supervise medical students, cardiovascular research master students and students from the School of laboratory Sciences (HLO) doing their final thesis. I enjoy teaching and spreading knowledge, and believe that a combination of theory and practice in small groups is optimal for learning.

## Publications since 2021

(1-49)

1. Alipour Symakani RS, Bartelds B, Merkus D, Bogers A, Taverne Y. Guiding interventions for secondary tricuspid regurgitation: follow the intricate interplay between form and function. *Cardiol Rev.* 2021.
2. Atiq F, van de Wouw J, Sorop O, Heinonen I, de Maat MPM, Merkus D, et al. Endothelial Dysfunction, Atherosclerosis, and Increase of von Willebrand Factor and Factor VIII: A Randomized Controlled Trial in Swine. *Thromb Haemost.* 2021;121(5):676-86.
3. Brandt MM, Cheng C, Merkus D, Duncker DJ, Sorop O. Mechanobiology of Microvascular Function and Structure in Health and Disease: Focus on the Coronary Circulation. *Front Physiol.* 2021;12:771960.
4. Broekhuizen M, Danser AHJ, Reiss IKM, Merkus D. The Function of the Kynurenine Pathway in the Placenta: A Novel Pharmacotherapeutic Target? *Int J Environ Res Public Health.* 2021;18(21).
5. Merkus D, Muller-Delp J, Heaps CL. Coronary microvascular adaptations distal to epicardial artery stenosis. *Am J Physiol Heart Circ Physiol.* 2021;320(6):H2351-H70.
6. Stam K, Clauss S, Taverne Y, Merkus D. Chronic Thromboembolic Pulmonary Hypertension - What Have We Learned From Large Animal Models. *Front Cardiovasc Med.* 2021;8:574360.
7. Taverne Y, Sadeghi A, Bartelds B, Bogers A, Merkus D. Right ventricular phenotype, function, and failure: a journey from evolution to clinics. *Heart Fail Rev.* 2021;26(6):1447-66.
8. Te Lintel Hekkert M, Newton G, Chapman K, Aqil R, Downham R, Yan R, et al. Preclinical trial of a MAP4K4 inhibitor to reduce infarct size in the pig: does cardioprotection in human stem cell-derived myocytes predict success in large mammals? *Basic Res Cardiol.* 2021;116(1):34.
9. van de Wouw J, Sorop O, van Drie RWA, Joles JA, Danser AHJ, Verhaar MC, et al. Reduced nitric oxide bioavailability impairs myocardial oxygen balance during exercise in swine with multiple risk factors. *Basic Res Cardiol.* 2021;116(1):50.
10. van de Wouw J, Steenhorst JJ, Sorop O, van Drie RWA, Wielopolski PA, Kleinjan A, et al. Impaired pulmonary vasomotor control in exercising swine with multiple comorbidities. *Basic Res Cardiol.* 2021;116(1):51.
11. Broekhuizen M, de Vries R, Smits MAW, Dik WA, Schoenmakers S, Koch BCP, et al. Pentoxifylline as a therapeutic option for pre-eclampsia: a study on its placental effects. *Br J Pharmacol.* 2022;179(22):5074-88.
12. Cai Z, Tian S, Klein T, Tu L, Geenen LW, Koudstaal T, et al. Kynurenine metabolites predict survival in pulmonary arterial hypertension: A role for IL-6/IL-6Ralpha. *Sci Rep.* 2022;12(1):12326.
13. Cai Z, Tian S, Klein T, Tu L, Geenen LW, Koudstaal T, et al. Kynurenine metabolites predict survival in pulmonary arterial hypertension: A role for IL-6/IL-6Ralpha. *Sci Rep.* 2022;12(1):12326.
14. Duncker DJ, Sorop O, van de Wouw J, Fen G, de Beer VJ, Taverne YJ, et al. Integrated control of coronary blood flow in exercising swine by adenosine, nitric oxide, and K(ATP) channels. *Am J Physiol Heart Circ Physiol.* 2022;323(6):H1080-H90.
15. Hamers J, Sen P, Merkus D, Seidel T, Lu K, Dendorfer A. Preparation of Human Myocardial Tissue for Long-Term Cultivation. *J Vis Exp.* 2022(184).
16. Pang L, Kottu L, Guo Z, Shi Y, Ferdous M, Zhao Y, et al. Dawning public health services dogma: An indigenous Southwest Chinese perspective in managing hypertension-with or without the "BPHS"? *Front Public Health.* 2022;10:1017795.
17. Schuttler D, Tomsits P, Bleyer C, Vlcek J, Pauly V, Hesse N, et al. A practical guide to setting up pig models for cardiovascular catheterization, electrophysiological assessment and heart disease research. *Lab Anim (NY).* 2022;51(2):46-67.
18. Steenhorst JJ, Hirsch A, Verzijl A, Wielopolski P, de Wijs-Meijler D, Duncker DJ, et al. Exercise and hypoxia unmask pulmonary vascular disease and right ventricular dysfunction in a 10- to 12-week-old swine model of neonatal oxidative injury. *J Physiol.* 2022;600(17):3931-50.
19. Tian S, Cai Z, Sen P, van Uden D, van de Kamp E, Thuillet R, et al. Loss of lung microvascular endothelial Piezo2 expression impairs NO synthesis, induces EndMT, and is associated with pulmonary hypertension. *Am J Physiol Heart Circ Physiol.* 2022;323(5):H958-h74.
20. van Zundert SK, Broekhuizen M, Smit AJ, van Rossem L, Mirzaian M, Willemsen SP, et al. The Role of the Kynurenine Pathway in the (Patho) physiology of Maternal Pregnancy and Fetal Outcomes: A Systematic Review. *Int J Tryptophan Res.* 2022;15:11786469221135545.
21. Zhang H, Merkus D, Zhang P, Zhang H, Wang Y, Du L, et al. Predicting protective gene biomarker of acute coronary syndrome by the circRNA-associated competitive endogenous RNA regulatory network. *Front Genet.* 2022;13:1030510.
22. Algul S, Dorsch LM, Sorop O, Vink A, Michels M, Dos Remedios CG, et al. The microtubule signature in cardiac disease: etiology, disease stage, and age dependency. *J Comp Physiol B.* 2023;193(5):581-95.
23. Alipour Symakani RS, Bartelds B, Merkus D, Bogers A, Taverne Y. Guiding Interventions for Secondary Tricuspid Regurgitation: Follow the Intricate Interplay Between Form and Function. *Cardiol Rev.* 2023;31(1):7-15.
24. Alipour Symakani RS, van Genuchten WJ, Zandbergen LM, Henry S, Taverne Y, Merkus D, et al. The right ventricle in tetralogy of Fallot: adaptation to sequential loading. *Front Pediatr.* 2023;11:1098248.
25. Chen Y, Ferdous MM, Kottu L, Zhao J, Zhang HL, Wang MY, et al. Can Measuring the 'Dual Anchors of Aorta' Enhance the Success Rate of TAVR?-A Single-Center Experience. *J Clin Med.* 2023;12(3).
26. Cruz-Lopez EO, Ye D, Stolk DG, Clahsen-van Groningen MC, van Veghel R, Garrelds IM, et al. Combining renin-angiotensin system blockade and sodium-glucose cotransporter-2 inhibition in experimental diabetes results in synergistic beneficial effects. *J Hypertens.* 2023.
27. Sen P, Shashikadze B, Flenkenthaler F, Van de Kamp E, Tian S, Meng C, et al. Proteomics- and Metabolomics-Based Analysis of Metabolic Changes in a Swine Model of Pulmonary Hypertension. *Int J Mol Sci.* 2023;24(5).
28. Sen P, Sorop O, Merkus D. Myocardial epigenetic modifications link chronic kidney disease to coronary microvascular disease. *Am J Physiol Heart Circ Physiol.* 2023;324(1):H175-H6.
29. Steenhorst JJ, Hirsch A, van den Berg LEM, Kamphuis LS, Merkus D, Boersma E, et al. Standardizing submaximal exercise intensities for use of supine push-pull exercise during cardiovascular magnetic resonance. *Clin Physiol Funct Imaging.* 2023;43(1):10-9.
30. Cruz-Lopez EO, Merkus D, Danser AHJ. Blood Pressure Monitoring Through Radiotelemetry: Exploring the Viability of Its Application in Multihoused Small Laboratory Animals. *Hypertension.* 2024;81(5):947-50.

31. Hamers J, Sen P, Murthi SR, Papanakli L, von Stumm M, Baessato F, et al. Trametinib alters contractility of paediatric Noonan syndrome-associated hypertrophic myocardial tissue slices. *ESC Heart Fail.* 2024.
32. Pang L, Kottu L, Guo Z, Ma M, Wang H, Zhao Y, et al. A tryst of 'blood pressure control- sex- comorbidities': the odyssey of basic public health services in Yunnan in quest for truth. *BMC Public Health.* 2024;24(1):490.
33. Pilz J, Gloddek N, Lindheimer F, Lindner MJ, Pühr-Westerheide D, Umutlu M, et al. Functional maturation and longitudinal imaging of intraportal neonatal porcine islet grafts in genetically diabetic pigs. *Am J Transplant.* 2024.
34. Sen P, Hamers J, Sittig T, Shashikadze B, d'Ambrosio L, Stockl JB, et al. Oxidative stress initiates hemodynamic change in CKD-induced heart disease. *Basic Res Cardiol.* 2024.
35. Steenhorst JJ, Helbing WA, van Genuchten WJ, Bowen DJ, van den Bosch A, van der Velde N, et al. Cardiac dysfunction during exercise in young adults with bronchopulmonary dysplasia. *ERJ Open Res.* 2024;10(3).
36. van Drie RWA, van de Wouw J, Zandbergen LM, Dehairs J, Swinnen JV, Mulder MT, et al. Vasodilator reactive oxygen species ameliorate perturbed myocardial oxygen delivery in exercising swine with multiple comorbidities. *Basic Res Cardiol.* 2024.
37. Zhang H, Sen P, Hamers J, Sittig T, Woestenburg B, Moretti A, et al. Retinoic acid modulation guides human-induced pluripotent stem cell differentiation towards left or right ventricle-like cardiomyocytes. *Stem Cell Res Ther.* 2024;15(1):184.
38. Alipour Symakani RS, van Genuchten WJ, Zandbergen LM, Hirsch A, Wielopolski PA, Bove T, et al. Ventriculo-arterial coupling in pulmonary regurgitation following transannular patch repair of pulmonary stenosis. *Am J Physiol Heart Circ Physiol.* 2025.
39. Bartelds B, Merkus D. Taming the flame: SerpinB1 suppression of pyroptosis in pathological cardiac hypertrophy. *Cardiovasc Res.* 2025;121(1):4-5.
40. Baur C, Geml A, Wimmer KS, Heim F, Holschbach A, Elbs K, et al. An Expendable Player in Positive Vascular Remodeling? ADAMTS13 Deficiency Does Not Affect Arteriogenesis or Angiogenesis. *Int J Mol Sci.* 2025;26(18).
41. Broekhuizen M, Allenberg H, van der Ley CP, van Zundert SKM, Cai Z, van Faassen M, et al. Pregnancy complications affect kynurenine pathway metabolite concentrations in umbilical cord blood. *Reprod Biol Endocrinol.* 2025;23(1):105.
42. Cai Z, Tu L, Tian S, Deng L, Fu Y, Phan C, et al. IDO-1 Promotes Pulmonary Vascular Remodeling Via Kynurenine Pathway in Pulmonary Arterial Hypertension. *J Am Heart Assoc.* 2025;14(16):e040896.
43. Elbs K, Bobrowski L, Arnholdt C, Kubler M, Gotz P, Rohrmoser MR, et al. P2Y(12)-Inhibitor Clopidogrel Promotes Collateral Artery Growth in a Murine Hindlimb Model of Arteriogenesis. *Biomedicines.* 2025;13(11).
44. Joosen RS, Dickinson MG, van de Veerdonk MC, Alipour Symakani RS, Merkus D, Voskuil M, et al. Right ventricular pressure-volume loop analysis in congenital heart disease. *Int J Cardiol Congenit Heart Dis.* 2025;22:100625.
45. Sen P, Sorop O, Merkus D. Increasing heart rate in heart failure with preserved ejection fraction: a sensible way to go? *Eur Heart J.* 2025;46(21):2027-8.
46. Sen P, Wang L, d'Ambrosio L, Bierschenk S, Hamers J, Ornek I, et al. Coronary microvascular disease in heart failure with preserved ejection fraction. *Physiol Rep.* 2025;13(16):e70521.
47. Sorop O, van de Wouw J, Merkus D, Duncker DJ. Coronary Microvascular Dysfunction in Ischaemic Heart Disease: Lessons From Large Animal Models. *Basic Clin Pharmacol Toxicol.* 2025;137(2):e70074.
48. Tune JD, Duncker DJ, Goodwill AG, Warne CM, Essajee SI, Tucker SM, et al. Potassium as an electro-metabolic signal for local coronary vasodilation. *Basic Res Cardiol.* 2025.
49. van Genuchten WJ, Steenhorst JJ, van Tussenbroek G, van der Velde N, Kamphuis LS, Reiss IKM, et al. Differences in Pulmonary Artery Stiffness Measured by CMR in Preterm-Born Young Adults With and Without Bronchopulmonary Dysplasia. *Circ Cardiovasc Imaging.* 2025;18(4):e017791.