Erasmus University Rotterdam – Taiwan Ministry of Education PhD Scholarship Program: Erasmus MC vacancies

PHD SCHOLARSHIP VACANCY BOOKLET

介紹 ERASMUS MC

Erasmus MC 的博士課程 - 概述

如何申請博士學位

PhD Scholarship Vacancies

選擇 Erasmus MC 的理由

CONTENTS

CONTENTS & PHD SCHOLARSHIP VACANCY OVERVIEW BY DEPARTMENT

介紹 ERASMUS MC

Erasmus University Medical Center, 被稱為 Erasmus MC

Erasmus大學的醫學院及其3所大學醫院全部整合到一個園區中，並由一個執行委員會領導。該教育中心於2012年開業，擁有400個學習場所和40個教學與演講室，最多可容納6,000名學生，並於2013年因其建築風格而獲獎。2018年，老醫院被最先進的單人病房，1,000臥室醫院所取代。 Erasmus MC 致力於通過研究和教育實現健康的人口和卓越的醫療保健 (www.erasmusmc.nl).

病人護理： Erasmus MC 只滿足於最好的護理，只有單間病房（VIP 醫院）以加速其醫療創新和使用最新、最具創新性的材料和程序治療患者的能力
https://www.youtube.com/watch?v=agYQOLrhmrQ

研究與創新： 伊拉斯謨醫學中心在各個臨床領域始終名列全球前 5-74 名，在臨床前和健康科學領域名列前 6-51 名（2022 年美國新聞學科排名，自然指數）。重要的是，其在臨床前、臨床和健康科學領域研究論文的世界影響力為2.32，(見第5頁，左表）。Erasmus MC 的整體研究目標是將實驗和研究成果轉化為臨床應用，涵蓋從臨床前研究、到臨床、再到健康科學研究的所有領域。

教育培訓： Erasmus MC提供BSc，MSc，PhD和Residency計劃，以培訓下一代醫學從業人員和研究人員。它是歐洲最大的醫學院之一，擁有約 2,500 名醫學生，每年有 220-250 名博士畢業。其醫學教育是，33%的醫學生發表過論文，70%在國外，20%選擇了醫學博士，（成為臨床醫生和科學家），非常出色。同樣，它希望博士生在畢業考試之前擁有4種或以上的研究發表（在研究領域排名前25%的期刊內）。所有博士生在入學時均擁有MSc，MD或DVM，並且大多數人具有個人獎學金或由研究補助金支付。

創新教育計劃： Erasmus MC 和 Delft University of Technology 是世界上第一個提供納米生物學（Nanobiology）BSc-MSc計劃的人，此跨領域學程結合了生物，物理，數學及電腦運算，所以它彌合了生命科學與技術之間的鴻溝。與技術大學的這種緊密合作產生了更廣泛的研究合作，並更多地關注社會上的直接應用。

監督率: 我們擁有約750名註冊醫學專家，約1000名居民和約1500名科學人員（加上600名博士後），而約有1,250名博士生，我們擁有世界上最好的主管比例之一（博士生至少有兩名主管）。

Erasmus MC和歐洲： 從研究發表數量和源自EC資助的研究（即FP7和Horizon計劃）的研究發表數量衡量，Erasmus MC 屬於歐盟10大醫學院校，並且是歐洲大陸上最成功的歐洲醫學院之一（Horizon2020 主題健康、人口變化與福祉; 見右表第 2 頁）。因此，它是通向歐洲研究網絡的誘人門戶，無論您的職業是在歐洲還是國外，這都是畢業後的一項好處。

與台灣的合作： Erasmus MC以其長期的合作和對合作夥伴的忠誠度而聞名。這種理念在高質量的研究合作中得到了體現。這通常要比台灣與更著名的合作夥伴（請參閱本頁頂部的表格）所享受的研究質量要好得多，而重要的是您一起發表的論文。因為合作比短暫的機會更為重要，所以我們更喜歡從事中荷合作和/或將荷蘭合作網絡帶回台灣的台灣博士研究生。

科技部龍門計劃： Erasmus MC 為龍門計劃的主辦機構之一，增加了與感興趣的台灣科學家合作的另一種方式。

台灣教育部核准及補助的PhD獎學金： 有興趣前往荷蘭Erasmus MC的學生，可經由此教育部連結 (*Taiwanese Ministry of Education*）申請全額補助獎學金。

ERASMUS MC 的博士課程 - 概述

選擇一所大學攻讀博士課程是以研究為導向的職業生涯中最重要的一步。它是大學提供的最高教育課程，博士培訓的結果決定了您職業生涯的下一步。由於博士學位本質上是一項研究培訓和教育計劃，因此您想報名參加的研究所的研究發表的質量非常重要。我們還注意到，歐洲和非歐洲大學代表團始終重視獲得歐洲研究資助。因此，如果您有在國際背景下從事職業的想法，請知道 Erasmus MC 在其研究論文的質量以及獲得歐洲研究資助（所謂的 Horizon2020 資助、主題健康、人口統計學）方面有著良好的記錄與福祉。

ERASMUS MC 的博士課程 - 概述

category normalized citation impact of publications in preclinical, clinical & health sciences 2019-2023 *InCites Clarivate dbase as of Oct, 17th, 2024*		
University or Med School*	**normaliz'd impact**	**publ**
Erasmus MC*	2.32	27,540
Stanford University	2.32	46,852
Univ Cambridge	2.31	22,543
Harvard Univ Med School*	2.29	98,680
U Penn Med School*	2.28	42,079
Johns Hopkins Med School*	2.22	47,129
UMC Utrecht*	2.06	19,472
Natl Univ of Singapore	2.01	22,470
Karolinska Institutet*	1.98	37,359
UCL Med School, UK*	1.79	7,957

Horizon2020 - Societal Challenge Health, Demographic Change & Wellbeing EC DASHBOARD SEP23rd *2020*		
ORGANIZATION (*med school only)	**country**	**earningS**
INSERM	FR	115.16 M€
University of Oxford	UK	76.64 M€
LSHTM	UK	74.20 M€
Erasmus MC*	**NL**	**61.26 M€**
Karolinska Institutet *	SE	61.17 M€
Radboud University	NL	57.26 M€
University College London	UK	55.75 M€
UMC Utrecht*	NL	53.89 M€
Imperial College London	UK	50.42 M€
Kings College London	UK	49.69 M€

Horizon Europe - Global Challenge Health EC DASHBOARD OCT 17th *2024*		
ORGANIZATION (*med school only)	**country**	**projects**
INSERM	FR	67
Karolinska Institutet*	SE	55
Erasmus MC*	**NL**	**48**
KU Leuven	BE	43
Charite Berlin*	DE	39
Amsterdam UMC*	NL	41
Radboud UMC*	NL	40
Region Hovedstaden	DK	37
University of Oxford	UK	36
UMC Utrecht*	NL	32

- ***左表***：*世界影響：這組研究發表的引用影響指數與世界影響指數相比（世界平均值為1,00）。InCites-Clarivate 出版物：2024 年 10 月 17 日在 InCites 數據庫中發現的 2019-2023 年臨床前、臨床和健康科學聯合領域的研究發表*
- ***右上表***：*歐洲研究資助計劃"地平線 2020"中最成功的組織——主題健康、人口變化與福祉，根據 2020 年 9 月 23 日在歐盟儀表板上獲得的歐元金額排名。Erasmus MC是第一所大陸醫學院，自法國的INSERM是一個全國性組織，另外兩個成功的組織是英國。*
- ***右下表***：*歐洲研究資助計劃"地平線 Europe"中最成功的組織——主題健康、根據 2024 年 10 月 17 按項目數量排名*

ERASMUS MC 的博士課程 - 概述

- Erasmus MC**博士課程的目標**是使您成為一名獨立的研究人員，能夠根據科學證據來解決複雜的問題。畢業生將具有評估科學研究的能力，並朝著成為生物醫學學者的方向邁出了重要的一步。博士生最適合成為大學醫學中心、研究型大學、研究機構的未來（臨床）研究人員，和/或填補工作人員和政策職位，例如管理生物醫學大學、醫院和其他醫療保健組織、生物醫學和製藥公司、部委等等。

- 我們**教育理念**的核心是，良好的科學培訓需要主動學習。這意味著我們以小組甚至有時單獨授課的方式來教授博士和研究型碩士生，並且以綜合方式教授理論知識和實踐技能。因此，激發學生積極地使用他們新獲得的知識，這既嵌入了他們的知識，又提高了他們的研究質量。融合是提高我們各級教育的多學科性和跨學科性的重要驅動力。學生向在各自領域處於領先地位、具有國際經驗且其研究小組與其他（國際）國家研究小組合作的教師學習。

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一個典型的博士學位課程將花費4年，並且候選人必須擁有其理學碩士，醫學或DVM學位。在健康科學領域，應聘者將其博士學位研究與健康科學專業碩士相結合。候選人的雅思成績必須達到 7.0 或托福成績達到 100，但在攻讀博士學位期間，他們的英語寫作和演講技巧會得到進一步提高。

ERASMUS MC 的博士課程 - 概述

培訓和指導：作為博士研究生，您將註冊Erasmus MC研究生學院，該研究生學院提供通用和高度專業化的課程。然而，博士課程是高度個性化的，在最初的幾個月內，您將與您的導師一起開發最適合您的科學需求以及您理想職業道路的課程。重要的是，我們還希望您能夠獨立工作（我們會訓練您這樣做），並且敢於主動，我們會激發您競爭旅遊船，海報獎或進行其他相關的課外活動。

- *您將進行*一項獨立的科學研究並將結果呈現在論文中。
- *您將受到*一名全職教授的監督，並由一名或兩名共同指導教授提供支持
- *您將參加*至少30個EC點的課程，研討會和會議（您可以從Grad School的150門課程中選擇，並且可以參加Erasmus MC以外的課程）
- *您將參加*一個多學科，跨國和資助驅動的最新研究環境
- 根據您的項目，有可能出國（研究訪問）在另一個環境中學習

您的博士學位論文：每個研究項目都不同，每個博士生都不同，知識和實驗室經驗也可能不同，因為博士生來自不同的大學。但是，我們為擁有世界上最高的博士學位考試要求之一而感到自豪。當您邁向職業生涯的下一步時，這將為您帶來巨大的優勢。有關獲得博士學位後成果的範例，請查看下表：

在2019年從伊拉斯姆斯大學畢業的最後10名外國博士研究生的產出

country	publications	Conferences, courses, research abroad	honors & awards	teaching
Brazil	5 publications in top 3 journals, 1x top 25%, 1x other	6 conference visits + 1 conference organization	1 grant, editorial board, 4x coordinator research projects	lecturer, 4 MSc interns,
Poland	2x top 10, 2x top 25%, 1x other	3 conference visits	1 scholarship, 2 travel grants	3 BSc + 4 MSc interns
Romania	1x top 10, 3x top 25%, 2x other, 2 book chapters	1 conference + 2x course organizer, 1x course co-chairman	1 grant, editorial board	1 MSc intern
U.K.	4x top 25%, 6x other	1 course, 4 conferences	4 awards, board AAV	teaching assistant, 1 MSc intern
P.R. China	2x top 3, 1x top 5, 1x top 25%, 13 other	3 conference visits, 1 research visit	1 scholarship + 5 awards	1 MSc intern
Sudan	1x top 3, 4x top 5, 1x top 10, 2x top 25%, 12x other	6 courses/workshops, 232 conferences	2 grants	not reported
Italy	2x top 3, 1x top 5, 4x top 25%, 2x other, 2 in preparation	1 research visit,2 workshops, 71 conference presentations	1 scholarship + 3 awards	1 MSc intern
India	3x top 25%, 8x other	8 conferences	2 awards	teaching assistant, 2 MSc interns
Mexico	1x top 10, 11x top 25%, 1x top 50% journal	4 courses, 6 conferences	1 scholarship + 5 awards, JHP Editorial Board EHF	teaching assistant, 1x intern JMS
Syria	1x top 1, 9x top 25%, 3x other	8 conferences	1 award	2x teaching assistant med school, 1x teaching nurse school
U.S.A.	2x top 3, 1x top 10, 14x other	12 conferences & workshops	not reported	5x teaching at courses, 2x advisor, 1x MSc intern
Germany	4x top 3, 1x top 10, 3x top 25%,	5 conferences, 3 courses	not reported	lecturer at med and at nursing school, residents, 2x med and 1x MSc intern
Morocco	1x top 5, 2x top 25%, 5x other	10 conferences, 6 courses	1 grant	not reported
Indonesia	1x top 3, 4x top 5, 3x top 10 , 4x top 25%, 3x Top 50% journals	1 course, 4 conferences	1 grant + 4 awards	teaching at Med School and MSc Program, 1 intern BSc student
Thailand	3x top 25%, 1x submitted, 2x in preparation	13 conferences	5 travel grants, co-chair, committee member at national science days	teaching endocrinology course

圖註

country – 博士畢業生的原籍國,

publications – 博士學位論文發表，其質量由該期刊在研究生研究領域中的排名來表示,

conferences abroad – 國外會議，課程和研究訪問的次數,

honors & awards – 獲得的贈款和獎勵，學者或旅費，委員會或董事會成員的數量,

teaching – 博士研究生開設的課程和對學生的指導.

在您獲得論文博士學位後，您與我們的聯繫將不會停止：熟悉我們的員工和我們的研究並了解西方研究資助的動態，您將從研究生轉變為有價值的海外同事和研究夥伴：表格第2頁顯示了我們與國外科學家的合作出版物所獲得的引用平均得分高於在世界各地擁有一些大學的外國科學家的引用數量。這是只有您才能做到的，因為我們許多成功的合作都是與我們以前的校友合作。

如何申請博士學位

如何使用此空缺手冊

本手冊概述了Erasmus MC幾個選定部門中與台灣實驗室合作或正在尋求合作的各個實驗室的博士生職位。空缺以通用方式編寫，目的是使您對他們研究的主題有所了解，但也可以讓您靈活地提出一些與主題相關的建議。有關更多信息或問題，您可以隨時通過電子郵件聯繫相關教授（職位空缺包括相關教授的聯繫數據）或通過Erasmus MC 的研究發展辦公室 RDO

寫動機或求職信

這些職位空缺有簡短的研究描述，並顯示了一些研究發表。這是進一步閱讀的來源。主管希望博士候選人寫一封好的動機信函，將他們的興趣描述為教授的研究興趣，以及候選人之前獲得的經驗將如何匹配或添加到博士項目中。

由於Erasmus MC的幾乎所有博士生的職位都是基於研究資助或自己的博士獎學金，因此建議您一下，當您被教授錄取時，您將申請博士學位獎學金。這將是您教育部的博士獎學金計劃或其他可用的獎學金，例如基於大學或大學醫院的博士獎學金。獲得獎學金可能是一種要求，但我們認為這是一個額外的步驟，可以作為您職業生涯後期質量的證明。這也是您未來的主管將在您的獎學金申請的研究部分中為您提供幫助的原因。

您被教授錄取了，現在怎麼辦？

一旦您接受了面試（或多次面試）並被錄取，在大多數情況下，您將申請獎學金。您的主管將為您的博士獎學金申請的科學描述提供幫助，並且通常您需要獲得獎學金申請的錄取通知書。您的主管可以通過 RDO 獲得這些信息。

提交申請後，不久之後，您的獎學金將被授予，您將通知未來的指導教授。他們將把您，他們的新博士生，通知人事和人力資源部（HR），其他一些 Erasmus MC員工也會與您聯繫。通常，HR只會在您預計到達的兩個月之前與您聯繫。

人力資源所需的文件，以準備您的申請和註冊

- 護照的彩色複印件（所有書面和蓋章頁）；
- 在荷蘭承保的醫療保險證明；如果您沒有保險，則可以在荷蘭後安排醫療保險；
- 獨立證明：例如津貼，助學金，贊助，定期付款，任命書或僱傭合同。
- 證明您具有進行研究的適當資格的證書副本；您的文憑或大學證書。文憑或大學證書必須由公證人或市政當局批准；
- 由您的指導教授簽名的研究建議書的副本。

除上述強制性文件外，還建議提交

- 出生證明的副本，該副本經合法化或帶有加蓋公章的印章，用於確定市政個人記錄數據庫（GBA）的個人詳細信息。

注意：這些文件必須由官方翻譯人員翻譯成英文，荷蘭文或法文。

DEPARTMENT OF BIOCHEMISTRY

Project: Molecular mechanisms is viral infection and tumorigenesis using patient-derived organoid platforms

Supervisor information:

Prof dr. Tokameh Mahmoudi t.mahmoudi@erasmusmc.nl https://eheg.nl, https://www.mahmoudilab.nl

Grants: European Commission and Research Council: ERC Starting grant and Erasmus+, Public-Private-Partnership Health Holland grants together with Pharma companies as well as Dutch governmental and national consortia research grants (NWO and ZonMw)

Supervision of PhD students/info over research group: I have trained 8 PhD students (theses defended), 7 post-docs, who have successfully transitioned onto academic or industry careers and am training 5 other PhDs who will graduate in the next 2.5 years. Many have successfully applied for and obtained funding to support their research in my lab and in transition to their next positions.

Select important recent publications:

2024. *iScience.* Crespo R et al,. 27(3):109152.
2024. *Nature Review Urology.* Olislagers M et al., doi: 10.1038/s41585-024-00914-7.
2024. *Heliyon.* Rao S et al., 10(10):e30740.
2024. *Communications Medicine.* Hossain et al., 4(1):123
2024. *Cancer Research.* Jones RT et al., 84(10):1699-1718.
2023. *Science Advances.* Prins HAB et al., 9(11):eade6675.
2023. *Science Translational Medicine*. de Jonge FC et al., 15(697):eabn4118.
2022. *Nucleic Acids Research.* Ne E. Crespo R. et al., 50(10):5577-5598.
2021. *Elife.* de Crignis et al., doi: 10.7554/eLife.60747
2021. *Nature Communications. Rao S. et al.,* 12(1):2475
2020. *Science Advances.* Stoszko M et al., 6(32):6617-6629
2019. *Current Opinion in Virology*. Stoszko M, Ne E et al., 38:37-53.
2018. *Cell Chemical Biology.* Marian C et al., 25(12):1443-1455.e14
2018. *Science Advances.* Palstra RJ et al., 4(2):e1701729.
2016. *EBioMedicine*. Stoszko et al., 3:108-121.

I believe in team science and am convinced that innovation and impact lies at the interface of disciplines, most effectively accomplished via an international, collaborative, and multidisciplinary approach. My international scientific background, having worked and trained in various academic centers of excellence in the United States (Bachelor's degree from UC Berkeley and post-doctorate training at UC San Francisco), Canada (Master's degree from University of Toronto), the United Kingdom (first year PhD at UCL - Cancer Research UK), and The Netherlands (PhD from Leiden University Medical Centre and post-doctoral training at the Hubrecht Institute) resulted in a wide national and international interdisciplinary network of collaborators. Combining this network and translational expertise is central to the quality, valorization, clinical translation and overall impact of our research.

Abstract:

The objectives of the various research projects running in my lab is understand the molecular events and key molecular players that drive human disease. My team and I study these mechanisms in a range of human diseases such as the pathogenesis resulting from infection with HIV and HBV, and tumorigenesis in bladder or in liver related to HBV infection. Our approach in the lab is to tackle translational bench-to-bedside questions in HIV – HBV cure research and in research into tumorigenesis using innovative strategies. We use an integrated experimental approach to study molecular and functional determinants of gene regulation and leverage these data to modulate and target processes in viral persistence or tumorigenesis. Key to the understanding of these complex systems is an interdisciplinary approach of virology, immunology, pathology, biochemistry, genetics, high throughput, single cell omics, combined with clinical data and patient derived (organoid) models. The goal of this approach is to develop innovative tools to understand disease mechanisms and discover "drug-able" molecular targets for therapeutics.

Requirements of candidate:

We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.

- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal)
- Master degree or MD degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF BIOSTATISTICS

Project:	**Advancing Causal Methods in Rare Diseases: Formalizing Challenges and Integrating Real-World Evidence**
Supervisor information:	**Prof. dr. Bettina E Hansen** *b.hansen@erasmusmc.nl* **dr. Richard AJ Post** *r.a.j.post@erasmusmc.nl* ***Recent publications:*** 1. Hansen BE et al; Global ALagille Alliance (GALA) Study Group. Event-free survival of maralixibat-treated patients with Alagille syndrome compared to a real-world cohort from GALA. *Hepatology 79(6), 1279-1292 (2024).* DOI: 10.1097/HEP.0000000000000727 2. Murillo Perez CF, Fisher H, …, Wason J, Hansen BE; GLOBAL PBC Study Group and the members of the UK-PBC Consortium. Greater Transplant-Free Survival in Patients Receiving Obeticholic Acid for Primary Biliary Cholangitis in a Clinical Trial Setting Compared to Real-World External Controls. *Gastroenterology 163(6), 1630-1642 (2022)* DOI: 10.1053/j.gastro.2022.08.054 3. Post RAJ et al. Flexible Machine Learning Estimation of Conditional Average Treatment Effects: A Blessing and a Curse. *Epidemiology 35(1), 32-40 (2024).* DOI: 10.1097/EDE.0000000000001684 4. Post RAJ et al. The built-in selection bias of hazard ratios formalized using structural causal models. *Lifetime Data Anal 30, 404–438 (2024).* DOI: 10.1007/s10985-024-09617-y
Abstract:	This project seeks to advance statistical methods for rare diseases by integrating causal inference techniques tailored to the unique challenges of limited data and treatment variability. With a growing reliance on real-world data (RWD) to address the scarcity of randomized controlled trials in rare diseases, this PhD project will explore two pressing issues: (1) treatment switching from control to promising treatment—a common scenario in ethical rare disease trials, and (2) the use of RWD as external or synthetic controls to supplement limited experimental data. To build a robust framework, we aim to formalize the challenges inherent to rare diseases within the potential outcomes framework, ensuring a clear causal interpretation that accounts for biases introduced by treatment switching and data quality issues in RWD. We will further adapt the target trial framework to the rare disease setting, where small sample sizes and high heterogeneity present unique obstacles. Through the careful implementation of causal inference methods, this project will develop rigorous strategies to harmonize experimental and RWD sources, enhancing the reliability of treatment effect estimation in rare disease research. Supported by supervision from experts in rare disease statistics and causal inference, this research will bridge methodological gaps, contributing novel insights to improve treatment evaluation and decision-making for rare disease populations.
Requirements of candidate:	*We seek a highly motivated and diligent student to join our biostatistics team. Ideal candidates should possess a solid quantitative background, demonstrate exceptional critical thinking skills, and have a strong drive to contribute to the advancement of statistical methodologies.* • *Master's degree in statistics or mathematics, clinical epidemiology or in an equivalent discipline, or candidates with a Master's in health sciences or medicine with experience in statistical programming* • *Scholarship that will, at least, cover subsistence allowance and international airplane ticket (your future supervisors could help with the scientific part of your scholarship proposal)* • *Experience with statistical programming in Python or R.* • *The student should be fluent in English (IELTS min 7.0), TOEFL 100 (min 20 for all subs) and have good communicative skills both in speech and in writing.*

DEPARTMENT OF BIOSTATISTICS

Project: From Machine Learning to Human Understanding: Tools for effective risk communication

Supervisor information:

Prof. Bettina Hansen b.hansen@erasmusmc.nl https://www.erasmusmc.nl/en/research/researchers/hansen-bettina
Dr. Elrozy Andrinopoulou e.andrinopoulou@erasmusmc.nl https://www.erandrinopoulou.com/

Grants:

Prof. Bettina Hansen: Industrial research grants from IPSEN pharma (1.2 mil euro)
Dr. Elrozy Andrinopoulou: Cystic Fibrosis Foundation awards

Recent publications:

1. Andrinopoulou ER, Harhay MO, Ratcliffe SJ, Rizopoulos D. Reflection on modern methods: dynamic prediction using joint models of longitudinal and time-to-event data. International Journal of Epidemiology. 2021 Oct 1;50(5):1731-43.
2. Andrinopoulou ER, Clancy JP, Szczesniak RD. Multivariate joint modeling to identify markers of growth and lung function decline that predict cystic fibrosis pulmonary exacerbation onset. BMC pulmonary medicine. 2020 Dec;20:1-1.
3. Andrinopoulou ER, Eilers PH, Takkenberg JJ, Rizopoulos D. Improved dynamic predictions from joint models of longitudinal and survival data with time-varying effects using P-splines. Biometrics. 2018 Jun;74(2):685-93.
4. Selles RW, Andrinopoulou ER, Nijland RH, Van Der Vliet R, Slaman J, van Wegen EE, Rizopoulos D, Ribbers GM, Meskers CG, Kwakkel G. Computerised patient-specific prediction of the recovery profile of upper limb capacity within stroke services: the next step. Journal of Neurology, Neurosurgery & Psychiatry. 2021 Jun 1;92(6):574-81.
5. Dorr MC, Andrinopoulou ER, Sewnaik A, Berzenji D, van Hof KS, Dronkers EA, Bernard SE, Hoesseini A, Rizopoulos D, Baatenburg de Jong RJ, Offerman MP. Individualized Dynamic Prediction Model for Patient-Reported Voice Quality in Early-Stage Glottic Cancer. Otolaryngology–Head and Neck Surgery. 2024 Jan;170(1):169-78.

Abstract:

Despite the rapid advancement of predictive models, many remain underutilized due to limited accessibility for end-users, particularly in clinical settings. Precision medicine, propelled by advancements in artificial intelligence (AI) and data sources like wearable devices, offers new potential for personalized care. However, effective integration of predictive tools is hindered by challenges in transparency, interpretability, and usability.

The rapid expansion of predictive modeling, particularly through machine learning (ML) and advanced statistical methods, has opened unprecedented opportunities to improve personalized care. The demand for transparency and interpretability in such models has never been more critical, particularly when these models inform decisions that impact patient care or public policy. Machine learning plays a critical role in handling the large volumes of data that accompany modern healthcare, enabling patterns to emerge that were previously undetectable. Yet, these ML algorithms also face challenges akin to those of traditional statistical methods, including overfitting, sampling biases, and improper feature selection. Our research will focus on developing and validating pipelines that address these challenges, ensuring ML-based models are not only reliable and accurate but also clinically relevant.

The project will, moreover, focus on creating a model-independent framework to transform various predictive models into accessible, user-friendly tools. Emphasizing intuitive interfaces and clear visualizations, the project aims to enable healthcare providers to interpret disease risk profiles and progression patterns without extensive technical knowledge, fostering seamless integration into daily clinical workflows. By bridging the gap between methodology and practical healthcare application, our project empowers healthcare professionals with practical, easy-to-use tools that enhance the clinical utility of predictive models. We believe this approach will improve patient outcomes and support data-driven decision-making in healthcare delivery.

Requirements of candidate:

We seek a highly motivated and creative student to join our team in the department of Epidemiology, Biostatistics. Ideal candidates should demonstrate creative thinking skills, and have a strong drive to contribute to the advancement of new methodologies.

- Master's degree in mathematics, statistics, biostatistics, health sciences research, public health or in an equivalent discipline.
- Scholarship to cover subsistence allowance and travelling
- Experience with statistical programming (R)
- The student should be fluent in English (IELTS min 7.0), TOEFL 100 (min 20 for all subs) and have good communicative skills both in speech and in writing.

DEPARTMENT OF CARDIOLOGY

Project:	**Innovation in Diagnosis and Therapy of Cardiac Arrhythmias**
Supervisor information:	*Prof dr. Natasja MS de Groot* *n.m.s.degroot@erasmusmc.nl* ***Website:*** https://www.linkedin.com/in/prof-dr-natasja-de-groot-md-phd-emc-65760662/ https://www.erasmusmc.nl/en/research/researchers/groot-natasja-de , https://www.medicaldelta.nl/onderzoek/medical-delta-cardiac-arrhythmia-lab ***Grants:*** *EU-LSH, Dutch-German Heart Foundation grant, Cardiovascular research Netherlands, personal grants: Dutch Heart Foundation Junior Staffmember, VIDI; multiple companies (e.g. Johnson&Johnson, Bayer)* ***Most important publications:*** Zhang, D., et al. (2019) ***Nature Communications,*** Calkins, H., **Heart Rhythm,** de Groot, N., (2016) **Circulation-Arrhythmia and Electrophysiology;** Knol, W. G., et al. (2019). **Heart Rhythm,** Starreveld, R., (2019) **Europace,** Kharbanda R. (2020) **JACC EP.**
Abstract:	*Our projects are aimed at unravelling the pathophysiology of complex cardiac tachyarrhythmias, developing and testing developing novel diagnostic tools (in close collaboration with Technical university Delft) and therapies for cardiac arrhythmias. Main topics are high resolution mapping studies of cardiac arrhythmias in particular atrial fibrillation, unravelling bio-electrical mechanisms of (post-operative) cardiac arrhythmias, dysrhythmias in patients with congenital heart disease and neuromodulation of atrial fibrillation. For this purpose, we have developed a unique way of recording and processing cardiac signals to perform mapping procedures in the surgical rooms and catheterization laboratory. In addition, we have access to biomimetic set ups for tissue slices and an ex-vivo-heart perfusion model.* *Our innovative scientific contributions include: discovery of novel mechanisms underlying persistence of atrial fibrillation, introduction endovascular mapping approach guiding ablative therapy of atrial tachyarrhythmias in patients with congenital heart disease, development of a novel, intra- operative epicardial mapping approach, discovery of the role of Bachmann's bundle in development of atrial tachyarrhythmias, performed worldwide the first high resolution mapping studies in pediatric patients, discovery conduction properties in pediatric patients with congenital heart disease.* *In our cardiac bio-electricity lab, we combine expertise of developmental biology, cardiac electrophysiology with macro- and microscopic cardiac morphology. We perform clinical and experimental studies in surgical rooms, EP labs, outpatient clinic and animal lab. We have several multi-disciplinary collaborations and electrical-, biomechanical engineers, a variety of medical doctors and molecular biologist are part of our research group.*  ***Keywords:*** *cardiac surgery, electrophysiology laboratory, biomarkers, human-, animal-, clinical-, experimental mapping studies, electrical activity, ECG analysis, electrograms, biomarkers and medical technology.*
Requirements of candidate:	• We are looking for highly motivated, hardworking students to join our very international team. Our strength is in using team work to tackle large scientific questions. • Master degree or MD • Scholarship that will, at least, cover subsistence allowance and international airplane ticket (we could help with the scientific part of your scholarship proposal) • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF CLINICAL GENETICS

Project:	**From complexity to cure: Addressing heterogeneity in lysosomal disease through in vivo precision medicine**
Supervisor information:	**Dr Leslie Sanderson** **l.sanderson@erasmusmc.nl** **Website:** https://orcid.org/0000-0002-8026-406X; **hosting lab page**: https://www.erasmusmc.nl/en/research/groups/barakat-lab-non-coding-genome-in-clinical-genetics **Grants:** Erasmus MC Startersbeurs**,** Marie Skłodowska-Curie COFUND LEaDing Fellows Programme Postdoctoral Fellowship **Supervision of PhD students/info over research group:** My team generates and characterizes *in vivo* models (using zebrafish) of rare neurodevelopmental disorders, particularly those with metabolic and/or membrane trafficking defects, which are also used in preclinical studies. We also develop novel *in vivo* genomic engineering techniques to address complex genetic questions. I currently co-supervise a last-year PhD student and two master interns, advise on multiple PhD projects, and participate in several mentoring programs. We are embedded in the Barakat lab, where we have extensive experience with guiding PhD students. Each student has a team of 3 co-promotors with complementary expertise, ensuring continuous support over the PhD trajectory. ***Five important recent publications:*** Deng et al, Acta Neuropathologica, 2023 https://doi.org/10.1007/s00401-023-02579-9; Berdowski et al, Acta Neuropathologica, 2022 https://doi.org/10.1007/s00401-022-02440-5; Martin et al, Science, 2022 https://doi.org/10.1126/science.abm4459, Sanderson et al, Brain, 2021 https://academic.oup.com/brain/article/144/3/769/6187999; Sofou et al, EMBO Molecular Medicine, 2021 https://doi.org/10.15252/emmm.202013376
Abstract:	*In recent years there has been an increasing awareness of the diversity and essentiality of lysosomal functions, made clear by the wide range of both severity and symptomology seen in lysosomal storage diseases (LSDs). These diseases are individually rare but collectively prevalent and present with a wide range of symptoms covering everything from immune deficits to cardiovascular disease, typically accompanied by particularly strong impacts on the central nervous system. Recently, we have published several LSD-like diseases (ex. VPS16 and VPS41) where defects in membrane trafficking reduce global access to the lysosome. Similarly to many LSDs, we also see substantial heterogeneity within and between patient cohorts, likely resulting in part from the different impacts of specific gene variants.* *This project aims to uncover the roles of lysosome function and membrane trafficking in neurodevelopmental disorders by leveraging two parallel and complementary approaches. First, we will examine how and why symptoms manifest across different tissues by examining cell-type specific lysosome functions and the role of lysosomes in regulating general processes such as cell fate decisions. To do this, we will employ genetic tools including CRISPR/Cas9, lineage-specific and global gene knock-outs, and misexpression systems to manipulate trafficking pathways involved in lysosomal targeting or biogenesis in vivo in the developing zebrafish. Cell behaviours will be observed through confocal live imaging using fluorescent reporters and other tools. These data are anticipated to be informative for a wide range of LSDs. Second, we will dissect the heterogeneity seen between patients within a single cohort by comparing multiple patient "avatars" – zebrafish lines carrying the precise genetic mutations identified in patients – which can subsequently be applied to individualized therapy development. The generation of patient avatars will be facilitated by a novel genomic engineering strategy currently under development in the lab that will enable the rapid, parallel generation of multiple precise gene variants in vivo. In addition to aiding investigations into lysosome biology, validation of this technique will more readily enable the pursuit of precision medicine for a wider range of patients and reduce the barriers to exploring treatments for other diseases with high cohort variability. This project encourages student agency and is well suited for creative and ambitious candidates.*
Requirements of candidate:	We are looking for a highly motivated, enthusiastic, and proactive student to join our very international team. We tackle large scientific questions through teamwork and thus require a student with good communication skills. • Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal) • Master degree or MD degree • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)* • Motivated, enthusiastic, and proactive. Active communicator. • Molecular biology experience desirable.

DEPARTMENT OF CLINICAL GENETICS

Project:	**Neurodevelopmental disorders: from chromatin biology to personalized medicine**
Supervisor information:	**Dr. Kristina Lanko** **Email: k.lanko@erasmusmc.nl** **Website:** https://orcid.org/0000-0002-0749-0079 **Hosting lab page: https://www.erasmusmc.nl/en/research/groups/barakat-lab-non-coding-genome-in-clinical-genetics** **Grants:** PhD funded by H2020 Marie Skłodowska-Curie ITN. In 4,5 years after the PhD total funding obtained via **individual grants €600000:** BBRF Young Investigator Grant (NARSAD, USA); Dutch National talent scheme (NWO) – VENI grant; Innovative research grants (ZonMW) – OffRoad, PSIDER Breakthrough project. **Supervision of PhD students/info over research group:** My team is focusing on stem-cell based models for neurodevelopmental disorders and functional studies to understand the disease mechanism. I'm currently co-supervising a last-year PhD student (supported by CSC scholarship), a research technician and master/bachelor internships. We are embedded in the Barakat lab, where we have extensive experience with guiding PhD students. Each student has a team of 3 (co)-promotors with complementary expertise ensuring continuous support over the PhD trajectory. ***Five important recent publications:*** Brain, vol 144(3), 2021, p.769-780 *https://academic.oup.com/brain/article/144/3/769/6187999; Genetics in Medicine 23 (11), 2122-2137 https://doi.org/10.1038/s41436-021-01246-2; Acta Neuropathologica 146 (2), 353-368 https://doi.org/10.1007/s00401-023-02579-9; Journal of medicinal chemistry 63 (9), 4562-4578 https://pubs.acs.org/doi/full/10.1021/acs.jmedchem.9b01828; Genome medicine 13, 1-27 https://link.springer.com/article/10.1186/s13073-021-00980-1*
Abstract:	*Neurodevelopmental disorders (NDD) present a major cause of disability early in life and a significant burden to the health system. Despite improved diagnostic yield of genetic testing, our understanding of the NDDs disease mechanisms remain incomplete. This project focuses on a group of NDDs caused by variants in chromatin modifiers (genes responsible for the regulation of gene expression) and will investigate fundamental aspects of complex NDD phenotypes as well as novel treatment options.* *We have previously established the first iPSC-based models for novel NDDs (e.g.SETD1B, BICRA), including human excitatory neurons and cerebral organoids. PhD candidate will use in vitro models to gain knowledge on regulatory functions of chromatin modifiers in neurons (ChIP-, ATAC-, RNA-seq techniques) and investigate their functionality by using multi-electrode array (MEA). Based on clinical and in vitro data, the candidate will also perform preclinical testing of modulators of disease-specific pathways aiming to develop new treatment options. We will also employ the multiplexed cerebral organoids approach as innovative method to investigate brain-related NDD phenotypes. Cerebral organoids from a pool of patient-derived induced pluripotent stem cells allow to simultaneously evaluate several pathogenic variants in different cell-types. The tracking of multiple cell-type differentiation and their (affected) transcriptional profile is enabled by the single-cell RNA-sequencing readout, generating a powerful dataset to understand the neuropathology of NDDs. Another aspect of NDDs that we are working on are immunity-related problems, such as recurrent infections – frequently observed in NDD patients' phenotype. In our work we aim to unravel the contribution of multiple NDD-relevant chromatin modifiers to infection phenotype in a systematic manner. We hypothesize that certain chromatin modifiers are involved in regulating host response at an early phase of infection. To investigate this we employ a synergistic approach combining virology and epigenetic analysis to examine the dynamics of chromatin accessibility together with direct transcriptional output of the host cell. Our approach includes conducting single-cell knock-down screens with chromatin accessibility readout to define the key chromatin modifiers regulating the host response and their cooperation. Ultimately we will reveal how the disrupted gene regulation in NDDs impacts the course of infection. In our research we take a comprehensive approach and address both neural and non-neural aspects of NDDs. This offers excellent opportunities for scientific development of the PhD candidate and creates a multilayered picture of the disease, that can help to develop new care strategies for the patients..*
Requirements of candidate:	We are looking for a highly motivated, hardworking student to join our dynamic international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. • Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal) • Master degree or MD degree • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)* • *Proactive approach to research* • *Previous cell-culture and molecular biology experience is a plus*

DEPARTMENT OF CLINICAL GENETICS

Project:	**Noncoding Genomics and Missing heritability**
Supervisor information:	**Dr Stefan Barakat, PhD, MD, MSc,** **t.barakat@erasmusmc.nl** **Website:** https://www.erasmusmc.nl/en/research/groups/barakat-lab-non-coding-genome-in-clinical-genetics https://orcid.org/0000-0003-1231-1562 https://scholar.google.nl/citations?hl=nl&user=2_0A8fkAAAAJ https://www.linkedin.com/in/stefan-barakat-456601141/ **Grants:** amongst others EMBO Fellowship, Marie Curie Sklodowska Fellowship, ZonMw Veni, ZonMw Vidi (Dutch talent program), KNAW Early Career Award, ERC funding, CURE Epilepsy Award, American Society of Human Genetics Charles J. Epstein Award for Excellence in Human Genetics; NARSAD Brain & Behavior Research Foundation Young Investigator Award, total funding since 2017 > 8 million euro. **Supervision of PhD students/info over research group:** you will be supervised in the Barakat lab. We are a multinational team of ~15 researchers at all career stages with a multidisciplinary background (both wet lab and dry lab). I have supervised >30 scientists from 20 different countries in my team. Previous PhD students have published multiple first-author papers and acquired competitive postdoc grants after successfully finishing their PhDs and supervised postdocs started their own groups. We have multiple international collaborations, including with prestigious institutes in US, UK and Europe. ***Selected important recent publications (IF= impact factor):*** *Jonkers et al **Cell** 2009 (IF:36), Gontan et al **Nature** 2012 (IF:42), Barakat et al **Molecular Cell** 2014 (IF:15), Barakat et al **Cell Stem Cell** 2018 (IF: 21), Gontan et al **Nature Communications** 2018 (IF:12), Oegema et al 2020 **Nature Reviews Neurology** (IF 42), Perenthaler et al **Acta Neuropathologica** (IF: 18), Hengel et al **Nature Communications** 2018 (IF:12), AlMuhaizea et al **Acta Neuropathologica** 2020 (IF 18), Barrish et al **American Journal of Human Genetics** 2020 (IF:11), Radio et al **American Journal of Human Genetics** 2021 (IF:11), Sanderson et al **Brain** 2021 (IF;14), Yousefi et al 2021 **Genome Medicine** (IF:11), Medico Salsench et al **Brain** 2021 (IF:14), Calame et al **Annals in Neurology** 2022 (IF:10), Claus et al **Kidney International** 2023 (IF:20), Pagliara et al **American Journal of Human Genetics** 2023 (IF:10), Deng et al 2023 A**cta Neuropathologica** (IF 18), Huang et al **Developmental Cell** 2024 (IF:12), Kalm et al **American Journal of Human Genetics** 2024 (IF:10), Delgado-Vega et al **Nature Genetics** 2024 (IF: 27).* All publications can be found at: https://pubmed.ncbi.nlm.nih.gov/?term=tahsin+stefan+barakat
Abstract:	*In the field of clinical genetics, we still do not know the cause of genetic disorders for more than 50% of our patients despite all technological advancements such as next generation based sequencing technologies. My laboratory aims to reduce this missing heritability in the context of brain disorders such as intellectual disability and epilepsy. To this end, we are studying on the one hand novel disease genes to validate their involvement in human disease, and on the other hand develop novel technologies to decipher the role of the non-coding genome and gene regulatory elements such as enhancers in causing disease. For the disease modelling projects, we make use of genetic studies, in vitro cell models (including patient-derived iPS cells, differentiated neurons and brain organoids), CRISPR-Cas9 based tools, and in vivo modelling using zebrafish including therapy development. For our work on deciphering the role of the noncoding genome, we make use of functional genomics tools, including massively parallel reporter assays, CRISPR based screens and computational analysis. The latter includes multi-omics integration, the development of novel artificial intelligence based algorithms to assess functionality of noncoding genome sequences and analysis of (short/long read) whole genome sequencing data from patients affected by rare disorders. Our close bridging to the diagnostics and clinical teams at our university enables rapid impact of our research findings.* *We are always looking for highly motivated and outstanding PhD students to work on either disease modelling or computational studies in our team. Previous experience in one of these domains, as testified by (co)-authored publications, would be a strong plus.*
Requirements of candidate:	We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. • Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal) • Master degree or MD degree • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF EPIDEMIOLOGY

Project: Distributed Machine Learning in application for large-scale omics studies

Supervisor information:

Dr. Gennady Roshchupkin *email: g.roshchupkin@erasmusmc.nl* *webpages: www.roshchupkin.org ; www.bigr.nl*

Personal Grants:

Gennady Roshchupkin is (co-PI) of Dutch, European and USA research grants, including on NIH R01 (750 kEuro), NVIDIA research grant. He received personal VENI grants (280kEuro) and Erasmus MC fellowship award (400 kEuro). Total research funding over last 10 years is more than 5 MEuro. He has supervised 5 PhD students and >20 master students

Most important publications:

- Hofer, E., Roshchupkin, G.V., Adams, H.H… Niessen WJ… Sudha Seshadri ., 2020. Genetic correlations and genome-wide associations of cortical structure in general population samples of 22,824 adults. Nature Communications, 11(1), pp.1-16..
- Wang, J., Knol, M.J., Tiulpin, A., Dubost, F., de Bruijne, M., Vernooij, M.W., Adams, H.H., Ikram, M.A., Niessen, W.J. and Roshchupkin, G.V., 2019. Gray matter age prediction as a biomarker for risk of dementia. Proceedings of the National Academy of Sciences, 116(42), pp.21213-21218..
- Roshchupkin GV, Gutman BA, Vernooij MW, Jahanshad N, Martin NG, Hofman A, McMahon KL, Van Der Lee SJ, Van Duijn CM, De Zubicaray GI, Uitterlinden AG, Wright MJ, Niessen WJ, Thompson PM, Ikram MA, Adams HHH. Heritability of the shape of subcortical brain structures in the general population. Nature Communications. 2016;7.
- Roshchupkin GV, Adams HHH, Vernooij MW, Hofman A, Van Duijn CM, Ikram MA, Niessen WJ. HASE: Framework for efficient high-dimensional association analyses. Scientific Reports. 2016;6.
- Grasby, K.L., Jahanshad, N., Painter, J.N., Colodro-Conde, L., Bralten, J., Hibar, D.P., Lind, P.A., Pizzagalli, F., Ching, C.R., McMahon, M.A.B. and Shatokhina, N., 2020. The genetic architecture of the human cerebral cortex. Science, 367(6484), p.eaay6690
- van Hilten, A., Kushner, S.A., Kayser, M., Ikram, M.A., Adams, H.H., Klaver, C.C., Niessen, W.J. and Roshchupkin, G.V., 2021. GenNet framework: interpretable deep learning for predicting phenotypes from genetic data. Communications biology, 4(1), p.1094.

Abstract:

Artificial Intelligence *field has seen dramatic advances in the past few years with much excitement around the use of deep learning (DL), many-layered convolutional neural networks (CNN). The world has witnessed striking advances in the ability of machines to understand and manipulate data, including images, language, and speech. CNN showed ability to detect a complex pattern in high-dimensional data, but also are able to integrate data from various resources by having many input channels into neural network. Human genetics can benefit immensely from DL. However, the application of AI in genetics analysis is still quite limited. The main issue is the restriction for data sharing between cohorts and loss of power, compare to the pooled analysis.*

Distributed Learning is a distributed machine learning approach which enables model training on a large corpus of decentralized data.

The main goal of this project *is to develop new distributed learning framework for multi-center genetics analysis in collaboration with* ***NVIDIA company****, which will be able to utilize machine learning approaches and increase power of gene discovery. We aim to apply these methods on large datasets from population-based Rotterdam study, UK Biobank as well as within* ***world-wide genetics consortiums****..*

Requirements of candidate:

- We are looking for a highly motivated, hardworking student to join our very international team. Successful candidates are expected to have a strong quantitative or computer science background, excel at critical thinking, with a strong motivation to engage in the development and application of advanced analytical methods.
- Master degree in mathematics, computer science, statistics, bioinformatics, physics, electrical engineering, or in an equivalent discipline.
- Experience with Python and Linux environment.
- Experience with machine learning and deep learning methods.
- The student should be fluent in English (IELTS *min 7.0)*, TOEFL 100 *(min 20 for all subs)* and have good communicative skills both in speech and in writing.

DEPARTMENT OF EPIDEMIOLOGY

Project: Unraveling Subclinical Atherosclerosis

Supervisor information:

Dr Daniel Bos, MD PhD
PI Imaging of Arteriosclerosis group | Epidemiologist | Deputy Chair Dept of Epidemiology
Email: d.bos@erasmusmc.nl
Profile: https://www.linkedin.com/in/daniel-bos/
Website: https://www.erasmusmc.nl/en/research/groups/imaging-of-arteriosclerosis

Most important grants and awards:

World Cancer Research Fund (2024)
Erasmus MC Grant (2023)
Innovation Center for AI – Stroke lab (2023)
NIH grant (2023)
European Commission Horizon 2020 - Research and Innovation Framework Programme (2019)
Netherlands Organisation for Scientific Research grant (2019)
BrightFocus Foundation Grant (2017)
Royal Academy of Arts and Sciences Grant (2016)
Lourens Penning Prize for best publication in Neuroradiology(2016)

Most important publications:

Alzheimers Dement 2024;20:2497.
Nature Genetics 2023; 55;10:1651.
Eur Heart J 2022; 43(39):3960.
JACC 2020;19(75):2387.
Plos Med 2020;17(5):e1003115.
Eur Heart J 2018;39:3369.
JACC 2018;72:582.
Eur Radiol 2018;28:3082.
Circulation 2017;135(22):2207.

Dr Maarten J.G. Leening, MD MSc PhD FESC
Preventive Cardiologist | Epidemiologist
Email: m.leening@erasmusmc.nl
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Most important grants and awards:

Dutch Heart Foundation grant (2024)
Alzheimer Foundation Netherlands grant (2023)
Netherlands Organisation for Scientific Research grant (2020)
Dutch Ministry of Health, Welfare, and Sports grant (2017)
Elizabeth Barrett-Connor Research Award American Heart Association (2014)
Young Investigator Award European Society of Cardiology (2014)

Most important publications:

Circulation 2024; in press.
JACC Img 2024; in press
Circulation 2020;142(9):838.
JACC 2018;71(2):259.
Circulation 2017;135(22):2207
JACC Img 2017;10(11):1405.
Eur Heart J 2017;38(20):1542.
JAMA 2016;315(14):1449.
JAMA 2014;311(14):1416.
Ann Intern Med 2014;160(2):122.
BMJ 2014;349:g5992.
Ann Intern Med 2012;157(6):389.

Abstract:

Most chronic conditions have a long preclinical phase before symptoms or complications occur. This provides a window for preventive interventions to avoid or delay clinical sequela. Atherosclerosis is a prime example of a chronic condition that develops over decades and can be readily identified on routine computed tomography (CT) imaging obtained for other clinical indications. Progression of atherosclerosis can be halted and reversed with effective and safe interventions in lifestyle and medication. As such, a vast preventive potential could be unlocked from everyday clinical CT imaging among individuals without manifest atherosclerotic disease.
This study aims to optimize automated quantification of subclinical coronary and cerebrovascular atherosclerosis on routine CT imaging. This includes validation of innovative software packages, describing distributions and localizations of subclinical atherosclerosis in unselected individuals, and linking quantitative measures of atherosclerosis to prognosis. In this project, the student will leverage highly detailed systematically collected data from unselected population-based cohorts (e.g. the Rotterdam Study) as well as large routine clinical care imaging datasets.
The student will work at the cross-section of Radiology, Epidemiology, and Cardiology. This setting provides a multidisciplinary environment with available expertise at all fronts in order to facilitate a unique learning experience that fosters scientific growth and productivity.

Requirements of candidate:

We are looking for a highly motivated, hardworking PhD student to join our international team. Our strength is in using team work to address important scientific questions and therefore requires a student with excellent communication skills.

- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisors can assist with preparing the scientific part of your scholarship proposal)
- MD degree or Master degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF EPIDEMIOLOGY

Project:	**Integration of population-based omics data to explore molecular mechanisms underlying age-related diseases**
Supervisor information:	**Dr. Mohsen Ghanbari,** Associate Professor and Principal Investigator of the 'Molecular & Systems Epidemiology' group **Email:** m.ghanbari@erasmusmc.nl https://www.erasmusmc.nl/en/research/researchers/ghanbari-mohsen https://pure.eur.nl/en/persons/mohsen-ghanbari https://scholar.google.com/citations?user=pwJpmOQAAAAJ&hl=en **Grants:** - EU4Health NutriBrain program, Modulation of brain-ageing with nutrition and healthy lifestyle. 2024-2027 - MODEM consortium, A national multi-centric grant for Mechanisms of Dementia. 2022-2027 - Alzheimer Nederland, Non-coding RNAs in metabolic pathways underlying Alzheimer's disease, 2022-2024. - Erasmus MC Fellowship, Atlas of genetic architecture and disease association of microRNAs, 2022-2026. - SOPHIA grant, A multi-centric H2020 grant for understating mechanism of Obesity. 2020-2023 - Alzheimer Nederland travel grant, Casual Inference and Alzheimer's disease, 2018 - European Fellowship for study of the Diabetes, Visiting Imperial College London, 2018 - European Society of Human Genetics fellowship, Advanced courses in Human Genetics, 2016 **Most important publications** (Dr. Ghanbari has so far published over 160 international peer-reviewed publications): **Genome Biology**. 2024 Oct 21;25(1):276. A comprehensive study of genetic regulation and disease … **Commun Biology.** 2024 Sep 9;7(1):1103. Genome-wide association study meta-analysis of NfL … **Biomarker Res**. 2024 Aug 13;12(1):83. Dysregulation of plasma circulating microRNAs in all-cause ... **Brain.** 2020 Apr 1;143(4):1220-1232. Plasma tau, neurofilament light chain and amyloid-β levels … **Cell.** 2020 Sep 3;182(5):1214-1231. The Polygenic and Monogenic Basis of Blood Traits and Diseases. **Diabetes Care.** 2020 Apr;43(4):875-884. Epigenetic Link Between Statin Therapy and Type 2 Diabetes. **Nature Communications.** 2019 Aug 20;10(1):3346. A metabolic profile of all-cause mortality risk … **Human Mutation.** 2019 Nov;40(11):2131-2145. A functional variant in the miR-142 promoter … **Nature Genetics.** 2019 Apr;51(4):636-648. Multi-ancestry genome-wide gene-smoking interaction … **Nature Communications.** 2019 Jan 22;10(1):376. Multi-ancestry study of blood lipid levels identifies … **Gastroenterology.** 2017 Oct;153(4):1096-1106. Epigenome-Wide Association Study Identifies …
Abstract:	Genetic and molecular epidemiology are emerging innovative fields of research in which molecular and biological concepts are incorporated into computational models and epidemiologic studies to identify genetic predispositions of complex diseases. This is made possible by recent rapid technological advances in high-throughput laboratory assays that measure various biomarkers from biological samples. Although traditional epidemiology has been proven valuable to identify associations between exposure and disease in populations; however, it does so without obtaining information of the biological processes that underlie the associations. Molecular epidemiology could enhance the measurement of exposure, effect, and susceptibility, and give insight into biological mechanisms. This knowledge will ultimately lead to the identification of early etiologic, diagnostic, and prognostic markers of diseases, allow us to better target preventive strategies and yield new therapeutics for complex diseases. Within the Molecular & Systems epidemiology research line at the Department of Epidemiology, we conduct cutting-edge research to identify the genetic determinants and novel biomarkers for age-related diseases (e.g., Alzheimer's disease, fatty liver disease, cardiovascular disease). To this end, we integrate omics data (genomics, epi-genomics, transcriptomics, proteomics, metabolomics) from the Rotterdam Study, a large population-based cohort of ~18,000 participants followed since 1990, employ advanced analytical methods, and conduct collaborative in-vitro studies. Moreover, we closely collaborate with several renowned international population-based cohort studies across Europe and United States to validate our findings.
Requirements of candidate:	• We are looking for a highly motivated, bright student to join our international and multidisciplinary team. For this projects, using big data and often collaborating in consortia, we require strong bioinformatics and good communication skills. • The student should have an MD or Master degree in Biology, Epidemiology, Biostatistics or a related field, and should be fluent in English (IELTS≥7.0 (≥6.0 for all subs), TOEFL ≥100 (≥20 for all subs). • We offer: Supervision, data access, advanced courses in genetic epidemiology and biostatistics, research infrastructure, and other training. Your salary and living expenses should be covered by the scholarship. We could help with the scientific part of the proposal. For more information related to this proposal, please contact dr. Mohsen Ghanbari (m.ghanbari@erasmusmc.nl).

DEPARTMENT OF EPIDEMIOLOGY

Project: Population Impact of Innovations in Preventive Cardiology

Supervisor information:

Dr Maarten J.G. Leening, MD MSc PhD FESC
Preventive Cardiologist | Epidemiologist
Email: m.leening@erasmusmc.nl
Profile: https://www.linkedin.com/in/maarten-j-g-leening-1a29a657

Most important grants and awards:
Dutch Heart Foundation grant (2024)
Alzheimer Foundation Netherlands grant (2023)
Netherlands Organisation for Scientific Research grant (2020)
Dutch Ministry of Health, Welfare, and Sports grant (2017)
Elizabeth Barrett-Connor Research Award American Heart Association (2014)
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Most important publications:
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Circulation 2020;142(9):838.
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Eur Heart J 2017;38(20):1542.
JAMA 2014;311(14):1416.
BMJ 2014;349:g5992.
JACC Img 2024; in press
JACC 2018;71(2):259.
JACC Img 2017;10(11):1405.
JAMA 2016;315(14):1449.
Ann Intern Med 2014;160(2):122.
Ann Intern Med 2012;157(6):389.

Dr Daniel Bos, MD PhD
PI Imaging of Arteriosclerosis group | Epidemiologist | Deputy Chair Dept of Epidemiology
Email: d.bos@erasmusmc.nl
Profile: https://www.linkedin.com/in/daniel-bos/
Website: https://www.erasmusmc.nl/en/research/groups/imaging-of-arteriosclerosis

Most important grants and awards:
World Cancer Research Fund (2024)
Innovation Center for AI – Stroke lab (2023)
Erasmus MC Grant (2023)
NIH grant (2023)
European Commission Horizon 2020 - Research and Innovation Framework Programme (2019)
Netherlands Organisation for Scientific Research grant (2019)
BrightFocus Foundation Grant (2017)
Royal Academy of Arts and Sciences Grant (2016)
Lourens Penning Prize for best publication in Neuroradiology(2016)

Most important publications:
Alzheimers Dement 2024;20:2497.
Eur Heart J 2022; 43(39):3960.
Plos Med 2020;17(5):e1003115.
JACC 2018;72:582.
Circulation 2017;135(22):2207.
Nature Genetics 2023; 55;10:1651.
JACC 2020;19(75):2387.
Eur Heart J 2018;39:3369.
Eur Radiol 2018;28:3082.

Abstract:

Over the past decade, a major shift in diagnostic tests and treatment options have emerged in the field of preventive cardiology and cardiovascular disease prevention at large. Imaging of subclinical atherosclerosis and blood biomarkers can identify asymptomatic individuals at very high risk of future atherosclerotic events. New drug classes (e.g. PCSK9-inhibitors, Lp(a)-lowering, low-dose colchicine, SGLT2-inhibitors, and GLP1-receptor antagonists) have emerged as potent options to lower cardio-metabolic risks in a wide spectrum of patients.

The potential impact at population level of these new diagnostic and therapeutic options remains poorly understood. In this project, the student will leverage highly detailed systematically collected data from unselected population-based cohorts (e.g. the Rotterdam Study) as well as international registries of patients with stable coronary heart disease (e.g. ESC EUROASPIRE V and VI). Eligibility, potential population risk reductions, numbers needed to treat and numbers needed to screen for a wide range of imaging and blood biomarkers, as well as new drug classes will be evaluated. Findings of these studies will be informative to practicing clinicians and clinical practice guideline committees alike.

The student will work at the cross-section of Cardiology, Vascular Medicine, Epidemiology, and Radiology. This setting provides a multidisciplinary environment with available expertise at all fronts in order to facilitate a unique learning experience that fosters scientific growth and productivity.

Requirements of candidate:

We are looking for a highly motivated, hardworking PhD student to join our international team. Our strength is in using team work to address important scientific questions and therefore requires a student with excellent communication skills.

- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisors can assist with preparing the scientific part of your scholarship proposal)
- MD degree or Master degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF EPIDEMIOLOGY

Project: Deep Learning in Omics Data Analysis and Precision Medicine

Supervisor information:

Prof.dr. M. Arfan Ikram
Secondary affiliation: Adj. professor at Harvard Chan School of Public Health, Boston
Email: m.a.ikram@erasmusmc.nl
Website: https://www.erasmusmc.nl/en/research/researchers/ikram-arfan-m

dr Gennady Roshchupkin
g.roshchupkin@erasmusmc.nl
www.roshchupkin.com

Personal Grants MA Ikram:
Total research funding over last 10 years is more than 15 MEuro, including ERC Starting Grant, European JPND grant, multiple Horizon 2020 consortium collaborations, multiple NIH R01-subcontract PI. He has supervised 28 PhD students.

Personal Grants Roshchupkin:
Gennady Roshchupkin is (co-PI) of Dutch, European and USA research grants, including on NIH R01 (750 kEuro), NVIDIA research grant. He received personal VENI grants (280kEuro) and Erasmus MC fellowship award (400 kEuro). Total research funding over last 10 years is more than 5 MEuro. He has supervised 5 PhD students and >20 master students

Most important publications:

Satizabal CL. Nat Genetics 2019
Hibar DP. Nat Commun 2017
Roshchupkin GV. Nat Commun 2016
Ikram MA. NEJM 2009
Wang J. PNAS 2019
Adams HH. Nat Neurosc 2016
Ikram MA. Nat Genetics 2012

Abstract:

A central goal of human genetics is to understand the relationship between genetic variation and diseases or traits. There are many different technologies, study designs and analytical tools for identifying such relations. Recent technological advances and biobank initiatives have allowed studies involving hundreds of thousands, and even millions, of individuals. Moreover, many studies have started collected other omics data beyond genetic data, including ***gene expression, methylation, proteins, metabolites, and microbiome****. This allows getting closer to the trait's etiology. However, by nature most of the analytical tools and methods are either univariate or cannot handle multi-omics data. Therefore, cross-omics methods are missing. Human genetics needs new types of approaches to solve such problems for improving the diagnosis, treatment, and classification of complex diseases.*
Deep learning (DL) *is a rapidly growing field. The application of the neural networks has become a golden standard in many research areas. DL algorithms have shown successful ability to detect a complex pattern in high-dimensional data, and also are able to integrate data from various resources by having many input channels into neural network*

The main goal of this project is to develop new DL methods for multi-omics analysis, which will be able to integrate prior biological knowledge and improve our understanding of the etiology of complex traits, such as dementia and cognition*. An additional dimension in this project will be to combine the various omics data to brain MRI-imaging. We aim to apply these methods on large datasets from population-based* ***Rotterdam study, UK Biobank*** *as well as within* ***international CHARGE consortium****.*
Co-supervision in this project will be done by dr. Gennady Roshchupkin.

Requirements of candidate:

- We are looking for a highly motivated, hardworking student to join our very international team. Successful candidates are expected to have a strong quantitative or computer science background, excel at critical thinking, with a strong motivation to engage in the development and application of advanced analytical methods.
- Master degree in mathematics, computer science, statistics, bioinformatics, physics, electrical engineering, or in an equivalent discipline.
- Experience with Python and Linux environment.
- Experience with machine learning and deep learning methods.
- The student should be fluent in English (IELTS *min 7.0)*, TOEFL 100 *(min 20 for all subs)* and have good communicative skills both in speech and in writing.

DEPARTMENT OF GASTROENTEROLOGY & HEPATOLOGY

Project:	**Dissecting the role of microplastics on the infection and inflammation in the gut-liver axis**
Supervisor information:	**Dr. Pengfei Li; PhD** **Email: *p.li@erasmusmc.nl*** **Website: *https://www.erasmusmc.nl/en/research/researchers/li-pengfei*** **Grants (ongoing):** ***Young Investigator Grant (Erasmus MC): € 200,000*** ***ZonMw-Pandemic Preparedness: € 50,000*** **Most important publications:** 1. Li P, Pachis ST, Xu G, Schraauwen R, Incitti R, de Vries AC, Bruno MJ, Peppelenbosch MP, Alam I, Raymond K, Pan Q. Mpox virus infection and drug treatment modelled in human skin organoids. Nature Microbiology. 2023 Nov;8(11):2067-2079. 2. Li P, Du Z, Lamers MM, Incitti R, Tejeda-Mora H, Li S, Schraauwen R, van den Bosch TPP, de Vries AC, Alam IS, Haagmans BL, Hoogduijn MJ, Pan Q. Mpox virus infects and injures human kidney organoids, but responding to antiviral treatment. Cell Discovery. 2023;9(1):34. 3. Li P, Wang Y, Lavrijsen M, Lamers MM, de Vries AC, Rottier RJ, Bruno MJ, Peppelenbosch MP, Haagmans BL, Pan Q. SARS-CoV-2 Omicron variant is highly sensitive to molnupiravir, nirmatrelvir, and the combination. Cell Research. 2022;32(3):322-324. 4. Li P, Wang Y, Lamers MM, Lavrijsen M, Iriondo C, de Vries AC, Rottier RJ, Peppelenbosch MP, Haagmans BL, Pan Q. Recapitulating infection, thermal sensitivity and antiviral treatment of seasonal coronaviruses in human airway organoids. EBioMedicine. 2022;81:104132. 5. Li P, Li Y, Wang Y, Liu J, Lavrijsen M, Li Y, Zhang R, Verstegen MMA, Wang Y, Li TC, Ma Z, Kainov DE, Bruno MJ, de Man RA, van der Laan LJW, Peppelenbosch MP, Pan Q. Recapitulating hepatitis E virus-host interactions and facilitating antiviral drug discovery in human liver-derived organoids. Science Advances. 2022 Jan 21;8(3):eabj5908. **Publication link (2 last authors, 19 first authors):** **https://pubmed.ncbi.nlm.nih.gov/?term=%28%28Pengfei+Li%29+OR+%28%28Li+P%29+AND+%28Jiang+S%29%29%29+AND+%28%28Erasmus+Medical+Center%29+OR+%28%28department+of+preventive+veterinary+medicine%29+AND+%28Shandong+Agricultural+University%29%29%29&sort=date**
Abstract:	*Widespread waste of micro- and nano-plastics (MNPs) have been associated with a range of physiological and pathological issues in animals and humans. With the accumulation of MNPs in the environment, the increased risk of human exposure to MNPs and the possible consequences for human health are eminent. On the one hand, through daily food and water consumption, MNPs from plastic package can accumulated in the human digestive system, particularly in the liver and gut. We hypothesize that this accumulation of MNPs may induce detrimental effect to the liver and gut, such as triggering the inflammatory response in gut-liver axis.* *On the other hand, evidence suggests that MNPs can act as carriers for pathogenic viruses. Alarmingly, there are a large amount of food- and water-borne viruses (e.g., hepatitis E virus, rotavirus), which can attach to MNPs and eventually enter the digestive system. We further hypothesize that MNPs carrying these viruses may enhance viral infectivity and pathogenesis, leading to severe infections that harm the gut and liver.* *This project aims to investigate the role of MNPs in viral infections and inflammatory responses within the gut-liver axis. Human organoids are superior models in comparison to classical cancer cell lines, which have been increasingly used for studying infectious and non-infectious diseases. To effectively achieve the project, the PhD candidate will specifically employ human tissue-derived liver and intestinal organoids for simulating the gut-liver axis.*
Requirements of candidate:	• **We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.** • **Master degree or MD degree** • **English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)***

DEPARTMENT OF GASTROENTEROLOGY & HEPATOLOGY

Project:	**Combating emerging viral diseases**
Supervisor information:	**Dr. Qiuwei Abdullah Pan; PhD** **Email: g.pan@erasmusmc.nl** **Most relevant recent publications:** Pengfei Li, Jaffar A. Al-Tawfiq, Ziad A. Memish, Qiuwei Pan*. Preventing drug resistance: combination treatment for mpox. *Lancet*. 2023 Nov 11;402(10414):1750-1751. Pengfei Li, Spyridon T. Pachis, Guige Xu, Rick Schraauwen, Roberto Incitti, Annemarie C. de Vries, Marco J. Bruno, Maikel P. Peppelenbosch, Intikhab S. Alam, Karine Raymond, Qiuwei Pan*. Mpox virus infection and drug treatment modelled in human skin organoids. *Nature Microbiology*. 2023 Nov;8(11):2067-2079. Li Y, Zhang R, Wang Y, Li P, Li Y, Janssen HLA, de Man RA, Peppelenbosch MP, Ou X, Pan Q*. Hepatitis E virus infection remodels the mature tRNAome in macrophages to orchestrate NLRP3 inflammasome response. *Proc Natl Acad Sci U S A*. 2023 Jun 20;120(25):e2304445120. Li P, Li Y, Wang Y, Liu J, Lavrijsen M, Li Y, Zhang R, Verstegen MMA, Wang Y, Li TC, Ma Z, Kainov DE, Bruno MJ, de Man RA, van der Laan LJW, Peppelenbosch MP, Pan Q*. Recapitulating hepatitis E virus-host interactions and facilitating antiviral drug discovery in human liver-derived organoids. *Science Advances*. 2022 Jan 21;8(3):eabj5908. Li P, de Vries AC, Kamar N, Peppelenbosch MP, Pan Q*. Monitoring and managing SARS-CoV-2 evolution in immunocompromised populations. *Lancet Microbe*. 2022 May;3(5):e325-e326.
Abstract:	Despite advances in modern medicine, viral diseases consistently pose major public health, economic and societal burdens throughout the world. This is largely due to the ability of viruses to emerge and re-emerge frequently in humans from natural reservoirs such as wild and domesticated animals, leading to unpredictable outbreaks. Just over the past 100 years, several major epidemics and pandemics have been caused by an infectious disease, each with over one million recorded deaths. The current COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infiltrated every corner of the world resulting in over 7 million deaths officially recorded by WHO so far, which is likely an underestimation. In the meantime, a global outbreak of monkeypox virus (MPXV) emerged, with Europe as the first epicentre. Over 200 virus species are known to cause diseases in humans, but current efforts of therapeutic development only target a few percent of them, leaving a large number of pathogenic viruses neglected. We dedicate to understanding the pathogenic mechanisms and developing therapeutics for a wide range of emerging and re-emerging viruses, including hepatitis D virus, hepatitis E virus, coronaviruses, monkeypox virus and flaviviruses.
Requirements of candidate:	• **We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.** • **Master degree or MD** • **English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs).***

DEPARTMENT OF GASTROENTEROLOGY & HEPATOLOGY

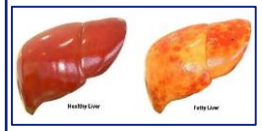
Project: Molecular Characterization of Immunological Pathways in NASH

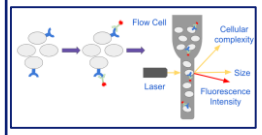
Supervisor information:

Prof.dr. Andre Boonstra
p.a.boonstra@erasmusmc.nl

Dr. Gulce Sari
g.sari@erasmusmc.nl

Dr. Willem Pieter Brouwer
w.p.brouwer@erasmusmc.nl





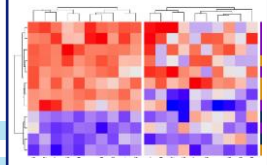
For information about our research and laboratory:

www.viralhepatitis.nl www.escalon.eu (EU funded ESCALON project) https://www.erasmusmc.nl/en/research/groups/chronic-viral-hepatitis-liver-cancer

Recent publications by the team:

- Beudeker BJB, ….Boonstra A. Validation and optimization of AFP-based biomarker panels for early HCC detection in Latin America and Europe. Hepatol Comm. 2023 Sep 15;7(10):e0264.
- Montanari NR, …Boonstra A. Multi-parametric analysis of human livers reveals intrahepatic inflammation variation across chronic hepatitis B infection phase. J Hepatol. 2022. 77(2): 332-343.
- Osmani Z, Boonstra A. Recent insights into the role of B cells in chronic viral hepatitis infections. Pathogens 2023 12(6): 815.
- Vanwolleghem T, ….Boonstra A. Hepatitis B core-specific memory B cell responses associate with clinical parameters in patients with chronic HBV. J Hepatol. 2020 Jul;73(1):52-61.
- Debes J, …..Boonstra A. Levels of Cytokines in Serum Associate With Development of Hepatocellular Carcinoma in Patients With HCV Infection Treated With Direct-Acting Antiviral Gastroenterology. 2018. Feb; 154(3):515-517.
- Debes J, … Boonstra A. Serum Biomarkers for the Prediction of Hepatocellular Carcinoma. Cancers. 2021; 13(7):1681.

Abstract:



The research group of professor Boonstra is devoted to understand the immune responses in hepatitis. Besides this, a major effort of his team focusses on the search for new biomarkers to predict the development of fibrosis and hepatobiliary cancers at early stages in patients at risk.

NASH is becoming increasingly prevalent worldwide, especially in developed countries, largely due to the epidemic of obesity and metabolic syndrome. Understanding its mechanisms and finding effective treatments are critical to address this growing public health concern. NASH can progress to advanced liver diseases such as cirrhosis, liver failure, and hepatocellular carcinoma (liver cancer) and imposes a significant economic burden on healthcare systems due to its associated complications, including hospitalizations, liver transplants, and ongoing medical care. Currently, there are no FDA-approved pharmacological treatments specifically for NASH. Research efforts aim to identify potential therapeutic targets and develop effective interventions to halt or reverse the progression of the disease. It is a multifactorial disease with complex pathogenesis involving interactions between genetic, environmental, metabolic, and immunological factors. Our research group aims to identify potential therapeutic targets and develop effective interventions to halt or reverse the progression of the disease.

The research, conducted by both biologists and medical doctors within the group, combines basic immunology and state-of-the-art systems biology, genetic manipulations as CRISPR-Cas tools and molecular biology methods together with translational studies using patient cohorts. Examples of current projects include but not limited to: multicolor microscopy imaging with Imaging Mass Cytometry (Hyperion), single cell RNASeq studies on liver aspirate biopsies, studies to examine the functionality of B cells, the search for biomarkers to predict fibrosis progression in NASH and early stage of hepatocellular carcinoma to improve patient survival. These translational studies are facilitated by extensive biobanks and databases that have been set up over the years by the research group, as well as by participation in longitudinal clinical studies focused on improvement of therapy, and participation in numerous multi-center Phase I/II clinical trials.

The research is conducted in close collaboration with clinicians and researchers of the department of Hepatology, Pathology, Virosciences and Infectious Diseases. In addition, the team participates in many national and international consortia, and professor Boonstra is the main applicant and coordinator of the EU Horizon2020 grant ESCALON, aimed at improving early detection and diagnosis of cancers to the liver, the bile ducts and the gall bladder. The ESCALON consortium consists of members from 11 countries and enables the team to conduct long-lasting collaborative studies with the South American partners in Chile, Argentina, Peru, Colombia, Brazil and Ecuador.

Requirements of candidate:

- **We are looking for highly motivated, talented students with a Master degree or MD, to join our research team. The scholarship will, at least, cover subsistence allowance and an international airplane ticket.**
- **Working in the lab requires that the student has good communication skills. Therefore, we have English language requirements: IELTS 7.0 (min 6.0 for all subs), TOEFL 100 (min 20 for all subs), for In addition, at the start of the research project, the student needs to be vaccinated and have protective antibody titers to HBV.**

DEPARTMENT OF GASTROENTEROLOGY & HEPATOLOGY

Project:	**Biliary complications after liver transplantation**
Supervisor information:	**Dr. Caroline M. den Hoed, MD PhD** **Email: c.denhoed@erasmusmc.nl** **Website: C.M. (Caroline) den Hoed, MD PhD - Researcher - Erasmus MC** ***Current functions:*** - **Medical director Liver transplant Program Erasmus MC** - **Board Member of the National Council for Livertransplantation (LOL)** - **Board Member Transplantation Institute Erasmus MC** - **Most important publications:** 1. One-year transplant-free survival following hospital discharge after ICU Admission for ACLF in the Netherlands. Journal of Hepatology 2024; S0168-8278(24)00155-7 2. Recent outcomes of liver transplantation for Budd-Chiari syndrome: A study of the European Liver Transplant Registry (ELTR) and affiliated centers. Hepatology 2024 Jul 1;80(1):136-151 3. Three-year results of renal function in liver transplant recipients on low-dose sirolimus and tacrolimus: a multicenter, randomized, controlled trial. Liver Transplantation 2023; 29 (2): 184 4. The Role of PIVKA-II as a Predictor of Early Hepatocellular Carcinoma Recurrence-Free Survival after Liver Transplantation in a Low Alpha-Fetoprotein Population. Cancers 2023; 16(1):4. 5. High antibody response in relation to immunosuppressive blood levels in liver transplant recipients after SARS-CoV-2 vaccination: an observational, cohort study. Gut 2022; 71(12): 2605 6. Location and allocation: Inequity of access to liver transplantation for patients with severe acute-on-chronic liver failure in Europe. Liver Transplantation 2022; 28(9):1429 7. COVID-19 in liver transplant candidates: pretransplant and post-transplant outcomes - an ELITA/ELTR multicentre cohort study. Gut 2021; 70 (10): 1914 8. Identification of genetic loci associated with Helicobacter pylori serologic status. JAMA 2013; 309(8):1912
Abstract:	*One of the most significant complications with a large impact on morbidity and graft survival are biliary complications such as biliary leakage, ischemic type biliary lesions (ITBL), anastomotic strictures (AS) and non-anastomotic (strictures). Though a lot of work is done on preservation and machine perfusion to prevent biliary complications we still see biliary complications in ~ 20% of postmortal liver transplantations and ~30-50 % of living donor liver transplantations.* *Despite the significance of this issue the optimal treatment is not known. In this research project the aim is to identify the optimal treatment methods used worldwide, work on optimizing treatment options and identify patients and grafts at risk.* *This clinically focused research project will contain all aspects of research with a retrospective data study, an international questionnaire study and prospective studies with focus on newer treatment options, the effects on patients and a smaller basal part on therapeutic options.*
Requirements of candidate:	• **We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using teamwork to tackle large scientific questions and thus requires a student with good communication skills.** • **Master degree or MD degree** • **English language requirement: IELTS 7.0 (min 6.0 for all subs), TOEFL 100 (min 20 for all subs)**

DEPARTMENT OF GASTROENTEROLOGY & HEPATOLOGY

Project:	**Modelling the role of H. pylori in gastric carcinogenesis**
Supervisor information:	***Ass Prof dr Gwenny M Fuhler, PhD*** ***Email:*** *g.fuhler@erasmusmc.nl* ***Websites:*** • *https://www.erasmusmc.nl/en/research/departments/gastroenterology-hepatology* • *https://www.erasmusmc.nl/en/research/researchers/fuhler-gwenny#3b3d488c-4710-48bf-8337-be4d5c0d2a86* • ***Grants:*** - *2021. NPO, coaching program for students (€240.000)- coordinator..* - *2023 Dutch Cancer Society, Early detection of pancreatic cancer (€700.000) – co-applicant* • ***Most important publications:*** 1. Matute JD, et al.. **J Exp Med**. 2023 https://pubmed.ncbi.nlm.nih.gov/36413219/ 2, Grootjans J, et al. **Science**. 2019 https://pubmed.ncbi.nlm.nih.gov/30819965/ 3. Fuhler GM et al. **Gastroenterology** 2019 https://pubmed.ncbi.nlm.nih.gov/31499039/ 4. Lam SY et al **Gastroenterology** 2022 https://pubmed.ncbi.nlm.nih.gov/35031300/ 5. van der Giessen J, et al. **Gut** 2019 https://pubmed.ncbi.nlm.nih.gov/31167813/ 6. Janmaat VT, et al. **Nat Commun**. 2021 https://pubmed.ncbi.nlm.nih.gov/34099670/ 7. Mommersteeg MC, et al. **Gut Microbes** 2022 https://pubmed.ncbi.nlm.nih.gov/34965181/ 8. Yu B, et al. **Front Immunol**. 2023 https://pubmed.ncbi.nlm.nih.gov/37006300/
Abstract:	*Gastric cancer remains one of the most common and deadly diseases, but its prevalence varies globally. The main risk factor for development of gastric cancer is infection with the bacterium H. pylori, which can cause chronic gastritis. While half the world's population is infected with this bacterium, only a small fraction of patients go on to develop gastric atrophy, gastric intestinal metaplasia or gastric cancer.* ***We aim to better understand the host- or bacterial factors contributing to this discrepancy.*** *To this end, we will derive gastric organoids from patients with gastric premalignant lesions to test patient-specific responses to H. pylori. We will set up co-culture models of gastric organoids with human primary gastric fibroblasts, in order to better mimic the gastric microenvironment. We will investigate how H. pylori affects gastric epithelial and fibroblast cellular proliferation, differentiation, DNA methylation and RNA expression profiles. In addition, we will create overexpression models of the H. pylori virulence factor CagA to investigate whether Eastern and Western strains of this bacterium have different effects on gastric epithelial cells, which may explain the global differences in gastric cancer incidence.*
Requirements of candidate:	• We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. • Master degree or MD • Experimentation skills and experience with basic scientific techniques such as Western blotting, PCR, ELISA, cell culture etc. • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF GASTROENTEROLOGY & HEPATOLOGY

Project:	**META-TARGET: Cancer Testis Antigen TARGETed immunotherapy to treat liver cancer micro-METAstases after surgery**
Supervisor information:	***Dr Sonja Buschow, PhD :*** *s.buschow@erasmusmc.nl Website: Dr Buschow* ***Dr Dave Sprengers, MD, PhD :*** *d.sprengers@erasmusmc.nl Website: Dr Sprengers* ***Grants:*** - 3x Health Holland grants for public private partnerships with ISA pharmaceuticals (2017, 2021 & 2023 > 1.500k€ in total) focused on preforming a phase I trial & ancillary research to test a new peptide-based therapeutic vaccine for chronic HBV infection - 3x Dutch cancer fund (KWF; 2017, 2020, 2022; ~1000k€ in total; one as collaborator) focused on developing a therapeutic vaccine/ T cell therapy for hepatocellular carcinoma - Research funding from several private partners to support collaborative projects (i.e. ISA pharma, Pfizer, Merus, Numab,ao.) ***Most important publications:*** 1. Induction of broad multifunctional CD8+ and CD4+ T cells by hepatitis B virus antigen-based synthetic long peptides ex vivo Front Immunol 2023 Sep 13:14:1163118. 2. Immunopeptidome of hepatocytes isolated from patients with HBV infection and hepatocellular carcinoma (2022) JHEP Reports, 4 (11) 3. Systemic T-cell and humoral responses against cancer testis antigens in hepatocellular carcinoma patients (2022) OncoImmunology, 11 (1) DOI: 10.1080/2162402X.2022.2131096 4. An Engineered IL15 Cytokine Mutein Fused to an Anti-PD1 Improves Intratumoral T-cell Function and Antitumor Immunity Cancer Immunol Res 2021 Oct;9(10):1141-1157 5. Reduction of immunosuppressive tumor microenvironment in cholangiocarcinoma by ex vivo targeting immune checkpoint molecules J Hepatol 2019 Oct;71(4):753-762
Abstract:	***Goal:*** *To identify targets in micro-metastases of liver cancer, for personalized antigen specific immunotherapy as adjuvant treatment to prevent early HCC recurrence after primary tumor resection.* ***Background:*** *Hepatocellular Carcinoma (HCC), is the 3rd cause of cancer-related death in the world. Surgical tumor resection is presently the only potentially curative therapy. Unfortunately, 40% of operated patients experience local cancer recurrence within 2 years after resection, and die soon thereafter. Early HCC recurrence likely originates from liver micro-metastases. Patients at risk of HCC recurrence cannot be identified yet, and there is no therapy to prevent recurrence. A promising new form of therapy is Antigen Specific Immune Therapy (ASIT) that can facilitate adaptive responses to antigens that are specifically expressed in tumor cells but not in healthy tissues, so called tumor associated antigens (TAA). Examples of ASIT are therapeutic vaccination with TAA-derived synthetic long peptides (SLPs) or mRNAs, or with TAA loaded dendritic cells (DCs) or alternatively the adoptive transfer of TAA specific T cells. Also, ASIT has thus far shown limited clinical efficacy in HCC. We believe this due to: 1) the use of ineffective ASIT platforms 2) the targeting of ineffective TAA not sufficiently specific to tumor cells or not presented on tumor cell HLA; 3) wrong patient selection; those with advanced disease and large tumor volume have developed a strongly immunosuppressive tumor micro-environment that counteracts immune attack.* *Previously, we have found 12 different TAA of the cancer testis antigen (CTAs) subtype to be expressed in HCC (>10% of patients each, 80% of patients expressed 1 or more CTAs) but not in healthy liver tissue. In some patients, however, CTAs were also expressed at low levels in seemingly tumor-free liver tissue (TF) and this expression related to tumor recurrence as well as with patient survival after resection (n=100 of which n=55 CTA+ TFL), also in an independent patient cohort (n=89; n=26 CTA+ TFL).* ***Hypothesis:*** *CTA-positive cells in seemingly TFL are occult micro-metastasis that may develop into recurrent tumors. The CTA expressed by these cells may be targets for ASIT in an adjuvant setting when tumor burden and associated immune suppression is low.* ***Research questions*** *1) Are these CTA-expressing cells indeed micro-metastasis of previously resected HCC?* *2) How can expression of these CTAs in TFL be optimally sampled?* *3) What are the best CTA targets for post-operative ASIT?* *4) Considering CTA specific T cell quality and tumor CTA HLA presentation, what is the best ASIT platform to target these CTA in HCC?* ***Methods:*** *Cell isolation from human HCC, Cell culture, Multicolor flow cytometry, T cell assays, Immune histochemistry, HLA immunopetidomics, single cell RNA sequencing*
Requirements of candidate:	• We are looking for a highly motivated, hardworking student to join our very international and translation team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. • Master degree (biomedical sciences or similar) or MD degree with demonstrated affinity for (tumor)immunology • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF GASTROENTEROLOGY & HEPATOLOGY

Project:	**Metabolic dysfunction-associated steatotic liver disease (MASLD) in Inflammatory Bowel Disease (IBD)**
Supervisor information:	*Annemarie de Vries MD PhD Associate professor* ***Email:*** *a.c.devries@erasmusmc.nl* *Willem Pieter Brouwer MD PhD* ***Email***: w.p.brouwer@erasmusmc.nl *Lauranne Derikx MD PhD* ***Email***: l.derikx@erasmusmc.nl ***Most important publications Annemarie de Vries:*** Li P, de Vries AC, Kamar N, Peppelenbosch MP, Pan Q. Monitoring and managing SARS-CoV-2 evolution in immunocompromised populations. *Lancet Microbe*. 2022 May;3(5):e325-e326. Sleutjes JAM, Roeters van Lennep JE, van der Woude CJ, de Vries AC. Lipid Changes After Induction Therapy in Patients with Inflammatory Bowel Disease: Effect of Different Drug Classes and Inflammation. *Inflamm Bowel Dis*. 2022 May 19:izac100. Goetgebuer RL, Kreijne JE, Aitken CA, Dijkstra G, Hoentjen F, de Boer NK, Oldenburg B, van der Meulen AE, Ponsioen CIJ, Pierik MJ, van Kemenade FJ, de Kok IMCM, Siebers AG, Manniën J, van der Woude CJ, de Vries AC. Increased Risk of High-grade Cervical Neoplasia in Women with Inflammatory Bowel Disease: A Case-controlled Cohort Study. *J Crohns Colitis*. 2021 Sep 25;15(9):1464-1473. Beelen EMJ, Nieboer D, Arkenbosch JHC, Regueiro MD, Satsangi J, Ardizzone S, López-Sanromán A, Savarino E, Armuzzi A, Janneke van der Woude C, de Vries AC. Risk Prediction and Comparative Efficacy of Anti-TNF vs Thiopurines, for Preventing Postoperative Recurrence in Crohn's Disease: A Pooled Analysis of 6 Trials. *Clin Gastroenterol Hepatol*. 2021 Oct 20:S1542-3565(21)01134-4. ***Most important publications Willem Pieter Brouwer:*** pubmed
Abstract:	*Inflammatory bowel disease (IBD) patients have a higher risk of metabolic dysfunction-associated steatotic liver disease (MASLD) compared with the general population. Hepatic fibrosis is a consequence of an inflammatory response to MASLD, which is referred to as steatohepatitis (MASH). Hepatic fibrosis is the most important prognostic factor in patients with liver disease, and could be treated with targeted interventions if apparent. However, oftentimes hepatic fibrosis is not diagnosed until the latest stages, when liver cirrhosis is already apparent and the prognosis of patients is poor without a liver transplantation. Easy to use, non-invasive hepatic fibrosis and steatosis risk scores may be useful to screen for MASLD in IBD patients, in order to detect presence of liver disease at an early stage. The association between non-invasive scores and presence of MASLD at ultrasonography requires further study. Furthermore, the consequences of a diagnosis of MASLD in IBD are unclear, most particular with regard to drug survival/ effectiveness and side effects, including liver enzyme disturbance. Data of prospective studies are available to study these associations.*
Requirements of candidate:	• We are looking for a highly motivated, hardworking student to join our international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. • Master degree or MD degree • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF GASTROENTEROLOGY & HEPATOLOGY

Project:	**Unraveling the role of RNF43 and ZNRF3 in cancers**
Supervisor information:	*Assistant Professor Ron Smits, PhD* **Email:** *m.j.m.smits@erasmusmc.nl* **Website:** *M.J.M. (Ron) Smits, PhD - Researcher - Erasmus MC* ***Most important publications:*** **1.** **Cancer Research** 84: 1443-1459 (2024). 2. **Nature Medicine** 28: 2162-2170 (2022). 3. **Nature Communications** 12: 3354 (2021). 4. **Cancer Research** 80: 5619-5632 (2020). 5. **Gastroenterology** 158: 1029-1043 e1010 (2020). 6. **Oncogene** 39: 3458-3472 (2020). 7. **Nature Communications** 11: 1961 (2020). 8. **Biochim Biophys Acta Rev Cancer** 1872: 74-79 (2019). 9. **Gastroenterology** 153: 1133-1147 (2017).
Abstract:	*The Wnt/β-catenin signaling pathway is one of the most commonly deregulated pathways among cancers. In many tumor types this pathway is constitutively activated through mutational (in)activation of one of the core elements of the β-catenin destruction complex. For example, in about 70-80% of colorectal cancers loss-of-function mutations are observed in the APC gene, leading to hyperactivation of β-catenin signaling. A second main mechanism has been uncovered in the past decade, namely the mutation of the RNF43 and ZNRF3 proteins, which are involved in fine-tuning the levels of Wnt-receptors on the cellular membrane. Their mutation leads to tumors that rely on Wnt-ligand exposure to support growth. Therefore, many pharmaceutical companies are developing therapies targeting this specific characteristic of these tumors. In addition to this well-established function of RNF43/ZNRF3, several other aspects of these proteins are being discovered that may be relevant for cancers.* *In this PhD project we plan to look into more detail at the mechanisms that may support RNF43/ZNRF3-driven tumorigenesis. We will make use of various molecular and cellular techniques such as CRISPR-cas gene editing of cell lines/organoids, immunofluorescence, flow cytometry, next-generation RNA sequencing, mass-spectrometry and others. These techniques will be complemented with database analyses and patient material when needed. Ultimately, we expect to increase our knowledge on how RNF43/ZNRF3 mutations contribute to cancer.*
Requirements of candidate:	• We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. • Master degree or MD degree • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF GASTROENTEROLOGY & HEPATOLOGY

Project: Liquid biopsy for detection of gastric cancer and its precursor lesions

Supervisor information:

Prof Manon Spaander, MD, PhD,
Email: *v.spaander@erasmusmc.nl*
Website: *Prof. M.C.W. (Manon) Spaander, MD PhD - Researcher - Erasmus MC..*

Dr Judith Honing, MD, PhD,
j.honing@erasmusmc.nl
https://www.researchgate.net/profile/Judith-Honing-2,

Dr Saskia Wilting, PhD
s.wilting@erasmusmc.nl
https://pure.eur.nl/en/persons/saskia-wilting

Prof. Manon Spaander *has an extensive international track record in high-quality research regarding screening and surveillance of premalignant gastrointestinal conditions. She is part of the advisory board of our Dutch colorectal screening program, co-editor of Endoscopy journal and editor-in-chief of Best Practice and Research: Clinical Gastroenterology. Currently her research team is involved in two large EU-Horizon calls regarding gastric cancer screening. Besides her research activities she is involved in numerous national and international committees, involved in the new MAPS guideline and lead of the gastroenterology division at our hospital.*

Dr. Judith Honing *has recently joined the team of prof.Spaander at the Erasmus MC and focusses on surveillance and treatment of upper gastrointestinal conditions. Prior to this position she worked as a Clinical Fellow with the world-renowned team of prof.R.Fitzgerald at the University of Cambridge. She has a specific interest in translational research and during her PhD she has worked for several years in the oncology laboratory. Currently, she is part of the international team participating in the two Horizon calls regarding gastric cancer and establishing an independent research group with a specific interest in biomarkers for the detection of premalignant conditions.*

Dr. Saskia Wilting*: Saskia is a molecular biologist focusing on the use of liquid biopsies to improve both early detection and disease monitoring in cancer patients. She is an assistant professor at the department of oncology and recently obtained two large grants to improve measurement of circulating tumour DNA to improve colorectal cancer care.*

Most important publications

1. Effect of Colonoscopy Screening on Risks of Colorectal Cancer and Related Death | New England Journal of Medicine (nejm.org)
2. Detection of residual disease after neoadjuvant chemoradiotherapy for oesophageal cancer (preSANO): a prospective multicentre, diagnostic cohort study - The Lancet Oncology
3. Young-onset colorectal cancer - PubMed (nih.gov)
4. HOXA13 in etiology and oncogenic potential of Barrett's esophagus - PubMed (nih.gov)
5. Population-Based Colonoscopy Screening for Colorectal Cancer: A Randomized Clinical Trial - PubMed (nih.gov)
6. Accuracy of upper endoscopies with random biopsies to identify patients with gastric premalignant lesions who can safely be exempt from surveillance - PubMed (nih.gov)
7. Endoscopic surveillance with systematic random biopsy for the early diagnosis of hereditary diffuse gastric cancer: a prospective 16-year longitudinal cohort study - PubMed (nih.gov)
8. A comparison of carboplatin and paclitaxel with cisplatinum and 5-fluorouracil in definitive chemoradiation in esophageal cancer patients - PubMed (nih.gov)
9. Adequacy of endoscopic recognition and surveillance of gastric intestinal metaplasia and atrophic gastritis: A multicentre retrospective study in low incidence countries - PubMed (nih.gov)
10. The genomic landscape of metastatic breast cancer highlights changes in mutation and signature frequencies - PubMed (nih.gov)
11. Whole genome sequencing of metastatic colorectal cancer reveals prior treatment effects and specific metastasis features - PubMed (nih.gov)

Abstract:

The Challenge: *Worldwide gastric cancer (GC) is still ranking third of all cancer-related deaths based on its poor 5-year survival <20%. The malignant sequence is induced by a Helicobacter pylori infection causing chronic inflammation which subsequently can lead to the oncogenic lesions gastric atrophy (GA) and gastric intestinal metaplasia (GIM) . GA/GIM and gastric cancer are currently only diagnosed during a gastroscopy as other screening modalities have low sensitivity. Lately attention has been directed at tumor-specific biomarkers in the plasma or gastric juice of gastric cancer patients to find less-invasive manners to predict neoplastic progression in patients with GIM.*

The clinical utility of one such biomarker, circulating tumor DNA (ctDNA), has evolved rapidly. Cell-free circulating DNA (cfDNA) fragments are released from all dying cells in the bloodstream, and ctDNA fragments are a fraction specifically released by the tumor cells. At the Erasmus MC, a cfDNA methylation assay was developed which was able to detect ctDNA in patients with advanced colon adenomas.

To further increase precision and clinical utility, it's advantageous to consider several predictive factors simultaneously. A polygenic risk score (PRS) is a composite variable of several single nucleotide polymorphisms (SNPs), each with an individually small effect on risk, that cumulatively reflects the variation in individual's genetic risk for gastric cancer. Thus, to further establish non-invasive markers of GIM progression, we will additionally calculate a PRS for gastric cancer.

The Novelty *of this approach is twofold: first, we assess if a novel biofluid, the gastric juice, together with blood could harbor ctDNA of gastric cancer and GIM patients, and second, we consider both molecules of a patient's germline susceptibility (PRS) and molecules reflecting tumor-specific biology (ctDNA).*

The Research Plan: *this proof-of concept study will consist of three parts for which we will approach patients under surveillance in the Erasmus University MC for gastric intestinal metaplasia(GIM) with or without dysplasia or referred for gastric cancer. In the first part of the study we will create a methylation ct-DNA profile specific for gastric cancer. Subsequently in the second part we will investigate if this specific profile can be detected in the serum and gastric juice of patients with GIM. In the third part, we will calculate a PRS score for GC risk among both GIM and GC patients and determine whether PRS can predict GC status. We aim to determine if PRS is an independent predictor of neoplastic progression and determine if PRS adds value to a ctDNA methylation profile for predicting GC risk.*

Requirements of candidate:

- We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.
- Master degree or MD degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF GASTROENTEROLOGY & HEPATOLOGY

Project:	**Prediction of functional cure after withdrawal of antiviral therapy in patients with chronic hepatitis B**
Supervisors information:	**Prof dr HLA Janssen MD PhD, department chair, gastroenterologist & hepatologist** *Email: h.janssen@erasmusmc.nl* *Website: https://www.linkedin.com/in/harry-janssen-89936470/* *Pubmed: https://pubmed.ncbi.nlm.nih.gov/?term=janssen+hl* ***Most important publications**:* 1. Off-Therapy Response After Nucleos(t)ide Analogue Withdrawal in Patients With Chronic Hepatitis B: An International, Multicenter, Multiethnic Cohort (RETRACT-B Study). Gastroenterology. 2022 Mar;162(3):757-771.e4. 2. Treatment of HCV infection by targeting microRNA. N Engl J Med. 2013 May 2;368(18):1685-94. 3. Pegylated interferon alfa-2b alone or in combination with lamivudine for HBeAg-positive chronic hepatitis B: a randomised trial. Lancet. 2005 Jan 8-14;365(9454):123-9. **Dr M.J. Sonneveld MD PhD, assistant professor, gastroenterologist & hepatologist** *Email: m.j.sonneveld@erasmusmc.nl* *Website: https://www.linkedin.com/in/milan-sonneveld-373b5923/* *Pubmed: https://pubmed.ncbi.nlm.nih.gov/?term=sonneveld+mj* ***Most important publications:*** 1. HBV DNA and HBsAg Levels at 24 Weeks Off-Treatment Predict Clinical Relapse and HBsAg Loss in HBeAg-Negative Patients Who Discontinued Antiviral Therapy. Gastroenterology. 2024 Jan;166(1):168-177.e8.. 2. Effect of the COVID-19 pandemic on procedure volumes in gastroenterology in the Netherlands. Lancet Gastroenterol Hepatol. 2022 Jul;7(7):595-598. 3. Optimisation of the use of APRI and FIB-4 to rule out cirrhosis in patients with chronic hepatitis B: results from the SONIC-B study. Lancet Gastroenterol Hepatol. 2019 Jul;4(7):538-544.
Abstract:	*Currently available nucleo(s)tide analogues achieve suppression of hepatitis B virus DNA in the majority of patients, but functional cure (loss of HBsAg from serum) is infrequently achieved. As a result, life-long treatment in required in most patients. Withdrawal of nucleo(s)tide analogue therapy has recently emerged as a novel strategy to increase the chance functional cure, but this potential benefit is counterbalanced by a significant risk of viral relapse, which can precipitate severe liver inflammation and even liver failure. Careful selection of patients is therefore essential.* *We are currently conducting an international multicenter retrospective cohort study of patients who discontinued antiviral therapy in expert centers across Northern America, Europe and Asia, and have already enrolled >1800 patients. These data will be used to study predictors of successful therapy withdrawal, with the ultimate goal of providing individualized recommendations for therapy cessation. Furthermore, blood samples have been obtained from a subset of the patients, allowing for assessment of novel biomarkers that could aid in risk stratification.*
Requirements of candidate:	• We are looking for a highly motivated, hardworking MD to join our team comprising multiple staff members, translational researchers and multiple PhD students. Since this project is part of an international collaborative effort, good English language and communication skills are key. • Master's degree or MD degree • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF INTERNAL MEDICINE - PHARMACOLOGY

Project: Migraine: the role of CGRP and cardiovascular safety of CGRP (receptor) blockade

Supervisor information:

Prof. Dr. Antoinette Maassen van den Brink ***a.vanharen-maassenvandenbrink@erasmusmc.nl*** ***https://pharma.erasmusmc.nl/migraine.html***

Grants:
- Dutch Research Council: Veni (2004), Vidi (2011), Vici (2020)
- Various Industry grants
- Dutch Heart Foundation, Dutch Brain Foundation, Berlin Institute of Health

Most important publications:

1. de Vries, T., Boucherie, D.M., van den Bogaerdt, A., Danser, A.H.J., MaassenVanDenBrink, A. (2023). Blocking the CGRP Receptor: Differences across Human Vascular Beds. Pharmaceuticals (Basel). 2023;16(8):1075.
2. Van Casteren, D.S., Kurth, T., Danser, A.H.J., Terwindt, G.M., MaassenVanDenBrink, A. (2021). Sex differences in response to triptans: A systematic review and meta-analysis. Neurology, 96:162-170.
3. MaassenVanDenBrink, A., Reekers, M., Bax, W.A., Ferrari, M.D., Saxena, P.R. (1998). Coronary side effect potential of current and prospective antimigraine drugs. Circulation, 98:25 30.
4. MaassenVanDenBrink, A., Meijer, J., Villalón, C.M., Ferrari, M.D. (2016). Wiping out CGRP - potential cardiovascular risks. Trends in Pharmacological Sciences, 37:779-88.
5. De Vries, T., MaassenVanDenBrink, A. (2019). Monoclonal antibody targeting CGRP in difficult-to-treat migraine. Nature Reviews Neurology, 15:688-689.
6. Al-Hassany, L., MaassenVanDenBrink, A. (2020). Targeting CGRP in migraine: a matter of choice and dose. Lancet Neurol, 19:712-713.
7. Mulder, I.A., Li, M., de Vries, T., Qin, T., Yanagisawa, T., Sugimoto, K., van den Bogaerdt, A., Danser, A.H.J., Wermer, M.J.H., van den Maagdenberg, A.M.J.M., MaassenVanDenBrink, A., Ferrari, M.D., Ayata, C. (2020). Anti-migraine CGRP receptor antagonists worsen cerebral ischemic outcome in mice, Ann Neurol, 88:771-784

Abstract:

Background*: Migraine is a highly disabling and prevalent disorder, occurring 2-3 times more often in females than in males. A novel class of antimigraine drugs consists of antibodies against Calcitonin Gene-Related Peptide (CGRP) or its receptor, as well as small molecule CGRP receptor antagonists (gepants). While blocking CGRP may be a big advantage for migraine patients without a good response to current therapies, the potential risks of 'wiping out' the vasodilator CGRP, which is thought to have a rescue function in case of threat of ischemia, should be well studied. Further, the role of CGRP, related peptides and their receptors may be different in male and female migraine patients, which is relevant in view of the predominance of migraine in females.*

Project description: *The current PhD project will focus on the (neuro)vascular role of CGRP, with a special emphasis on the role of sex hormones on the CGRP-ergic system. We will use animal in vivo models as well as human blood vessels in vitro. Depending on the interest of the PhD student, also human in vivo and/or epidemiological studies could be part of this project.*

Expected result*: A typical Dutch PhD thesis, containing multiple published papers in top pharmacological or neurological journals. The PhD student will work with an extensive team of basic scientists, clinicians, and technicians, allowing him/her to cover both preclinical and clinical research.*

PhD student profile: *Ideally, the student has a solid background in physiology and pharmacology, and some experience with animal research, biochemistry and molecular biology. He/she does not need to be a clinician.*

Requirements of candidate:

- We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.
- Master degree or MD
- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (we could help with the scientific part of your scholarship proposal)
- IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF INTERNAL MEDICINE – VASCULAR MEDICINE

Project: Untangling cell type-specific gene regulatory mechanisms of type II diabetes

Supervisor information:

Dr Annique Claringbould **Email:** annique.claringbould@erasmusmc.nl **Website:** BlueSky; Google Scholar

Grants:

2024 NWO Veni Grant
2024 Diabetes Foundation Junior Fellowship
2020 EMBL Interdisciplinary Postdoctoral Fellowship
(EU Horizon 2020 research and innovation programme)
2019, 2016 Simons Foundation Scientific Visit Grants (University of California Los Angeles, US; International Congress of Human Genetics, Kyoto, Japan)
2018 De Drie Lichten Foundation Scientific Visit Grant (University of Queensland, Australia)

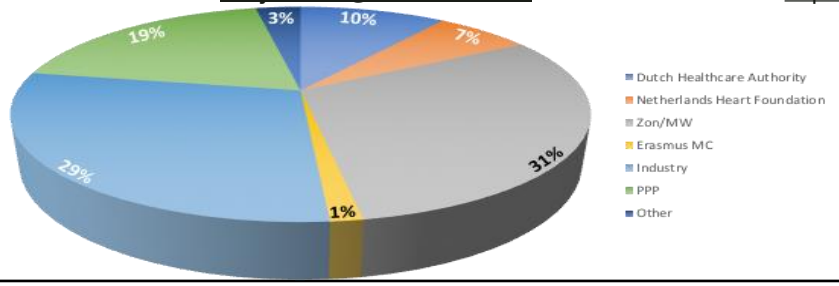
Five important recent publications:

Trindade Pons, Claringbould, et al., Genetic Epidemiology 2024; Kamal et al., Molecular Systems Biology 2023; Võsa, Claringbould* et al., **Nature Genetics** 2021; COVID-19 Host Genetics Initiative, **Nature** 2021; Chen et al., **Nature Genetics** 2021; Claringbould and Zaugg, Trends in Molecular Medicine 2021; Van der Graaf , Claringbould et al. **Nature Communications** 2020; Porcu et al., **Nature Communications** 2019*

Prof Dr Eric Sijbrands **Email:** e.sijbrands@erasmusmc.nl **Website:** https://www.erasmusmc.nl/nl-nl/patientenzorg/zorgverleners/sijbrands-ejg

Grants: Since arriving in Rotterdam in 2001, the research and innovation funding was approximately €29KK, including €4.3KK awarded by Regeneron that is waiting for legal approval and a yearly bonus of €350K for a Dutch Healthcare Authority project (see below). The distribution of the funding sources is shown in the figure. Private parties made investments in the context of private public partnerships (PPP's) of e-health projects.

A grant that successfully reached the production goal (vascular genetics) has been awarded infinite yearly funding (current total €5.6KK).



Important recent publications:

His H-index is 91, and his 100 publications in journals with the highest impact factor [IF] appeared in: 3 in the New England Journal of Med [91.245], 3 in the Lancet [79.321], 2 in JAMA [56.272], 5 in Nature [49.962], 2 in Cell [41.582], 2 in BMJ [39.890], 14 in Nature Genetics [38.330], 3 in Lancet Diabetes Endocrinology [32.069], 10 in European Heart Journal [29.983], 7 in Circulation [29.690], 7 in JACC [24.094], 11 in Diabetes Care [19.112], 3 in Nature Communications [14.919], 1 in JACC Cardiovascular Imaging [14.805], 2 in JAMA Cardiology [14.676], 1 in Pharmacology & Therapeutics [12.310], 1 in Plos Medicine [11.069], 2 in American Journal of Human Genetics [11.025], 2 in Hypertension [10.190], 9 in Diabetologia [10.122], 1 in Cardiovascular Diabetology [9.951], and 13 in Diabetes [9.461]. His current PubMed search retrieves 350 hits with an average IF of 12.382 and a median of 5.917.

Abstract:

We seek a motivated PhD student to join our lab at **Erasmus Medical Centre** in Rotterdam, exploring the **gene regulatory mechanisms in pancreatic β-cells** linked to **type 2 diabetes (T2D)**.

Genome-wide association studies (**GWAS**) have identified numerous genetic variants linked to type 2 diabetes (T2D); however, the biological mechanisms behind these associations remain unclear. To address this gap, polygenic scores can help identify individuals at high risk for developing T2D. Many of these genetic variants are enriched in pancreas-specific regulatory regions, where they exert subtle effects that collectively disrupt β-cell function, thereby increasing the likelihood of T2D onset.

In this project, we will employ **iPSC technologies** and **single-cell multiomics** to uncover how these variants affect gene regulation and function in β-cells. Using polygenic risk scores to identify genetic extremes will enable the in-depth exploration of combined genetic effects at the molecular level in disease-relevant cell types. The project will generate insights into diabetes biology that will bridge the gap between genetic discoveries and clinical application.

The PhD candidate will have the **flexibility** to focus on a bioinformatics-driven approach to build gene regulatory networks from multi-omics datasets, or to combine this with experimental work using iPSCs to model patient-specific pancreatic cells. Joining our **newly established lab**, the candidate will play a key role in shaping the project and contributing to innovative diabetes research, with the ultimate goal of advancing **personalized treatments**.

Requirements of candidate:

We are looking for a highly motivated, hardworking student to join our very international team. Collaboration is at the heart of our work, so we are looking for a student with good communication skills. Candidates with a background in bioinformatics, computational biology, genomics, or molecular biology with an interest in gene regulation, GWAS, or lipid metabolism are especially encouraged to apply.

- Scholarship that will, at least, cover subsistence allowance and international airplane ticket (your future supervisor could help with the scientific part of your scholarship proposal)
- Master degree or MD degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF INTERNAL MEDICINE – VASCULAR MEDICINE

Project: Integrative genetic scoring for personalised risk assessment of Familial Hypercholesterolaemia

Supervisor information:

Dr Annique Claringbould **Email:** annique.claringbould@erasmusmc.nl **Website:** BlueSky; Google Scholar

Grants:

2024 NWO Veni Grant
2024 Diabetes Foundation Junior Fellowship
2020 EMBL Interdisciplinary Postdoctoral Fellowship
(EU Horizon 2020 research and innovation programme)
2019, 2016 Simons Foundation Scientific Visit Grants (University of California Los Angeles, US; International Congress of Human Genetics, Kyoto, Japan)
2018 De Drie Lichten Foundation Scientific Visit Grant (University of Queensland, Australia)

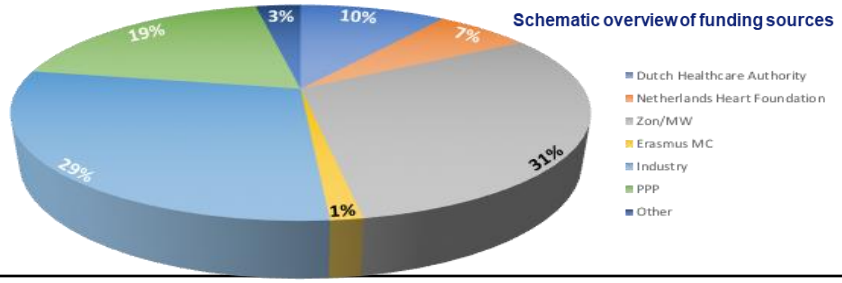
Five important recent publications:

Trindade Pons, Claringbould, et al., Genetic Epidemiology 2024; Kamal et al., Molecular Systems Biology 2023; Võsa*, Claringbould* et al., **Nature Genetics** 2021; COVID-19 Host Genetics Initiative, **Nature** 2021; Chen et al., **Nature Genetics** 2021; Claringbould and Zaugg, Trends in Molecular Medicine 2021; Van der Graaf , Claringbould et al. **Nature Communications** 2020; Porcu et al., **Nature Communications** 2019

Prof Dr Eric Sijbrands **Email:** e.sijbrands@erasmusmc.nl **Website:** https://www.erasmusmc.nl/nl-nl/patientenzorg/zorgverleners/sijbrands-ejg

Grants: Since arriving in Rotterdam in 2001, the research and innovation funding was approximately €29KK, including €4.3KK awarded by Regeneron that is waiting for legal approval and a yearly bonus of €350K for a Dutch Healthcare Authority project (see below). The distribution of the funding sources is shown in the figure. Private parties made investments in the context of private public partnerships (PPP's) of e-health projects.

A grant that successfully reached the production goal (vascular genetics) has been awarded infinite yearly funding (current total €5.6KK).



Important recent publications:

His H-index is 91, and his 100 publications in journals with the highest impact factor [IF] appeared in: 3 in the New England Journal of Med [91.245], 3 in the Lancet [79.321], 2 in JAMA [56.272], 5 in Nature [49.962], 2 in Cell [41.582], 2 in BMJ [39.890], 14 in Nature Genetics [38.330], 3 in Lancet Diabetes Endocrinology [32.069], 10 in European Heart Journal [29.983], 7 in Circulation [29.690], 7 in JACC [24.094], 11 in Diabetes Care [19.112], 3 in Nature Communications [14.919], 1 in JACC Cardiovascular Imaging [14.805], 2 in JAMA Cardiology [14.676], 1 in Pharmacology & Therapeutics [12.310], 1 in Plos Medicine [11.069], 2 in American Journal of Human Genetics [11.025], 2 in Hypertension [10.190], 9 in Diabetologia [10.122], 1 in Cardiovascular Diabetology [9.951], and 13 in Diabetes [9.461]. His current PubMed search retrieves 350 hits with an average IF of 12.382 and a median of 5.917.

Abstract:

We seek a motivated PhD student to join our lab at **Erasmus Medical Centre** in Rotterdam, focusing on the **genetic underpinnings of familial hypercholesterolemia (FH)** and its impact on cardiovascular disease (CVD) risk.

FH is a common genetic disorder characterised by **elevated blood cholesterol levels** from birth, significantly increasing the risk of cardiovascular disease. While FH is traditionally linked to LDLR, APOB, and PCSK9 gene mutations, recent studies have highlighted **the role of common genetic variants in lipid metabolism**. These variants, identified through genome-wide association studies (**GWAS**), affect gene expression and protein levels, contributing to the complexity of FH. Using only known rare mutations leaves significant room for improvement, making the inclusion of common variations highly relevant.

In this project, we develop an **integrative scoring** system that combines rare mutations, common variants, and molecular variants to provide a comprehensive genetic risk assessment for FH patients. By leveraging data from large-scale cohorts, we will predict cardiovascular complications. This approach will enhance our understanding of the genetic architecture of FH and improve patient stratification for **personalised treatment**.

The PhD candidate will primarily use **bioinformatics-driven** analysis to construct and validate the integrative score. Joining our interdisciplinary team, the candidate will play a crucial role in advancing innovative research in cardiovascular genetics, with the ultimate goal of improving clinical outcomes for FH patients.

Requirements of candidate:

We are looking for a highly motivated, hardworking student to join our very international team. Collaboration is at the heart of our work, so we are looking for a student with good communication skills. Candidates with a background in bioinformatics, computational biology, genomics, or molecular biology with an interest in gene regulation, GWAS, or lipid metabolism are especially encouraged to apply.

- Scholarship that will, at least, cover subsistence allowance and international airplane ticket (your future supervisor could help with the scientific part of your scholarship proposal)
- Master degree or MD degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF MOLECULAR GENETICS

Project: Nucleotide Excision Repair mechanisms and disease

Supervisor information:

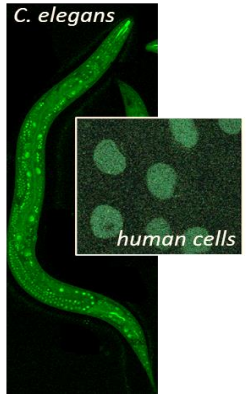
Dr. Hannes Lans, **Associate professor DNA repair mechanisms and disease** w.lans@erasmusmc.nl www.lanslab.eu

Grants:
2023 2x Dutch Cancer Society (€ 1469364**) 2022** Dutch Research Council (€ 321000); **2018** 2x Dutch Research Council (€ 568000); **2017** Dutch Cancer Society (€ 534000); **2014** WorldWide Cancer Research (€ 218000); **2012** ERC FP7-PEOPLE-ITN (€ 689000); **2008** Veni grant Dutch Research Council (€ 208000).

Selected publications:

2023 Recovery of protein synthesis to assay DNA repair activity in transcribed genes in living cells and tissues. ***Nucleic Acids Research* 31:gkad642**
2023 Different SWI/SNF complexes coordinately promote R-loop- and RAD52-dependent transcription-coupled homologous recombination. ***Nucleic Acids Research* 51:9055-9074**
2021 Tissue-Specific DNA Repair Activity of ERCC-1/XPF-1. ***Cell Reports*** *34*:108608
2020 Ubiquitin and TFIIH-stimulated DDB2 dissociation drives DNA damage handover in nucleotide excision repair. ***Nature Communications*** 11:4868
2019 The DNA damage response to transcription stress. ***Nature Reviews Mol Cell Biol*** 20:766-784
2018 DNA damage sensitivity of SWI/SNF-deficient cells depends on TFIIH subunit p62/GTF2H1. ***Nature Communications*** 9:4067
2018 Base and nucleotide excision repair facilitate resolution of platinum drugs-induced transcription blockage. ***Nucleic Acids Research*** 46:9537-9549
2014 Understanding nucleotide excision repair and its roles in cancer and ageing ***Nature Reviews Mol Cell Biol*** 15:465-81

Abstract:



DNA damage is a major cause of health issues like cancer and aging. Nucleotide excision repair (NER) is an important defense mechanism that protects cells against dysfunction by removing helix-distorting DNA damage, such as is induced by UV light and by platinum-based anticancer drugs. We study how NER functions on the molecular level and how knowledge of its function can help to prevent disease and improve cancer therapy.

We investigate NER by identifying and functionally characterizing novel regulatory proteins and mechanisms. For our studies, we use both C. elegans and mammalian cell culture as model systems. We pursue a multi-disciplinary approach, using molecular cell biology and genetics (e.g CRISPR- and RNAi-mediated screening) combined with live cell imaging and quantitative proteomics, to study NER mechanisms in different cell types. We are looking for a highly motivated PhD student who wants to work on this frontline ambitious project aimed at understanding how NER protects cells from the deleterious consequences of DNA damage. The results of this project will help to better understand the molecular pathogenesis associated with inherited NER deficiency and to develop therapies aimed at alleviating discomfort associated with cancer and aging.

Requirements of candidate:

- We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.
- Master degree or MD
- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (we could help with the scientific part of your scholarship proposal)
- IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF MOLECULAR GENETICS

Project: Investigation of tumorigenesis via advanced imaging and single cell -omics analysis

Supervisor information:

Dr. Miao-Ping Chien, *m.p.chien@erasmusmc.nl,* *http://www.mpchienlab.org/*

Selected Grants:

Oncode Institute Junior Fellow, KWF-TKI Grant, NWO Vidi award (NWO Talent Scheme) , KWF synergy grant, Oncode Technology Development Grant, Ammodo Science Award , Erasmus-TU Delft Convergence Grant, Oncode Institute Junior Fellow, Erasmus MC Fellowship, CancerGenomiCs.nl Junior PI's Grant, Dragon Gate Grant (Taiwan MoST), NWO Veni award (NWO Talent Scheme), CancerGenomiCs.nl Junior Fellow

Selected publications:

1. You, Li*, Su, P.R.*, Betjes, M.*, et al., Chien, M.P. "Linking the genotypes and phenotypes of cancer cells in heterogenous populations via real-time optical tagging and image analysis", ***Nature Biomedical Engineering***, 2022, https://doi.org/10.1038/s41551-022-00853-x
2. Su, P.R., et al., Chien, M.P., "Microscopy-based single-cell proteomic profiling reveals heterogeneity in DNA damage response dynamics". ***Cell Reports Methods***, 2022, DOI:https://doi.org/10.1016/j.crmeth.2022.100237
3. Smit M., et al., Chien M.P. Protocol for profiling intratumor heterogeneity using spatially annotated single cell sequencing. ***STAR Protocols***. 2023, 4(3):102447. doi: 10.1016/j.xpro.2023.102447.
4. Cheng, K.W., et al., Chien, M.P.*, Hsu, C.C.* "Investigating the Metabolic Heterogeneity of Cancer Cells Using Functional Single-Cell Selection and nLC Combined with Multinozzle Emitter Mass Spectrometry". ***Analytical Chemistry***. 2024, 96, 2, 624–629. https://doi.org/10.1021/acs.analchem.3c03688.
5. Chien M.P et al. "Photoactivated voltage imaging in tissue with an archaerhodopsin-derived reporter", ***Science Advances***, 2021: Vol. 7, no. 19, eabe3216

Miao-Ping Chien received her PhD in chemistry and biochemistry from the University of California, San Diego in 2013, and went on to do a postdoc at Harvard University, working on technology development for biology (combining biophysics, computation and optical instrumentation). She joined Erasmus MC as a group leader in June 2017 and became a principal investigator at Oncode Institute in 2019. Her current research focuses on developing and applying multidisciplinary technologies (advanced microscopy and imaging, computation, single cell technology, bioinformatics, (photo)chemistry) to investigate the underlying mechanisms of tumorigenesis, particularly of rare cancer-driving cells. She is also a founder of UFO Biosciences, which aims to enable better cancer care by creating treatment options for rare, cancer-driving cell populations that escape traditional treatment

Abstract:

The Chien Lab is looking for self-motivated PhD students with a strong interest in working in a multidisciplinary lab. In our lab, we develop single cell technologies combining optical, biomedical and bioinformatics methods to address biological questions, particularly in cancer biology and immuno-oncology.
The candidate will have a chance to work on wet-lab projects, dry-lab projects or a combination of these two. For the wet-lab projects, the candidate can apply the technologies developed in Dr. Chien's group, including advanced imaging and single cell sequencing (analysis), to cancer cell lines or patient-derived primary cultures to investigate molecular mechanisms of tumorigenesis and therapy resistance. We also have a project for people with advanced imaging or optical engineering background. For the dry-lab projects, the candidate can work on advanced imaging analysis including machine learning-based approaches or bioinformatics analysis (-omics data analysis).

Requirements of candidate:

- We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.
- Master degree or MD
- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (we could help with the scientific part of your scholarship proposal)
- IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF NEUROSCIENCES

Project:	**Sensorimotor statistics govern the control and adaptation of balance**

Supervisor information:

Prof dr Maarten Frens
Email: m.frens@erasmusmc.nl

Dr Patrick Forbes
p.forbes@erasmusmc.nl

Website: www.neuro.nl

Grants:

- Dutch Scientific Organization Grant (VIDI/VENI/Top Talent, 2022/2019/2017)
- ESA Micro-Gravity Flight Campaigns (2016/2017/2018)
- European Research Commision (Marie Sklodowska-Curie Action, 2014)
- European FP7 ITN Grant (2009)

Important recent publications:

- **Nature Communications**, 2024, Mar 18;15(1):2351. doi: 10.1038/s41467-024-46398-2.
- **PNAS**, 2024 Aug 6;121(32):e2404909121. doi: 10.1073/pnas.2404909121
- **Human Brain Mapping**, 2024 Feb 1;45(2):e26565. doi: 10.1002/hbm.26565.
- **Communications Biology**, 2024, doi: 10.1038/s42003-024-06029-4
- **Journal of Neuroscience**, 2023, doi: 10.1523/JNEUROSCI.0987-22.2023
- **Annals of Neurology**, 2020, Mar;87(3):383-393. doi: 10.1002/ana.25679
- **Nature Communications**, 2019, doi: 10.1038/s41467-019-09738-1

Abstract:

Learning to balance relies on finely tuned sensorimotor mechanisms, where the vestibular system plays a crucial role by providing essential feedback on head orientation and movement relative to gravity. Prominent theories in motor control suggest that the natural variability of movement—and thus the statistical structure of sensory signals, such as those from the vestibular system—may be particularly important for learning since our ability to respond to behavioral errors depends on sensory feedback. For example, while larger errors require greater correction, studies show that as feedback errors increase, behavioral compensation may asymptote or even decline. This suggests an alternative possibility: larger errors might be less effective in driving adaptation or learning because they fall outside the natural statistics of sensory feedback and are therefore unlikely to occur. Indeed, evidence suggests that neural circuits, including those in the vestibular system, are adapted to the regular patterns of motion encountered in daily life. This proposal aims to bridge two lines of research: statistical optimality in learning and the adaptive design of vestibular circuits for motion, exploring how sensorimotor learning for balance control aligns with the typical statistical properties of vestibular input.

We will establish how sensorimotor learning for balance is optimized to the statistical properties of vestibular feedback. Specifically, we will examine how the correlation between natural motion and artificial vestibular activity can help or hinder the ongoing control of balance, and if the learning mechanisms essential for standing balance can be reshaped for non-naturally occurring sensory input patterns. Healthy participants will undergo adaptation in dynamic balance tasks, with progressive adjustments to vestibular stimuli (via controlled electric vestibular stimulation) that mimics or deviates from common motion patterns. This manipulation will help determine if learning adapts optimally to input patterns most similar to everyday vestibular feedback. We will assess learning effectiveness by measuring balance stability, response properties, and error correction across different training conditions.

This research has the potential to uncover foundational principles about how sensorimotor learning for balance is shaped by the statistics of vestibular input. These results could enhance balance training and rehabilitation by shaping the statistical properties of natural vestibular feedback. This insight may lead to innovative, individualized therapies for those with vestibular impairments or other balance-related disorders, ultimately contributing to more effective interventions for improving balance control.

Requirements of candidate:

We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.

- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal)
- Master degree or MD degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*
- *Programming skills (Matlab/Python) are appreciated*

DEPARTMENT OF NEUROSCIENCES

Project: The cost of stability: How metabolic efficiency shapes movement variability

Supervisor information:

Prof dr Maarten Frens
Email: m.frens@erasmusmc.nl

Dr Patrick Forbes
p.forbes@erasmusmc.nl

Website: www.neuro.nl

Grants:

- Dutch Scientific Organization Grant (VIDI/VENI/Top Talent, 2022/2019/2017)
- ESA Micro-Gravity Flight Campaigns (2016/2017/2018)
- European Research Commision (Marie Sklodowska-Curie Action, 2014)
- European FP7 ITN Grant (2009)

Important recent publications:

- **Nature Communications**, 2024, Mar 18;15(1):2351. doi: 10.1038/s41467-024-46398-2.
- **PNAS**, 2024 Aug 6;121(32):e2404909121. doi: 10.1073/pnas.2404909121
- **Human Brain Mapping**, 2024 Feb 1;45(2):e26565. doi: 10.1002/hbm.26565.
- **Communications Biology**, 2024, doi: 10.1038/s42003-024-06029-4
- **Journal of Neuroscience**, 2023, doi: 10.1523/JNEUROSCI.0987-22.2023
- **Annals of Neurology**, 2020, Mar;87(3):383-393. doi: 10.1002/ana.25679
- **Nature Communications**, 2019, doi: 10.1038/s41467-019-09738-1

Abstract:

Recent findings suggest that humans naturally adapt their gait in real time to minimize metabolic cost, an optimization strategy that often coincides with a reduction in head movement variability. This adaptive behavior highlights the potential link between energy efficiency and stability, as reduced variability may facilitate smoother, less energetically demanding motion. However, the direction of influence between metabolic cost and movement variability remains unclear. It is possible that minimizing energetic expenditure leads to consistent, stable movement patterns, reducing variability. Alternatively, inherent variability within natural movement patterns could drive metabolic efficiency by fostering adaptive, energy-saving adjustments. This project seeks to unravel this interplay, examining whether metabolic cost influences movement variability or if variability itself acts as a primary driver in minimizing energetic demands.

To investigate these interactions, we will use a combination of experimental protocols and analytical techniques focusing on human postural and locomotor stability. The study will recruit young and old participants who will undergo a series of controlled tasks involving standing and walking under conditions of varying stability requirements and energetic demands. Key components of the methodology include:

- Metabolic cost: Using indirect calorimetry, we will measure oxygen consumption and carbon dioxide production as participants perform stabilization tasks.
- Motion tracking/kinematic analysis: High-resolution motion capture will record detailed kinematic data, allowing us to quantify movement variability.
- Manipulation of real-time sensorimotor feedback: We will incorporate human-in-the-loop feedback systems to influence participants' stabilization strategies. For example, real-time feedback of head movement will drive vestibular stimulation to alter the sensorimotor relationships that drive the variability-cost relationship.
- Computational models: Models will be used to assess the muscle contributions to changing relationships in variability and metabolic cost.

This integrative approach will provide insights into how metabolic cost considerations shape adaptive motor strategies during stabilization. Understanding these mechanisms could advance sensorimotor rehabilitation by informing strategies that emphasize natural variability to promote energy-efficient, adaptable stability.

Requirements of candidate:

We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.

- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal)
- Master degree or MD degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*
- *Programming skills (Matlab/Python) are appreciated*

DEPARTMENT OF NEUROSCIENCES

Project: Bicycling through the labyrinth: unravelling the vestibular influence on human-machine balance control

Supervisor information:

Prof dr Maarten Frens
Email: m.frens@erasmusmc.nl

Dr Patrick Forbes
p.forbes@erasmusmc.nl

Website: www.neuro.nl

Grants:

- Dutch Scientific Organization Grant (VIDI/VENI/Top Talent, 2022/2019/2017)
- ESA Micro-Gravity Flight Campaigns (2016/2017/2018)
- European Research Commision (Marie Sklodowska-Curie Action, 2014)
- European FP7 ITN Grant (2009)

Important recent publications:

- **Nature Communications**, 2024, Mar 18;15(1):2351. doi: 10.1038/s41467-024-46398-2.
- **PNAS**, 2024 Aug 6;121(32):e2404909121. doi: 10.1073/pnas.2404909121
- **Human Brain Mapping**, 2024 Feb 1;45(2):e26565. doi: 10.1002/hbm.26565.
- **Communications Biology**, 2024, doi: 10.1038/s42003-024-06029-4
- **Journal of Neuroscience**, 2023, doi: 10.1523/JNEUROSCI.0987-22.2023
- **Annals of Neurology**, 2020, Mar;87(3):383-393. doi: 10.1002/ana.25679
- **Nature Communications**, 2019, doi: 10.1038/s41467-019-09738-1

Abstract:

For millions of years, humans have evolved to balance primarily on stationary ground; yet for a recent fraction of this evolutionary period, we have developed numerous devices (from tightropes to surfboards to Segways) that challenge our balance system in historically uncommon ways. A bicycle is one such device and is used daily by billions of people for transportation and recreation, yet it makes the rider vulnerable to fall injuries that are evolutionarily uncommon. Unlike walking, we are not born with an inscribed model of the complex dynamics of bicycling. A bicycle's stability depends on speed (it is unstable at low speeds) and requires counterintuitive control to maintain balance and direction—you must initially steer in the opposite direction of an intended turn. This makes the bicycle a challenging machine to master; yet we learn its basic operation relatively rapidly. With further practice, extreme athletes can even perform unimaginable maneuvers, such as riding on one wheel along a narrow edge. This project aims to uncover the sensorimotor control mechanisms of cycling and how they are adapted for balancing a bicycle. Our findings could provide the foundational science needed to develop active bicycle safety assistance that synergistically complements the plasticity of a cyclist's internal balance controller. This approach could, in turn, open new research paths, offering deeper insights into human sensorimotor control and the capacity to adjust control strategies during safety-critical human-machine interactions.

Although computational models of bicycling predict that the nervous system integrates sensory feedback maintain balance during bicycling, physiological mechanisms indicating how, when, and where this occurs in our sensorimotor control are completely unknown. Crucial to this process of bicycle balancing are signals that arise from the vestibular system (i.e. the labyrinth or balance organ), which encode our internal estimate of our body's and the bicycle's orientation and motion. This is perhaps best demonstrated by the fact that expert riders can balance a bike in absence of proprioceptive feedback of steering (i.e. no hands) and visual feedback (i.e. eyes closed). Here, we will answer the following questions: 1) What are the essential vestibular control loops of bicycle balancing? And: 2) How do these vestibular control loops adapt during balance-assisted cycling? This project will combine non-invasive sensory stimulation techniques together with a unique programmable bicycle to answer these questions and propose new physiologically-based human control models.

Requirements of candidate:

We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.

- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal)
- Master degree or MD degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*
- *Programming skills (Matlab/Python) are appreciated*

DEPARTMENT OF NEUROSCIENCES

Project:	**Optical dissection of the brain circuitry underlying epilepsy**
Supervisor information:	**Prof Dr Eric Lowet** **Email:** e.lowet@erasmusmc.nl **Website:** https://neuro.nl/research/lowet **Grants:** ERC starter grant, 2023, 1.63M$ ***Five important recent publications:*** - Neuron, 2018, 2020 - Nature Communications 2022,2023,2024, - Cell reports, 2023 - Nature Methods, 2024 - Elife, 2018
Abstract:	Epilepsy, a common neurological disorder, affects around 50 million people worldwide and is marked by recurring seizures due to excessive, synchronized neural activity. This can lead to various symptoms, such as uncontrolled motor activity and loss of consciousness. Epilepsy types vary by seizure location and pattern, with temporal lobe epilepsy (TLE) being the most common focal epilepsy (~60%), primarily affecting the hippocampus and related structures. While many anti-epileptic drugs (AEDs) have been developed, about 30% of patients experience drug-resistant epilepsy (DRE), defined as resistance to at least two AEDs. DRE significantly impacts quality of life, as uncontrolled seizures are linked to poorer outcomes and can hinder intellectual and social development, especially in children. The unclear neurobiological mechanisms underlying seizures and DRE represent an important knowledge gap, which has limited the development of more effective therapy. In this project, we will use optical fluorescence microscopy, chemo- and optogenetic approaches as well as electrophysiology to determine the changes in the hippocampal circuitry underlying DRE. Voltage fluorescence microscopy is a novel technique based on genetically encoded voltage indicators (GEVIs) that enables the recording of the membrane potential of single neurons at millisecond resolution in the awake mouse. We have previously published voltage imaging and optogenetic applications in the mouse hippocampus. In the first part, the PhD candidate will apply these techniques in vivo and ex-vivo epilepsy mouse models to record from neuronal (excitatory, inhibitory) and glial (astrocytes) cell types during seizures and as a function of seizure progression. We hypothesize that dysfunction of neuronal-astrocyte interactions is a key mechanism for the deregulation of excitatory-inhibitory balance and the emergence of DRE. In the second part, using optical causal as well as pharmacological interventions, we will seek to interfere with the circuitry to counteract seizures and DRE. This offers excellent opportunities for scientific development of the PhD candidate and creates a multilayered picture of the disease, that can help to develop new care strategies for the patients.
Requirements of candidate:	We are looking for a highly motivated, hardworking student to join our dynamic international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. • Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal) • Master degree or MD degree • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)* • *Proactive approach to research* • *Previous cell-culture and/or rodent experience is a plus*

DEPARTMENT OF NEUROSCIENCES

Project:	Cerebellar differentiation in motor control and neurodevelopmental disorders
Supervisor information:	**Prof dr Martijn Schonewille** **Email:** m.schonewille@erasmusmc.nl **Website:** www.neuro.nl/research/schonewille **Grants (examples):** EUR Fellowship (200k), NWO-Veni (250k), H2020 ERC-Starter (1500k), Janelia Visitor Program (2x, co-PI, 60k total), Convergence Flagship (consortium, 2000k), NWO ENW-M1 (366k). CSC Fellowships students, former: dr. Haibo Zhou (link), dr. Bin Wu (link); current: Chen Yang, Jie Yang (both CSC) and Heiling Lu (NRF, South Africa) ***Important publications:*** Wulff P*, **Schonewille M***, Renzi M, Viltono L, Sassoè-Pognetto M, Badura A, Gao Z, Hoebeek FE, van Dorp S, Wisden W, Farrant M, De Zeeuw CI. Synaptic inhibition of Purkinje cells mediates consolidation of vestibulo-cerebellar motor learning. ***Nat Neurosci***. 2009 Aug;12(8):1042-9. doi: 10.1038/nn.2348. Epub 2009 Jul 5. PMID: 19578381 **Schonewille M**, Gao Z, Boele HJ, Veloz MF, Amerika WE, Simek AA, De Jeu MT, Steinberg JP, Takamiya K, Hoebeek FE, Linden DJ, Huganir RL, De Zeeuw CI. Reevaluating the role of LTD in cerebellar motor learning. ***Neuron***. 2011 Apr 14;70(1):43-50. doi: 10.1016/j.neuron.2011.02.044. PMID: 21482355 De Zeeuw CI, Hoebeek FE, Bosman LW, **Schonewille M**, Witter L, Koekkoek SK. Spatiotemporal firing patterns in the cerebellum. ***Nat Rev Neurosci***. 2011 Jun;12(6):327-44. doi: 10.1038/nrn3011. Epub 2011 May 5. PMID: 21544091 Review. Wu B, Blot FG, Wong AB, Osório C, Adolfs Y, Pasterkamp RJ, Hartmann J, Becker EB, Boele HJ, De Zeeuw CI, **Schonewille M.** TRPC3 is a major contributor to functional heterogeneity of cerebellar Purkinje cells. ***Elife***. 2019 Sep 5;8:e45590. doi: 10.7554/eLife.45590. PMID: 31486767 Blot FGC, Krijnen WHJJ, Den Hoedt S, Osório C, White JJ, Mulder MT, **Schonewille M**. Sphingolipid metabolism governs Purkinje cell patterned degeneration in *Atxn1[82Q]/+* mice. ***Proc Natl Acad Sci U S A***. 2021 Sep 7;118(36):e2016969118. doi: 10.1073/pnas.2016969118. PMID: 34479994 *Osório C, White JJ, Lu H, Beekhof GC, Romana Fiocchi F, Andriessen CA, Dijkhuizen S, Post L,* **Schonewille M**. Pre-ataxic loss of intrinsic plasticity and motor learning in a mouse model of SCA1. ***Brain***. 2023 Jun 1;146(6):2332-2345. doi: 10.1093/brain/awac422. PMID: 36352508 Blot FGC, White JJ, Hattem A, Scotti L, Balaji V, Adolfs Y, Pasterkamp RJ, De Zeeuw CI, **Schonewille M**. Purkinje cell microzones mediate distinct kinematics of a single movement. ***Nat Comm.*** 2023 Jul 19;14(1):4358. doi: 10.1038/s41467-023-40111-5., PMID: 37468512
Abstract:	The perfect execution of a voluntary movement requires the appropriate integration of current bodily state, sensory input and desired outcome. To assure that this motor output is optimized, the brain needs to learn from previous movements. The cerebellum plays a central role in sensorimotor integration, yet there is no generally excepted theory for cerebellar functioning. We recently demonstrated that cerebellar modules, identified based on anatomical connectivity and gene expression, differ distinctly in spike activity properties. The long-term goal of the lab is to identify the ontogeny of anatomical and physiological differences between modules, and their functional consequences. To achieve this goal, we make use a variety of techniques including molecular biological approaches, anatomical reconstruction, in vitro and in vivo electrophysiology and behavioral paradigms. We aim to determine how differential gene expression patterns control the development of distinct physiological properties and anatomical connection patterns of the types of neurons in different cerebellar modules, and how this is related to neurodevelopmental disorders (project option 1). Moreover, we aim to determine how genetic differentiation underlies the proper cerebellar information processing for optimal coordination of timing and force of movements and how this is related to (neurodegenerative) movement disorders (project option 2). Combined with the growing body of evidence for a cerebellar role in higher order brain functions and neurodevelopmental disorders, this knowledge will be fundamental for understanding how the cerebellum contributes to every day functioning.
Requirements of candidate:	We are looking for: • A highly motivated student to join our international team; tackling large scientific questions requires a student with good communication skills for optimal performance in our collaborative environment • A scholarship that will, at least, cover subsistence allowance and international air plane ticket (the supervisor will help with the scientific part of your scholarship proposal) • Master degree or MD degree • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF NEUROSCIENCES

Project: Neurodevelopmental disorders: from chromatin biology to personalized medicine

Supervisor information:

Prof. Dr. Chris I. De Zeeuw c.dezeeuw@erasmusmc.nl https://neuro.nl/research/de-zeeuw

Personal Grants:

ERC Advanced Grant (ERC-Adv), 2014
ERC PoC grants (ERC-PoC), 2015, 2016, 2017
Dutch Scientific Organization (ALW-Open) Grants, 2021, 2023, 2024
ZonMw Grant, 2020, 2021
KNAW Grants, 2021, 2023

Most important publications:

- Nature Neuroscience 2021 24: 160
- Nature Communications 2020 11
- Nature 2018 563:113
- Science Adv 2018 and 2024
- Nature Neuroscience 2017 20:727
- Nature Reviews Neuroscience 2021 22:92
- Nature Communications 2019 10 and 2023
- Nature Communications 2018 9 and 2024
- Science 2017 356:1084 and Science 2024
- Neuron 2017 93:409 and Neuron 2024

Abstract:

Neurodevelopmental disorders (NDD) present a major cause of disability early in life and a significant burden to the health system. Despite improved diagnostic yield of genetic testing, our understanding of the NDDs disease mechanisms remain incomplete. This project focuses on a group of NDDs caused by variants in chromatin modifiers (genes responsible for the regulation of gene expression) and will investigate fundamental aspects of complex NDD phenotypes as well as novel treatment options.
We have previously established the first iPSC-based models for novel NDDs (e.g.SETD1B, BICRA), including human excitatory neurons and cerebral organoids. PhD candidate will use *in vitro* models to gain knowledge on regulatory functions of chromatin modifiers in neurons (ChIP-, ATAC-, RNA-seq techniques) and investigate their functionality by using multi-electrode array (MEA). Based on clinical and *in vitro* data, the candidate will also perform preclinical testing of modulators of disease-specific pathways aiming to develop new treatment options. We will also employ the multiplexed cerebral organoids approach as innovative method to investigate brain-related NDD phenotypes. Cerebral organoids from a pool of patient-derived induced pluripotent stem cells allow to simultaneously evaluate several pathogenic variants in different cell-types. The tracking of multiple cell-type differentiation and their (affected) transcriptional profile is enabled by the single-cell RNA-sequencing readout, generating a powerful dataset to understand the neuropathology of NDDs. Another aspect of NDDs that we are working on are immunity-related problems, such as recurrent infections – frequently observed in NDD patients' phenotype. In our work we aim to unravel the contribution of multiple NDD-relevant chromatin modifiers to infection phenotype in a systematic manner. We hypothesize that certain chromatin modifiers are involved in regulating host response at an early phase of infection. To investigate this we employ a synergistic approach combining virology and epigenetic analysis to examine the dynamics of chromatin accessibility together with direct transcriptional output of the host cell. Our approach includes conducting single-cell knock-down screens with chromatin accessibility readout to define the key chromatin modifiers regulating the host response and their cooperation. Ultimately we will reveal how the disrupted gene regulation in NDDs impacts the course of infection. In our research we take a comprehensive approach and address both neural and non-neural aspects of NDDs. This offers excellent opportunities for scientific development of the PhD candidate and creates a multilayered picture of the disease, that can help to develop new care strategies for the patients..

Requirements of candidate:

We are looking for a highly motivated, hardworking student to join our dynamic international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.

- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal)
- Master degree or MD degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*
- *Proactive approach to research*
- *Previous cell-culture and molecular biology experience is a plus*

DEPARTMENT OF ORAL & MAXILLOFACIAL SURGERY, SPECIAL DENTAL CARE & ORTHODONTICS

Project:

Supervisor information:

Dr Lea Kragt **Prof dr Fernando Rivadeneira** **Prof dr Eppo Wolvius**

Email: l.kragt@erasmusmc.nl https://oral-health.nl/ https://www.linkedin.com/company/oralcraniofacialhealth/posts/?feedView=all&viewAsMember=true

Grants:

1. EMC-TKI-LSH Match call for PPP allowance (2020), Name of Funding Organization: Health Holland (via Erasmus MC TKI LSH office), Amount Awarded: € 449,933
2. Open Mind Call for Convergence (2021); Name of Funding Organization: Health and Technology by Convergence, Amount Awarded: € 16.070
3. Erasmus MC Starting Grant (2023) Name of Funding Organization: Ministerie van Onderwijs, Cultuur en Wetenschap, Amount Awarded: € 240.000

Five important recent publications:

2016 Journal of Dental Research 95(4): 395-401 https://journals.sagepub.com/doi/10.1177/0022034515625470?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
2017 Journal of Dental Research 96(13): 1482-1489 https://journals.sagepub.com/doi/10.1177/0022034517723326?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
2023 Journal of Dental Research 102(3): 349-356 https://journals.sagepub.com/doi/10.1177/00220345221132268
2024 Bone 182: 117070 https://www.sciencedirect.com/science/article/pii/S8756328224000590
2024 Arch Oral Biol 161:105933 https://www.sciencedirect.com/science/article/pii/S0003996924000542?via%3Dihub
2024 Community Dent Oral Epidemiol Online ahead of print https://onlinelibrary.wiley.com/doi/10.1111/cdoe.13012

Abstract:

Oral and craniofacial health plays a critical role in the overall functioning of the human body and is a significant contributorto general health and well-being. Nearly half of the global population (48%) suffers from one or more oral conditions. Consequently, the World Health Organization (WHO) has emphasized the need for research into the risk factors associated with oral and craniofacial diseases and the development of effective (preventive) strategies to reduce the burden of these conditions. Several social, behavioral, genetic, and environmental factors have been identified as key contributors to the development of oral and craniofacial disorders, andthese conditions may also be interrelated. However, previous studies have been challenged by the complex and multidimensional nature of oral and craniofacial disorders. The chronicand congenital nature, as well as the dynamic progression, of most oral and craniofacial conditions necessitates longitudinal observations in a multidisciplinary setting.

The aim of our research group is to improve oral and craniofacial health through scientific investigation and the translationoffindings into tangible health applications. We pursue this mission by incorporating technological advances into an observational epidemiological framework. Within our group, we examine a wide range of determinants of oral health, including endocrine, environmental, genetic, epigenetic, microbiome, lifestyle, nutritional, infectious, and sociodemographicfactors. Furthermore, we aim to investigate the interrelationship between oral and systemic diseases, exploring how they interact and identifying common risk factors. We apply sophisticated advanced statistical method and strive to continuously improve our approach.

Our research is conducted within two large population-based cohort studies based in Rotterdam, the Netherlands: the Generation RStudy and the Rotterdam Study. The Generation R Study follows children from fetal life through to young adulthood, while the Rotterdam Study focuses on elderly individuals aged 45 years and older. In both cohorts, a variety of data, including behavioral, genetic, and social determinants of health, have been repeatedly collected. In additionto oral health, many other health outcomes are also assessed within these studies. These settings therefore provide an ideal environment to investigate the bidirectional relationship between oral and general health and to gain insights into the development of oral health across the lifespan.

Requirements of candidate:

- We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using teamwork to tackle large scientific questions and thus requires a student with good communication skills.
- Scholarship that will, at least, cover subsistence allowance and international air planeticket (your future supervisor could help with the scientific part of your scholarship proposal)
- Master degree or MD degree related to health sciences, biomedical sciences or dentistry
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF PATHOLOGY

Project:	**Dr. Jekyll and Mr. Hyde: Cancer Cells with Multiple Personality Disorders.**
Supervisor information:	**Prof. dr. Riccardo Fodde, PhD** **Email: r.fodde@erasmusmc.nl** **Website: https://labriccardofodde.nl** **Ongoing grants:** - **Dutch Cancer Society (KWF) 2019-24. Secretory Paneth-like cells as the origin of intestinal cancer** - **Mrace (Erasmus MC) 2019-24 Dr. Jekyll and Mr. Hide: phenotypic plasticity and epigenetic control of EMT in oral cancer metastasis.** - **Chinese Scholarship Council (CSC) 2020-2024. The role of alternative splicing in the regulation of epithelial-to-mesenchymal plasticity in colon and ovarian cancer.** **Most important publications:** 1. Verhagen MP, et al. Non-stem cell lineages as an alternative origin of intestinal tumorigenesis in the context of inflammation. Nat Genet. 2024 Jul;56(7):1456-1467. 2. Xu T, et al. Tropomyosin1 isoforms underlie epithelial to mesenchymal plasticity, metastatic dissemination, and resistance to chemotherapy in high-grade serous ovarian cancer. Cell Death Differ. 2024 Mar;31(3):360-377. 3. Stabile R, et al. The deleted in oral cancer (DOC1 aka CDK2AP1) tumor suppressor gene is downregulated in oral squamous cell carcinoma by multiple microRNAs. Cell Death Dis. 2023 May 22;14(5):337. 4. Xu T, et al. Alternative splicing downstream of EMT enhances phenotypic plasticity and malignant behavior in colon cancer. Elife. 2022 Nov 8;11:e82006. 5. Sacchetti A, et al. Phenotypic plasticity underlies local invasion and distant metastasis in colon cancer. Elife. 2021 May 26;10:e61461.. 6. Schmitt M, et al. Paneth Cells Respond to Inflammation and Contribute to Tissue Regeneration by Acquiring Stem-like Features through SCF/c-Kit Signaling. Cell Reports. 2018 Aug 28;24(9):2312-2328.e7. 7. Mohd-Sarip A, et al. DOC1-Dependent Recruitment of NURD Reveals Antagonism with SWI/SNF during Epithelial-Mesenchymal Transition in Oral Cancer Cells. Cell Reports. 2017 Jul 5;20(1):61-75. 8. Rodríguez-Colman MJ, et al. Interplay between metabolic identities in the intestinal crypt supports stem cell function. Nature. 2017 Mar 16;543(7645):424-427. 9. Schewe M, et al. Secreted Phospholipases A2 Are Intestinal Stem Cell Niche Factors with Distinct Roles in Homeostasis, Inflammation, and Cancer. Cell Stem Cell. 2016 Jul 7;19(1):38-51. 10. Schewe M,et al. The Organoid Reconstitution Assay (ORA) for the Functional Analysis of Intestinal Stem and Niche Cells. J Vis Exp. 2017 Nov 20;(129):56329..
Abstract:	*Phenotypic plasticity is defined as the ability of a single organism with one genotype to produce more than one phenotype when exposed to different environments, and is regarded as the most clinically relevant hallmark of cancer. This capacity of altering cell identity based on the environmental context allows cancer cells to detach from the primary mass and efficiently survive the long-distance trip to a distal organ where they will form metastases. The invasion-metastasis cascade is underlined by transient and reversible epigenetic alterations which continuously adapt to the ever changing environments en route to their metastatic destination. Phenotypic plasticity also confers cancer cells resistance to conventional radio- and chemotherapy.* *Apart from the very terminal stages of cancer progression, phenotypic plasticity also plays a key role in the initiation of the tumorigenic process. We have recently shown that the cell-of-origin of colon cancer in the context of inflammation (as in inflammatory bowel diseases but also in Western style diet-driven metaflammation) is not a stem cell as the current dogma predicts but rather a fully committed lineage that de-differentiate to acquire stem cell features and initiate a new tumor. We are now conducting follow-up functional studies to elucidate the molecular and cellular mechanisms which underlie these dedifferentiation processes.* *In our laboratory, the above are the main themes of research and the newly offered PhD position will work, depending on previous education and experience (wet-lab or computational), on a project on the role of phenotypic plasticity in either colon cancer initiation or ovarian cancer metastasis formation in the abdominal cavity. The latter is based on a newly identified therapeutic target (Tpm1) which splicing isoforms underlie Wnt activation and EMT in advanced stage high-grade serous ovarian cancer. Hence, the best candidate will be assigned to a specific PhD project that best suits his/her scientific profile.*
Requirements of candidate:	• **We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.** • **Master degree with knowledge of molecular, cellular, and computational biology** • **English language requirement: IELTS 7.0 (min 6.0 for all subs), TOEFL 100 (min 20 for all subs)**

DEPARTMENT OF PEDIATRIC SURGERY

Project:	**The molecular basis of congenital and perinatal lung disease: vascular and epithelial interactions**
Supervisor information:	*Prof dr R.J. Rottier* *r.rottier@erasmusmc.nl* *https://www.erasmusmc.nl/en/research/researchers/rottier-robbert* ***Grants:*** • *ZonMW MKMD-COVID19* • *Human Disease Model Award* • *ZonMw MKMD* • *Dutch Lung Foundation* • *NWO fellowship* ***Most important publications:*** EBioMedicine. 2022 Jul;81:104132. doi: 10.1016/j.ebiom.2022.104132 Elife. 2021 Jul 21;10:e57325. doi: 10.7554/eLife.57325 The Lancet Child & Adolescent Health 2018 Apr;2(4):290-297 Sci Rep. 2018 May 9;8(1):7349 J Mol Cell Biol. 2012;4:377-385 Sci Transl Med. 2022 Jun 8;14(648):eabe5407 Am J Respir Crit Care Med. 2020; 202(8): 1088-1104 Am J Physiol Lung Cell Mol Physiol. 2018 Aug 1; 315(2): L276-285 Am J Respir Cell Mol Biol. 2014;51:311-22 J Cell Biol. 2009;185:27-34
Abstract:	*The clinical challenges of patients with congenital lung diseases and the frustration of treatment failure by clinicians and families drives the quest to improve the fundamental understanding of lung development. The lungs develop by close interaction between the epithelium and the surrounding mesenchyme, including the vessels.* *In my laboratory, I currently have two positions, one focusing on the origin and development of the pulmonary vasculature, the other focusing on epithelial differentiation:* ***(1) pulmonary vascular development in light of congenital lung abnormalities*** *Alveolar Capillary Dysplasia (ACD) and Congenital Diaphragmatic Hernia (CDH) are two examples of pediatric anomalies with abnormal vascularization of the lungs resulting from defective development. The transcription factor FOXF1 is directly involved either directly by genomic alterations of the locus (ACD), or indirectly through processes leading to reduced expression of FOXF1 (CDH). However, the exact molecular mechanisms remain elusive, and therefore, the overall objective of this project is to further decipher the molecular basis of pulmonary vascular development, in health and (pediatric) disease using mouse models, human tissue and primary cells.* ***(2) Oxygen, lung damage and pulmonary neuroendocrine cells: a numbers game?*** *Treatment of patients with severe congenital or acquired lung diseases is still non-evidenced based concomitant with unpredictable therapy responsiveness. One potential underlying cause may be the intrinsic property of the lung, since many patients have increased numbers of Pulmonary Neuroendocrine Cells (PNECs). The overall objective is to investigate the contribution of PNECs to the origin and progression of lung disease in the CDH. Therefore, we propose to analyze factors involved in the differentiation of PNECs, and identify mechanisms that control their numbers in normal and abnormal lung development using human and mouse models.*
Requirements of candidate:	○ We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. ○ Master degree or MD ○ Scholarship that will, at least, cover subsistence allowance and international air plane ticket (we could help with the scientific part of your scholarship proposal) ○ IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF RADIOLOGY & NUCLEAR MEDICINE

Project:	**Analysis of advanced musculoskeletal magnetic resonance imaging (MRI) data from clinical and population-based studies**
Supervisor information:	*Professor Edwin H.G. Oei, MD, PhD* *e.oei@erasmusmc.nl* *www.admire-group.com* ***Personal Grants:*** Dutch Research Council (***NWO***) *GE Healthcare / National Basketball Association (NBA) Patellar Tendinopathy CFP 2016* *Radiological Society of North America (RSNA) 2014* ***Most important publications:*** Wu T et al. Thorax. 2024 Apr 15;79(5):448-456. Breda et al. J Magn Reson Imaging. 2021 Nov;54(5):1596-1605. De Vries et al. Semin Arthritis Rheum. 2020 Apr;50(2):177-182 Eijgenraam et al. Eur Radiol. 2019 Oct;29(10):5664-5672 Van Tiel et al., Radiology. 2016 May;279(2):523-31. Van der Heijden et al. Am J Sports Med. 2016 May;44(5):1172-8
Abstract:	*The ADMIRE group's research focuses on imaging of common musculoskeletal diseases such as osteoarthritis, osteoporosis, and sports injuries, with advanced imaging techniques. We develop, improve, and validate innovative MRI, CT, ultrasound methods with the aim to identify new sensitive imaging biomarkers for pathological tissue processes and structural and compositional changes in tissues such as cartilage, bone, meniscus and tendon. We apply our novel imaging techniques in various clinical studies in collaboration with clinical departments. Another important research focus is on musculoskeletal population imaging, in which we apply MRI in the large-scale population based Rotterdam Study among elderly and the Generation R cohort among children and adolescents to study and epidemiology, genetics, and development of musculoskeletal diseases and body composition. The aim of this project will be to analyze existing, readily available, but unexplored quantitative MRI datasets acquired in clinical and population cohorts. The exact focus of the project and datasets to be utilized, will be defined at a later stage depending on the candidate's expertise and interest, but may as an example the assessment of bone, cartilage and meniscus quality on MRI from clinical osteoporosis and osteoarthritis studies, and correlation with symptoms or clinical outcomes. In the population imaging studies, an example would be the analysis of body composition, knee or hip MRI scans in the Generation R study, and correlation with risk factors and genetics. The project would typically entail the reading, annotation and quantitative biomarker extraction from acquired MRI datasets and correlating these with clinical and/or epidemiological data. According to the PhD student's profile and preference, the level of technical or analytical (MR physics, MRI analysis, deep learning) versus clinical focus will be defined.*
Requirements of candidate:	○ We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. ○ Master degree or MD ○ Scholarship that will, at least, cover subsistence allowance and international air plane ticket (we could help with the scientific part of your scholarship proposal) ○ IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF RADIOLOGY & NUCLEAR MEDICINE

Project:	***Advanced image analysis for early prediction of musculoskeletal diseases***
Supervisor information:	**Assistant Professor Jukka Hirvasniemi, PhD** **Email:** j.hirvasniemi@erasmusmc.nl **Website:** https://bigr.nl/member/jukka/, https://scholar.google.com/citations?user=qY1z96UAAAAJ&hl **Selected grants:** Academy of Finland grant (year: 2017, grant sum: 256k€, my role: principal investigator(PI)), Marie Skłodowska-Curie COFUND programme fellowship (2019, 63k€, PI), ERC advanced grant (2023, 2.5M€, work package leader, PI of the project: Prof S. Bierma-Zeinstra**)** ***Five important recent publications:*** - *Hirvasniemi et al., The KNee OsteoArthritis Prediction (KNOAP2020) challenge: An image analysis challenge to predict incident symptomatic radiographic knee osteoarthritis from MRI and X-ray images. Osteoarthritis and Cartilage 2023. https://doi.org/10.1016/j.joca.2022.10.001* - *Hirvasniemi et al., A machine learning approach to distinguish between knees without and with osteoarthritis using MRI-based radiomic features from tibial bone. European Radiology 2021. https://doi.org/10.1007/s00330-021-07951-5* - *Thevenot et al., Assessment of Risk of Femoral Neck Fracture with Radiographic Texture Parameters: A Retrospective Study. Radiology 2014. https://doi.org/10.1148/radiol.14131390* - *Li et al., Comparison of bone texture between normal individuals and patients with Kashin-Beck disease from plain radiographs in knee. Scientific reports 2018. https://doi.org/10.1038/s41598-018-35552-8* - *Gebre et al., Discrimination of Low-Energy Acetabular Fractures from Controls Using Computed Tomography-Based Bone Characteristics. Annals of Biomedical Engineering 2021. https://doi.org/10.1007/s10439-020-02563-4*
Abstract:	*Musculoskeletal disorders are common, significantly impact the quality of life of an individual, and impose a substantial economic burden on society. Identifying individuals at high risk of developing musculoskeletal diseases, such as osteoarthritis, is crucial for preventing or slowing disease progression. Additionally, early diagnosis of the musculoskeletal disorders is essential for effective management. Medical imaging provides insights into both anatomy and physiological processes and plays an important role in the diagnosis of musculoskeletal disorders both in clinical and research settings. Recent advances in deep learning-based image and data analysis enable analysis of large datasets and generation of synthetic data when data is limited. These advancement offer significant potential to deepen our understanding of musculoskeletal disorders and improve early detection and prediction.* *Osteoarthritis is the most common joint disease consisting of multiple subtypes. It affects over 500 million people worldwide and its etiology is partly unknown. At the end stage of the disease, joint replacement surgery is the only available treatment option. However, during the early stages of osteoarthritis, the disease might be more amenable to modification. The aim of the PhD project is to develop image analysis techniques for early detection and prediction of musculoskeletal diseases such as osteoarthritis. We have multiple unique and large musculoskeletal imaging datasets (including plain radiographs, DXA, and magnetic resonance imaging (MRI)) and novel and advanced imaging data (PET/MRI, photon-counting computed tomography) available at Erasmus MC University Medical Center. These data can be used for studying problems such as synthetic data creation, domain adaptation for medical images, deep learning-based image segmentation, automatic disease and pathology detection and image classification, and prediction of a risk for disease incidence from medical images. Additionally, disease progression modelling methods can be used to identify osteoarthritis subtypes and sequence of features using existing and emerging datasets at Erasmus MC University Medical Center and public international datasets.*
Requirements of candidate:	We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. • Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal) • Master degree in a technical discipline preferably with an affinity for medical applications (biomedical engineering, computer science, physics, engineering, …) • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF RADIOLOGY & NUCLEAR MEDICINE

Project: Novel Theranostics to Image and Treat Cancer

Supervisor information:

Dr Yann Seimbille
Email: y.seimbille@erasmusmc.nl
- https://www.erasmusmc.nl/en/research/groups/radiopharmaceutical-chemistry
- https://www.linkedin.com/in/yann-seimbille-3265bb12/

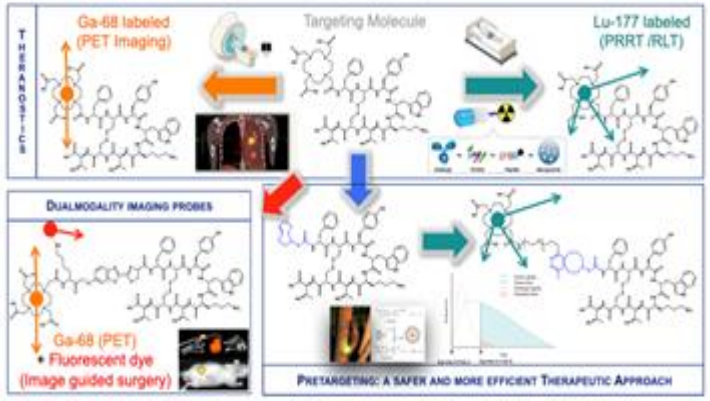
https://pure.eur.nl/en/persons/yann-seimbille
https://www.researchgate.net/profile/Yann_Seimbille,

Grants:
1) First-in-human assessment of a FAP-targeted probe for fluorescence guided surgery of pancreatic cancer, **Dutch Cancer Foundation**, 2025-2029. **2)** Elevating the future of cancer care with alpha theranostics, **EU-IHI**, 2025-2028. **3)** Molecular oncology twins advancing treatment and innovative cancer evaluation, **NWO**, 2025-2029. **4)** Theranostics hitting breast cancer: pointing the arrows at HER2 and GRPR, **Erasmus MC Grant**, 2021-2025

Five important recent publications:

1) Chapeau D, Beekman S, Piet A, Li L, de Ridder C, Stuurman D, **Seimbille Y**. *Bioconjugate Chemistry*, 2024 (https://doi.org/10.1021/acs.bioconjchem.4c00413). **2)** van der Heide C, Ma H, Hoorens M, Campeiro J, Stuurman D, de Ridder C, **Seimbille Y**, Dalm S. *EJNMMI Radiopharm and Chem*, 2024, 9:55 (https://doi.org/10.1186/s41181-024-00283-x). **3)** Chapeau D, Koustoulidou S, Handula M, Beekman S, de Ridder C, Stuurman D, de Blois E, Buchatskaya Y, van der Schilden K, de Jong M, Konijnenberg M, **Seimbille Y**. *Pharmaceuticals*, 2023, 16:985 (https://doi.org/10.3390/ph16070985). **4)** Handula M, Beekman S, Konijnenberg M, Stuurman D, de Ridder C, Bruchertseifer F, Morgenstern A, Denkova A, de Blois E, **Seimbille Y**. *EJNMMI Radiopharmacy and Chemistry*, 2023, 8:13 (https://doi.org/10.1186/s41181-023-00197-0). **The EANM Springer Prize: Best Paper 2024.** **5)** Murce E, Beekman S, Spaan E, Handula M, Stuurman D, de Ridder C, **Seimbille Y**. *Molecules*, 2023, 28:4022 (https://doi.org/10.3390/molecules28104022)

Abstract:



The research of the RadioPharmaceutical Chemistry (RPC) group at Erasmus MC is a molecular imaging-based program focused on **theranostics** and **multimodality imaging probes**, with an emphasis on developing these novel radiopharmaceuticals for clinical translation.
We are offering to work on a project aiming at the development of a new generation of theranostics pointing at the major Achilles' heels of tumors.
The new radioactive drugs will be capable of providing adequate diagnostic information and subsequently kill the tumor cells, when targeted radionuclide therapy is found appropriate. Addition of a fluorescent dye will provide dual-modality imaging probes for pre-operative surgical planning and intraoperative surgical guidance, whereas conjugation of a potent antineoplastic drugs will yield small-molecule drug conjugates (SMDC) for targeted chemotherapy. Preclinical evaluation of our theranostics will enable identification of lead candidates that could potentially be translated to the clinic.

Requirements of candidate:

We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.
- Scholarship that will, at least, cover subsistence allowance and international air plane ticket (your future supervisor could help with the scientific part of your scholarship proposal)
- Master degree or MD degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF SURGERY

Project:	**Exploring the regenerative potential of organoids in liver disease and transplantation**
Supervisor information:	**Prof. dr. Luc van der Laan** l.vanderlaan@erasmusmc.nl **Selected publications:** - van der Laan LJW, Bosker T, and Peijnenburg WJG. Deciphering potential implications of dietary microplastics for human health Nat Rev Gastro Hep 2023 - van Tienderen G et al. Hepatobiliary tumor organoids for personalized medicine: a multicenter view on establishment, limitations and future directions. Cancer Cell. 2022 40 (3): 226-230 - Roos FJM, Verstegen MMA, van der Laan LJW. Human branching cholangiocyte organoids recapitulate functional bile duct formation. Cell Stem Cell. 2022 May 5;29(5):776-794 - Marsee A, Roos FJM, Spee B/van der Laan LJW. Building consensus on definition and nomenclature of hepatic, pancreatic, and biliary organoids. Cell Stem Cell 2021, 28(5):816-832 - Willemse, van der Laan & Verstegen, et al. Fast, robust and effective decellularization of whole human livers using mild detergents and pressure controlled perfusion. Mater Sci Eng C Mater Biol Appl. 2020 Mar:108:110200 - Broutier ,Verstegen, van der Laan & Huch, et al. Human primary liver cancer-derived organoid cultures for disease modeling and drug screening. Nat Med 2017 Dec;23(12):1424-1435. - Blokzijl, Verstegen, van der Laan & van Boxtel et al. Tissue-specific mutation accumulation in human adult stem cells during life. Nature. 2016 Oct 13;538(7624):260-264.
Abstract:	*Although the adult liver is well-known for its regenerative capacity, the cellular events that drive this repair are pleiotropic and not fully elucidated. The two liver epithelial cell types, hepatocytes and cholangiocytes, have self-renewal capacity to maintain homeostasis and in response to liver injury. Moreover to the plasticity of epithelial cells, bipotent progenitor cells are found within the canals of Hering, the smallest branches of the biliary tree in the liver. These bipotent progenitor cells can differentiate into both mature hepatocytes and cholangiocytes. In larger bile ducts, including in the extrahepatic bile ducts, typical peribiliary glands harbor biliary progenitor cells which provide a proliferative response upon damage of the bile duct providing new cholangiocytes to restore the biliary lining. With the development of the 3D organoid culture technique, epithelial cells, including those found in the liver can be expanded in vitro (Huch et al, Cell, 2015) and used as model for stem cell biology and liver diseases such as Metabolic Associated Fatty Liver Disease (MAFDL) or primary liver cancer.* *The projects in our lab involve the use of biliary organoids to model liver-related disease (MAFLD, Allagile Syndrome, Cystic Fibrosis), study liver and bile duct regeneration (by developing liver-on-a-chip technology), and liver and bile duct tissue engineering (decellulairsation techniques and extracellular matrix analysis). During* ***liver transplantation*** *performed in Erasmus MC, biopsies are collected from liver and extrahepatic bile duct from donor and recipient (explanted liver) to be used in research projects. These biopsies are analyzed using histological techniques (immunohistochemistry, immunofluorescence, conventional, confocal and light-sheet microscopy) and molecular biological techniques (qPCR, RNA-expression arrays and whole genome sequencing). In addition, the LGR5-positive, Wnt-responsive adult stem cells from liver and the extrahepatic bile duct, will be cultured and expanded as organoids to be used as (patient-specific) models for liver regeneration and/or disease, including primary liver cancer.* ***Main methodology and techniques****: 3D biliary organoid cultures from healthy donor and patient biopsies (NASH, primary liver cancer). Gene expression analysis (single cell RNA sequencing, RT-qPCR), high resolution imaging (OIC-confocal, fluorescence microscopy), protein expression analysis (FACS, Immunohistochemistry, Western blotting).*
Requirements of candidate:	• We are looking for a highly motivated PhD student who has received excellent scientific and practical training in the areas of stem cell biology, transplantation medicine and/or regenerative medicine to join our research team. • The student should be fluent in English (IELTS *min 6.0)*, TOEFL 100 *(min 20 for all subs).* • Master degree or MD degree

DEPARTMENT OF SURGERY

Project : Determining the effects of aging on biliary regeneration

Supervisor information:

dr Iris de Jong,
Email: i.dejong@erasmusmc.nl,

Prof dr Luc van der Laan
l.vanderlaan@erasmusmc.nl

Prof dr Robert Porte
r.j.porte@erasmusmc.nl

Most important publications:

1. Hepatology 2022;75:814-830, de Jong & Porte et al. 10.1002/hep.32166
2. Hepatology 2019;69:1719-1734, de Jong & Porte et al. 10.1002/hep.30365
3. J Hepatol 2023;79:1396-140, de Jong & Porte et al. 10.1016/j.jhep.2023.08.010
4. Nat Commun 2023;14:7880, de Jong & Porte et al. 10.1038/s41467-023-43368-y
5. Transplantation 2023;107:e161-e172, de Jong & Porte et al. 10.1097/TP.0000000000004531

Abstract:

Bile duct complications after a liver transplantation, such as nonanastomotic strictures, carry high mortality and morbidity rates as they are often therapy resistent and may ultemately require a re-transplantation. It has been demonstrated that impairment of large bile duct regeneration after liver transplantation contributes to the development of bile duct complications. Biliary epithelia are severely damaged after ischemia, which is aggrevated after subsequent reperfusion; so-called ischemia-reperfusion injury. If wound healing of the ducts fails, pathological scarring occurs which translates to symptomatic stricturing of the large bile ducts.

Many variables determine the biliary regenerative potential after ischemia-reperfusion injury, including the extent of initial damage (determined by warm and cold ischemia times and donor variables), and more specifically: damage to the peribiliary glands and the peribiliary vascular plexus. Peribiliary glands are a reservoir of stem/progenitor cells; stand-by to regenerate the large bile ducts after severe damage. Older donor age is associated with the development of biliary complications. However, it is unknown whether older peribiliary glands are architecturally and genetically in a disadvantage to regenerate lost epithelia, predisposing the recipient to the development of biliary complications.

To study matrix and cell-related determinants of biliary aging, fresh and archival human extrahepatic bile duct samples (from the explanted liver) are available as well as decellularized scaffolds and patient-derived biliary organoids.

***Frequently used techniques in our lab are**: Gene expression analyses (single cell RNA sequencing, RT-qPCR), protein expression analyses (FACS, ELISA, immunohistochemistry/immunofluorescence, Western blotting), high resolution imaging (OIC-confocal, fluorescence microscopy), and extracellular matrix analyses (SILAC).*

Requirements of candidate:

- We are looking for a highly motivated PhD student who has received excellent scientific and practical training in the areas of stem cell biology, transplantation medicine and/or regenerative medicine to join our research team.
- Master degree or MD degree
- The student should be fluent in English (IELTS *min 6.0)*, TOEFL 100 *(min 20 for all subs).*

DEPARTMENT OF SURGERY

Project:	**The impact of euthanatica on the outcome after transplantation of livers donated after euthanasia**
Supervisor information:	**Dr. Wojciech Polak** w.polak@erasmusmc.nl **Dr. Monique Verstegen** m.verstegen@erasmusmc.nl **Prof. Dr. Robert J. Porte** r.j.porte@erasmusmc.nl ***Selected publications:*** 1. Broere R, Luijmes SH, de Jonge J, ***Porte RJ***. Graft repair during machine perfusion: a current overview of strategies. Curr Opin Organ Transplant. 2024. 2. Thorne AM, ….***Porte RJ***, de Meijer VE. Bile proteome reveals biliary regeneration during normothermic preservation of human donor livers. Nature Commun. 2023;14:7880. ***3.*** ***Porte RJ***. Improved organ recovery after oxygen deprivation. Nature 2022;608:273-274. 4. van Rijn R… ***Porte RJ***; Hypothermic Machine Perfusion in Liver Transplantation - A Randomized Trial. N Engl J Med 2021;384:1391. 5. van Reeven M,...***Polak WG***. Evaluation of Liver Graft Donation After Euthanasia. JAMA Surg 2020;155:917-924. 6. Willemse J, ….. ***Verstegen MMA***. Design by Nature: Emerging Applications of Native Liver Extracellular Matrix for Cholangiocyte Organoid-Based Regenerative Medicine. Bioengineering. 2022;9(3):110 7. Shi S, ***Verstegen MMA*** et al. Recapitulating Cholangiopathy-Associated Necroptotic Cell Death In Vitro Using Human Cholangiocyte Organoids, Cell Mol Gastroenterol Hepatol. 2022;13(2):541-564
Abstract:	*Only a few countries have accepted euthanasia as an alternative for individuals suffering unbearably from physical or mental illness. The Netherlands was the first country to legalize euthanasia and since 2012 it has allowed to procure organs from donors after euthanasia. Similar to the more commonly performed donation after circulatory death type III (DCD-III) liver transplantation, organs donated after euthanasia face a period of donor warm ischemia (dWIT) that triggers the occurrence of post-transplant complications such as primary non-function, early allograft dysfunction or ischemic cholangiopathy, worsening long-term outcomes. According to the modified Maastricht criteria, organs donated after euthanasia are considered the fifth subtype of donation after circulatory death (DCD-V).* *A recent study showed that despite shorter donor warm ischemia times in DCD-V compared to the standard DCD type III, the outcome of liver transplantation was similar in both groups. However, a recent observation from the Dutch liver transplant centers brought a caution for the use of DCD-V liver grafts due to the unexpectedly high incidence of primary non-function (PNF) and biliary complications. Therefore, as of 2024 it was nationwide decided that all DCD-V livers need to undergo viability assessment either using ex-situ normothermic machine perfusion or normothermic regional perfusion in the donor, before considering the graft for transplantation.* *One of possible explanations for the higher PNF rate and biliary complications after DCD-V liver transplantation is the toxic effect of the euthanatica on the function and viability of hepatocytes and cholangiocytes. Of note, in Belgium the use of donor organs after euthanasia is not related to high PNF rates and shows less biliary complications. This might be related to the differences in euthanasia procedures between these countries.* *In the Netherlands, thiopental sodium or propofol are mostly used to induce coma, after which a high dosage of rocuronium bromide is given as a neuromuscular blocker, which causes hypoxia leading to circulatory arrest. Especially the latter medication, rocuronium bromide, is metabolized by the liver and excreted by the kidneys. We hypothesise that this high dosage, in combination with dWIT, is toxic to the donor organs, which could explain the inferior outcomes of DCD-V liver transplantation. However, in Belgium, atracurium is mostly used as a neuromuscular blocker for euthanasia, which is not metabolized by the liver and kidneys but metabolized through a non-enzymatic Hoffman elimination.* *This project will focus on assessing the impact of euthanatica on the function of hepatocytes and cholangiocytes. As all DCD-V liver will undergo either normothermic regional perfusion in the donor or ex-vivo normothermic perfusion, perfusate samples will be taken at the different stages of perfusion to assess if and how much of the euthanatica is still present in perfusate.To model this and study how different euthanatica affect hepatocytes and cholangiocytes, liver-derived and extrahepatic bile duct-derived organoids will be cultured and analysed for cell viability, cell proliferation and affected cellular pathways.* ***Main methodology and techniques****:* *The research will consist of (retrospective) clinical research, as well as laboratory research using organoid culture systems.*
Requirements of candidate:	• We are looking for a highly motivated PhD student who has received excellent scientific and practical training in the areas of transplantation medicine and/or regenerative medicine to join our research team. • Master degree or MD degree • The student should be fluent in English (IELTS *min 7.0)*, TOEFL 100 *(min 20 for all subs)* and have good communicative skills both in speech and in writing.

DEPARTMENT OF SURGERY AND DEPARTMENT OF INTERNAL MEDICINE-NEPHROLOGY

Project: Enhancing Transplant Organ Compatibility: Modulating Immunogenicity for Improved Graft Acceptance

Supervisor information:

Dr MJ. Hoogduijn, in collaboration with Dr S. Heidt and Prof dr L. van der Laan
Email: m.hoogduijn@erasmusmc.nl
Website:
https://loop.frontiersin.org/people/29382/overview
https://www.rotterdamtransplantationlab.nl/
Grants:
European FP7, Dutch Kidney Foundation, Dutch Scientific Organization, industry, and others
Supervision of PhD students:
10 completed PhD trajectories, 9 current PhD students
Five important recent publications:
Transpl Int. 2024 Apr 18;37:12468. Interactions of the Immune System with Human Kidney Organoids. https://pubmed.ncbi.nlm.nih.gov/38699175/
Cell Discov. 2023 Apr 3;9(1):34. Mpox virus infects and injures human kidney organoids, but responding to antiviral treatment. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10070611/
JCI Insight. 2023 Nov 8;8(21):e172681. Virus-specific TRM cells of both donor and recipient origin reside in human kidney transplants. https://pubmed.ncbi.nlm.nih.gov/37751288/
Sci Rep. 2022 Nov 30;12(1):20699. Creating a kidney organoid-vasculature interaction model using a novel organ-on-chip system. https://pubmed.ncbi.nlm.nih.gov/36450835/
Kidney Int. 2021 Jan;99(1):134-147. Human kidney organoids produce functional renin. https://pubmed.ncbi.nlm.nih.gov/32918942/

Abstract:

Organ transplantation is a life-saving treatment for end-stage organ failure patients. However, transplant patients require life-long immunosuppressive therapy to prevent rejection of their transplant organ. These immunosuppressive drugs have a range of serious side effects. There is therefore a need for alternative solutions for these patients. In recent years, breakthroughs in our understanding of developmental processes have allowed researchers to create stem cell-derived mini-organs, known as organoids. Organoids form an excellent human model to study transplant organ rejection. In the future, organoids may find application as a tool for regenerative medicine.

Our laboratories have gained expertise in generating kidney and liver organoids derived from stem cells (Figure 1). Kidney and liver organoids express the major antigens for allo-immune responses: Human Leukocyte Antigen (HLA) and ABO blood group antigens. In this project we aim to generate low immunogenic kidney and liver organoids by knocking out HLA by CRISPR/Cas9 editing and by removing ABO blood group antigens by enzyme clearing. We will subsequently examine the immunogenicity of kidney and liver organoids upon exposure to human immune cells through in vitro immune assays. The project will involve diverse techniques including organoid culture, gene editing, enzyme assays, flow cytometry and histology. The PhD student will be guided in publishing a number of manuscripts.

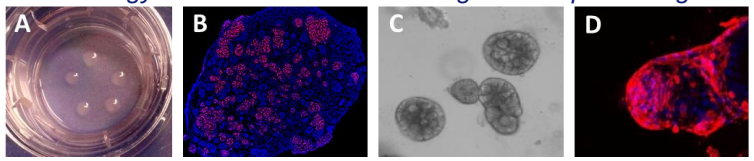
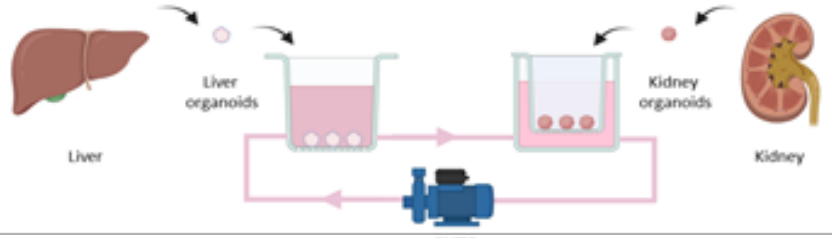


Figure 1. *A) Kidney organoids in a culture well. B) Section of a kidney organoid stained for the nephron marker WT1. C) Liver organoids. D) Albumin staining in liver organoid.*

Requirements of candidate:

- We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills.
- Master degree or MD degree
- English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

DEPARTMENT OF SURGERY AND DEPARTMENT OF INTERNAL MEDICINE-NEPHROLOGY

Project :	**Investigating the causes of acute kidney injury following liver transplantation using mini-organs**
Supervisor information:	**Prof dr L. van der Laan, Dr MJ. Hoogduijn** **Email:** l.vanderlaan@erasmusmc.nl m.hoogduijn@erasmusmc.nl **Grants:** European FP7, Dutch Kidney Foundation, Dutch Scientific Organization, industry, and others **Supervision of PhD students:** 25 completed PhD trajectories, 12 current PhD students ***Five important recent publications:*** - Sci. Transl. Med. 2024 Jan 16; 728. The extracellular matrix as hallmark of cancer and metastasis: From biomechanics to therapeutic targets. https://pubmed.ncbi.nlm.nih.gov/38170791/ - Cell Discov. 2023 Apr 3;9(1):34. Mpox virus infects and injures human kidney organoids, but responding to antiviral treatment. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10070611/ - Cell Stem Cell 2022 May 29;5:776-794. Human branching cholangiocyte organoids recapitulate functional bile duct formation. https://pubmed.ncbi.nlm.nih.gov/35523140/ - Sci Rep. 2022 Nov 30;12(1):20699. Creating a kidney organoid-vasculature interaction model using a novel organ-on-chip system. https://pubmed.ncbi.nlm.nih.gov/36450835/ - Kidney Int. 2021 Jan 99(1):134-147. Human kidney organoids produce functional renin. https://pubmed.ncbi.nlm.nih.gov/32918942/
Abstract:	*Liver transplantation is a life-saving treatment for end-stage liver disease patients. However, for unknown reasons half of liver transplant recipients experience acute kidney injury after the liver transplantation procedure, which leads to chronic kidney and heart disease, and even mortality. It is hypothesized that factors released from the transplant liver induce kidney injury. Identification of the factors that trigger acute kidney injury in liver transplant patients is challenging because liver transplantation affects multiple physiological systems in the body, which obscures the factors specifically impacting the kidneys. In recent years, breakthroughs in the understanding of developmental processes have allowed researchers to create* ***stem cell-derived mini-organs****, known as organoids, including liver and kidney organoids. These organoids form an excellent human model to study (transplant) organ injury. Recently, our laboratories have established a* ***liver-kidney organ-on-chip model*** *that simulates the micro-physiological environment of the human body and allows interaction between both organ compartments (Figure 1).* *In this project we will investigate the interaction between liver and kidney in* ***a novel model of liver transplantation-induced kidney injury in human organoids****. We will apply transplantation-related injury to the liver organoids in the form of hypoxia (1% O2) and inflammatory cytokines and examine whether injured liver organoids trigger events in kidney organoids that resemble acute kidney injury, we will determine cellular toxicity and morphological and functional changes in kidney organoids. Next, we will identify the factors released by liver organoids that are responsible for inducing kidney injury using stable isotope labeling with amino acids in cell culture (SILAC) and other assays. This research will lead to new avenues to treat this life-threatening complication.* ***Techniques*** *include organoid culture, organ-on-chip, immunohistochemistry confocal microscopy and flow cytometry. The PhD student will be guided in publishing a number of research articles.*  ***Figure 1. Schematic overview of the liver kidney multi-organ-on chip model. Liver and kidney organoids are placed in culture dishes that are connected through a fluidic system. Fluid flow is driven by a pump system.***
Requirements of candidate:	• We are looking for a highly motivated, hardworking student to join our very international team. Our strength is in using team work to tackle large scientific questions and thus requires a student with good communication skills. • Master degree or MD degree • English language requirement: IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 20 for all subs)*

選擇 ERASMUS MC 的理由

不用客氣：我們希望以您的博士生和未來的同事向您致意。我們希望您會感到賓至如歸，並在您職業生涯的任何後續步驟中與我們合作。

您職業生涯的下一步：在Erasmus MC獲得博士學位意味著您擁有4篇經過同行評審的國際研究發表，擁有研究發表對於您職業的下一步至關重要。在大多數大學中，他們只需要一份或更少的研究發表，因此來自Erasmus MC 意味著巨大的優勢（有關2019年最後10名外國博士畢業生的成就，請參閱第3頁)。

您的培訓和教育：我們擁有約1,500名科研人員，為少於1,250名博士生提供服務，並為約1,000名居民提供了約750名醫學專家，我們的監督率極高。更重要的是，博士生至少在Erasmus MC擁有2名導師，而且通常也可以聘請台灣導師，因為我們更願意以可以繼續在台灣進行研究的方式來培訓您。

無需學習荷蘭語：無需學習荷蘭語-荷蘭在過去兩年中英語水平排名第一，在過去十年中排名前三，鹿特丹在荷蘭城市中排名第一。因此，您無需講荷蘭語即可去雜貨店。

Taiwanese co-publications: domains of
PRECLINICAL, CLINICAL & HEALTH SCIENCES 2014-2023
Incites Clarivate dbase as of Oct, 17th, 2024

University or Med School*	normalized impact	co-publ
Erasmus MC*	18.89	407
UMC Utrecht*	17.99	171
Karolinska Institutet*	16.84	554
University of Cambridge	15.69	340
UCL Med School, UK*	15.60	141
U Penn Med School*	12.60	451
Harvard Med School*	10.04	1648
Johns Hopkins Med School*	9.05	769
Stanford University	7.95	1113
Natl Univ of Singapore	7.16	1496

你的社交生活：我們超過30%的博士生是外國人，我們在 Erasmus MC 和 Erasmus University Rotterdam 以及國際辦事處都有活躍的博士生組織。居住在歐洲最大的港口城市，在《孤獨星球》（Lonely Planet）2016年的城市排名中排名第5，這意味著您在阿姆斯特丹或安特衛普（乘汽車），布魯塞爾（乘火車），倫敦（乘飛機）或在柏林坐飛機1.5個小時，在巴黎坐火車2個小時。

我們的組織：Erasmus MC 是歐洲十大醫學院之一，也是歐盟委員會資助的臨床前、臨床和健康科學出版物的十大機構之一。我們與台灣同行的科學合作非常好，與其他外國大學相比，我們在台灣的合作質量（按平均引用/出版物表示，見右表）非常高，這在進行研究時是一個優勢合作回到台灣。此外，我們在各個臨床領域（見下表）排名世界第5-74 位，在生物醫學科學領域排名世界第 6-51 位 (Nature Index).

我們訓練台灣的年輕科學家希望他們能成為我們台灣下一代合作者。我們希望您能加入 Erasmus MC，並成為我們未來在荷蘭和您回到台灣後的同事，因為學位獲得後我們的聯繫不會停止。***重要的***, Erasmus MC 被列為久負盛名的主辦機構台灣科技部龍門計劃 因此，一旦您返回就可以發起合作。

Nature Index Ranking	World Rank
2021 Young Universities - Life Sciences	6
2024 Health Sciences	9
2019 Collaboration Big Science - Genetics	13
2021 Infectious Diseases	20
2023 Biological Sciences	29
2020 Cancer	51

在美國新聞網站上，鹿特丹伊拉斯姆斯大學醫學中心在指定的學科排名中被列為前幾名。

US News Ranking 2024	World Rank
Surgery	5
Microbiology	20
Infectious Diseases	25
Gastroenterology & Hepatology	28
Immunology	30
Neuroscience & Behavior	33
Radiology, Nucl Med, Med Imaging	36
Oncology	43
Clinical Medicine	46
Social Sciences & Public Health	49
Endocrinology & Metabolism	51
Cardiac & Cardiovascular Systems	58
Public, Env & Occup Health	64
Molecular Biology & Genetics	66
Psychiatry & Psychology	68
Pharmacology & Toxicology	74