Amsterdam UMC

Genetic innovation in motion

Collaborating for the future of healthcare, patients and society

Annual Report 2024 Department of Human Genetics Amsterdam UMC

Preface

Welcome

Welcome to the annual report 2024 of our department of Human Genetics.

June 2024 Prof. Marcel Mannens left us to finally enjoy his retirement, and I took over the position as head of department. These are big shoes to fill, not only because Marcel left a department that was blooming, but also because it will be difficult to match his wisdom and leadership. For all the work Marcel has done during his career in leading the diagnostic laboratory and the department, but also because of his scientific contributions, he was awarded a high royal honor, knight in the order of the Dutch Lion. This was of course an event that we celebrated with the entire department. »

Celebration

But there was more to celebrate, as you can read in this report. Just to show you the tip of the iceberg, members of our department received several important grants, including a Vidi for Dr. Amélie Fréal and an Amsterdam UMC Fellowship for Dr. Danai Riga, both from the section of Functional Genomics. Prof. Arthur Bergen was a leading member of the Lifelong VISION consortium that obtained a large NWO Gravitation grant, whereas Dr. Dimitra Micha received funding to further establish the CURGENE project to develop therapy for osteogenesis imperfecta. Other highlights were the formation of a new research section for Epigenetics, lead by Dr. Peter Henneman and the start of several projects supported by the national sector funds in collaboration with Emma Center for Personalized Medicine, which resulted in a much welcomed comeback of Dr. Daniël Warmerdam.

New professors, a President elect, a new laboratory head & a new clinic

In 2024 Dr. Wiep Scheper was appointed as full professor of Proteostatic Stress and Neurodegeneration, and Dr. Henne Holstege started a collaboration with the VIB-KU Leuven Center for Brain & Disease Research where she shares her job in our department with a position as PI and Professor. During the 2024 annual meeting Prof. Martina Cornel was chosen as President elect of the ESHG, an important position that she very much deserved after decennia of groundbreaking work in the field of Community Genetics and Public Health Genomics. Dr. Mariëlle van Gijn became head of the section of Genome Analysis, which includes DNA diagnostics, the NIPT laboratory and the Core Facility Genomics. She made a successful start by leading her team through the final stages of the reorganisation process that was necessary to move all five diagnostics laboratories to a single »

Marcel Mannens with mayor Hein van der Loo (Almere)

laboratory in 2025. Finally, Dr. Rob Wolthuis joined Prof. Mieke van Haelst to start a CRISPR clinic, with the goal to inform patients of current and future possibilities of gene therapy. This is not only important for patients, but also highlights the strength of having both clinical and research sections in the same department.

Collaboration & improvement

This collaboration between all sections to face future challenges is key. Whereas the field of Clinical Genetics has mainly evolved around improving clinical and laboratory diagnostics and understanding genetic disorders, this is now rapidly changing. On one side, our field will move towards screening and prevention, for instance by introducing genetic methods into neonatal screening. On the other side, due to major improvements in gene editing techniques, we will be more and more involved in treating and even curing patients, something we could hardly think of until a few years ago.

Prof. Arthur Bergen

Prof. Arthur Bergen was a frontrunner when it came to curing genetic diseases. He was the leader of our section of Ophthalmogenetics, and he was one of the first geneticists who moved from finding new genes for genetic diseases, in his case genetic eye diseases, towards actually curing them. For his groundbreaking work he received the Snellen Penning in 2023, the most prestigious award in the field of eye diseases in the Netherlands. September 2024 we received the devastating news that Arthur had suddenly passed away. This was a big loss, not only for our department, but also for the large number of national and international collaborators who worked with him, not to speak of his family. Supported by the board of directors of Amsterdam UMC and the board of division 9 it was decided that we will continue Arthur's work, and make sure that his legacy will be safeguarded. As a first step, we renamed our scientific award into the "Arthur Bergen award". This award is given twice a year during our Science day for the best poster and the best oral presentation. The first Arthur Bergen award was won by one of Arthur's PhD students, Isa van der Veen. It's a great comfort to know that she and other young scientists will continue his work. To quote Arthur, "the show must go on!" •

Prof. Arthur Bergen

Erik Sistermans
Head Department of Human Genetics

Excellent patient care

Successful clinical genetics training

At the Clinical Genetics section, headed by Prof. Mieke van Haelst, we offer an excellent training program for residents in clinical genetics. In 2024 four of our residents, who successfully finished their training, were welcomed to join the clinical genetics team. Dr. Fenne Komdeur and Dr. Marjoleine Broekema in cancer genetics, Dr. Lotte Kleinendorst in dysmorphology and developmental disorders and Dr. Philip Jansen in neurogenetics and developmental disorders. Lotte and Philip combine their clinical work with their assistant professor positions at Emma Center for Personalised Medicine (Emma Center).

Future Fellowship in Genetic Therapy

Clinical geneticist in training Dr. Eva van Walree joined the Emma Center for Personalised Medicine (Emma CPM) in September 2024. She is pioneering a future fellowship in genetic therapy. Such a future fellowship is new in the Netherlands and reflects developments in the field: today's clinical geneticists are increasingly involved in treatment and therapeutic patient care. Eva works at the intersection of clinical genetics and paediatrics, focusing on accelerating diagnostics and treatments for children with rare conditions. In close collaboration with laboratory specialists, paediatricians and others, she is involved in a project that integrates suggestions for existing therapy referrals to the right expert clinicians to discuss personalized treatment options. The DNA test »

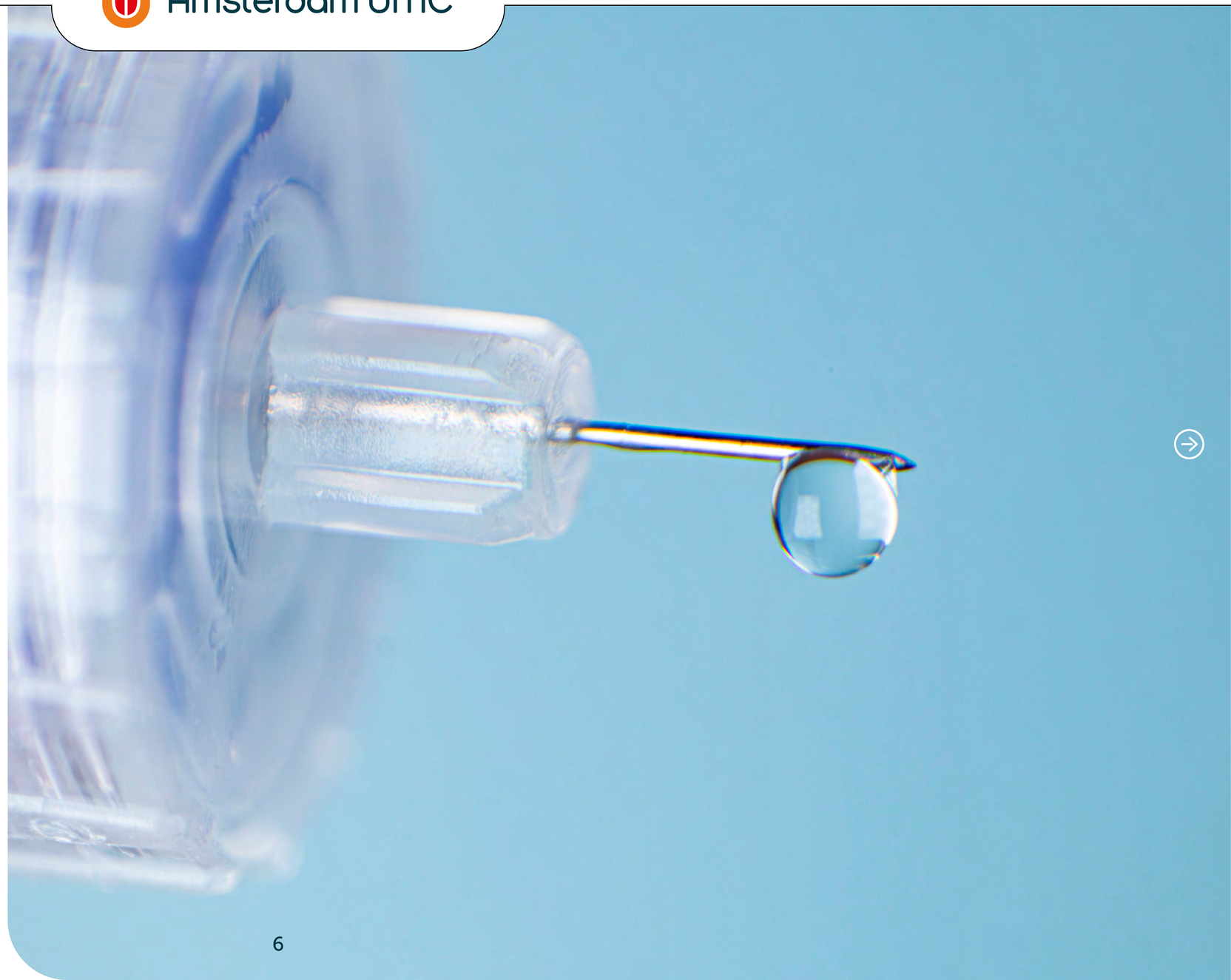
Fellow in genetic therapy Eva van Walree

result letter, issued by the Genome Laboratory Amsterdam UMC, helps this initiative, and minimises the delay of treatment.

At present, some children with metabolic diseases are receiving experimental treatment in the form of supplements or medications that have already been approved for other conditions (repurposing).

High-quality patient care

At our outpatient clinic and in many Centers of Expertise for Rare Diseases, we have continued to provide excellent patient care, which was highly appreciated by our patients (results patient evaluation). We also organized several well-attended clinical evenings, contributing to knowledge sharing and professional development in our field. •



Restructuring (a process)

Restructuring of the Laboratory for Genome Analysis

The - because of the AMC and VUmc merger - planned restructuring of the Laboratory for Genome Analysis (a section of the Human Genetics Department) was approved by Amsterdam UMC's Board of Directors on 1 November 2024. For the reorganisation team of Nadine Spoelder, Prof. Erik Sistermans, Bianca Heijdra, Dr. Elles Boon, Liesbeth Hage and Mischa Hornman, this adventure has been two years in the planning: a group effort during which about 184 employees from all five different locations across Amsterdam UMC were regularly updated and invited to provide input.

Ups and downs

Restructuring is a process with ups and downs and often fraught with uncertainty, but we are in the fortunate position that everybody affected will be able to keep their job. The section now is preparing for its next major milestone: relocating to one place, the Research & Diagnostics Center ADORE building in April 2025 (at location VU University Medical Center). With a streamlined structure and a brand-new location, we will be in great shape to deliver an innovative future! •

more information

Up to 2024

From the beginnings of the Epigenetics research group...

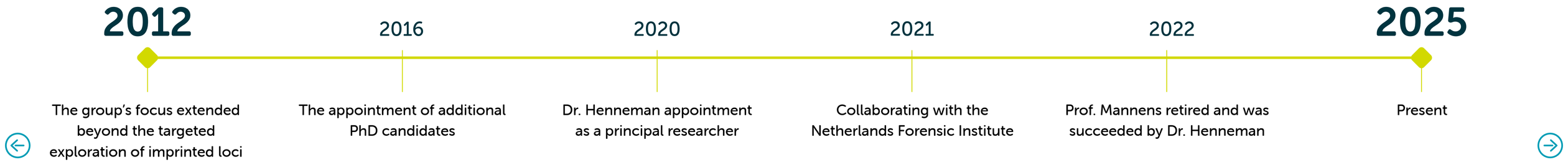
The Epigenetics research group was formally granted the status of a section within the Human Genetics Department. It can trace its proud history back to 2012 and its foundation as the Epigenetics of Disease research group under Prof. Marcel Mannens.

...towards a separate section in 2024

From its inception in 2012, Dr. Peter Henneman handled the day-to-day running of the Epigenetics group. Over the next five years, several PhD researchers joined on a collaborative basis, primarily focusing on epigenetic analyses related to trauma, Crohn's disease, and cardiovascular risk factors in Ghanaian migrants and non-migrants (RODAM study). From 2016 onward, a number of grants were awarded, some to Peter personally, leading to the appointment of additional PhD candidates and more intensive collaborative research on the above topics. Around 2020, episignature detection for rare Mendelian disorders was also implemented by the Epigenetics of Disease group, using state-of-the-art machine-learning algorithms, a strategy that was initially reported by Dr. Bekim Sadikovic of the London Health Sciences Centre (LHSC), Canada. Since machine learning inherently relies on large sample sizes, a long-term collaboration was established between Amsterdam UMC and LHSC. As a result, Amsterdam UMC's Human Genetics Genome Diagnostics has »

The Epigenetics team - Luke Carroll (PhD candidate) & Manasa Kayla Purushothama (postdoc) joined the team later in 2024

Proud history of the Human Genetics department



become the leading European provider of EpiSign diagnostic tests to date. These achievements led to Peter's appointment as a principal researcher in 2020 and associate professor in early 2023.

Epigenetics section to date

In 2022, Prof. Mannens retired and was succeeded by Dr. Henneman as head of the Epigenetics of Disease research group. Two years later, the group became an independent junior section within the Human Genetics Department at Amsterdam UMC. The section is working on the RODAM study, Crohn's disease, atherosclerosis and rare Mendelian disorders. In this context, the section participates in major EU projects (e.g. ERC, HORIZON, Marie Curie ITN) and is internally affiliated with the Emma Center for Personalized Medicine. One of its most notable projects involves a clinical trial that focuses on predicting the therapeutic response to monoclonal antibodies for Crohn's disease

Moving to a new location

In December 2024, the section was one of the first groups to move from location AMC to the brand-new Research & Diagnostics Center ADORE (at location VU University Medical Center). This state-of-the-art environment and the section's newly launched website (epigenetica.nu) are expected to boost group morale, enhance our already robust scientific output and further expand internal and external collaborations. •

more information

A new academic chair

Dr. Wiep Scheper appointed professor of Proteostatic Stress and Neurodegeneration

Dr. Wiep Scheper of the section Functional Genomics, Department of Human Genetics, is internationally renowned for her studies on the role of proteostatic stress mechanisms in the pathogenesis of neurodegenerative diseases. In further recognition of her work, she has been awarded a full professorship per 1 June 2024.

The role of proteostasis in neurodegenerative disorders

Following her training as an RNA biologist at Utrecht University, Dr. Scheper began work on the export of misfolded proteins from the endoplasmic reticulum during her time at Cambridge University, UK, and went on to develop a strong research programme in Amsterdam that examines the role of proteostasis in neurodegenerative disorders such as Alzheimer's disease, frontotemporal dementia and Parkinson's disease. In 2013, Dr. Scheper became a principal researcher at the Functional Genomics Section, building a multidisciplinary team and a prominent international reputation in the field, backed by prestigious publications and strong external funding. Dr. Scheper has also become a familiar face in the Dutch media, thanks to her outreach activities, fundraisers and talks aimed at a wider audience.

An academic chair

The purpose of the new academic chair is to initiate and conduct research to gain new insights and further deepen our understanding of the role that proteostatic stress mechanisms play in the pathogenesis of neurodegenerative diseases. These insights will lead to the identification of new targets for therapeutic intervention and associated biomarkers for therapy monitoring. Additionally, the chair focuses on utilising the results of this research by means of knowledge transfer to the business sector and science communication aimed at the general public. •


Prof. Wiep Scheper

more information

Henne Holstege joins VIB-KU Leuven Center

Genetic mechanisms

Dr. Henne Holstege joins VIB-KU Leuven - Center for Brain & Disease Research as new PI

On 1 November 2024, Dr. Henne Holstege, head of the section Genomics of Neurodegenerative Diseases and Ageing (a section of the Human Genetics Department), was appointed Principal Investigator at the Vlaams Instituut voor Biotechnologie at the Catholic University of Leuven (VIB-KU) Center for Brain & Disease Research. While taking on this new role, she will remain actively involved in Amsterdam UMC, continuing her research on the genetics of neurodegenerative diseases and healthy ageing. »

Understanding the genetic mechanisms

Dr. Holstege has dedicated her career to understanding the genetic mechanisms behind neurodegenerative diseases and cognitive resilience in patients. Her groundbreaking research on centenarians with good cognitive health has provided key insights into the biological factors that protect against age-related cognitive decline, potentially paving the way for new preventive strategies against Alzheimer's and other neurodegenerative diseases.

Hendrikje van Andel-Schipper

Her fascination with healthy ageing was sparked by the exceptional brain of Hendrikje van Andel-Schipper, who passed away at the age of 115, the oldest person ever recorded in the Netherlands. Despite her advanced age, her brain showed characteristics more typical of a 60-year-old. This discovery inspired Dr. Holstege to explore the genetic factors that contribute to healthy cognitive ageing.

Establishing and building

At Amsterdam UMC, she established a research section - Genomics of Neurodegenerative Diseases and Aging - focused on identifying genetic and genomic factors involved in neurodegenerative diseases, including Alzheimer's. She also built one of the world's largest cohorts of cognitively healthy centenarians, providing a valuable resource for studying resilience to dementia.

International collaboration

In her new position at VIB-KU Leuven, Dr. Holstege will further explore the molecular mechanisms of aging while maintaining her collaboration with Amsterdam UMC. By looking at why some individuals remain dementia-free, she aims to identify protective factors and translate these findings into therapies with the potential to benefit a broader population. Her dual affiliation strengthens international collaboration and innovation in the field of neurodegenerative disease research, fostering new insights into ageing and cognitive health. •

more information

Research & screening

50 years Heelprick Program

Fifty years of newborn screening

In 2024, the Netherlands' newborn blood spot screening programme marked its 50th anniversary. This successful public health programme detects serious treatable rare conditions at an early stage, preventing severe morbidity and mortality. In the Netherlands, this test – commonly known as the heel prick test – was initiated in 1974 to screen for the metabolic disorder phenylketonuria, expanding to include 27 conditions by 2024. To celebrate this anniversary, the National Institute for Public Health and the Environment (RIVM) organised a symposium for all stakeholders on 17 October 2024.

Chair at the advisory committee

Prof. Martina Cornel of the Community Genetics and Public Health Genomics section of Amsterdam UMC Human Genetics Department marked the occasion by giving a lecture on the impact of the heel prick test through the decades. Prof. Cornel chairs the screening advisory committee.

ZonMw PANDA study

The Community Genetics section has also actively participated in research on the screening of newborn babies. Prof. Lidewij Henneman, head of the section, led the ZonMw PANDA study (Psychosocial Aspects of Newborn Screening for Disorders Assessed), in close collaboration with TNO, RIVM and several patient organisations. The final paper was published in 2024. The PANDA study generated broad public and professional support for newborn screening and its expansion, citing the potential health benefits for greater numbers of children (van der Pal et al.). »

However, concerns and questions have also been raised, highlighting the need for ongoing engagement with diverse perspectives (van Dijk et al.). The project also examined the psychosocial impact of a false positive or inconclusive newborn blood spot screening result on parents (van den Heuvel et al.).

CRADLE study

In 2024, a new collaboration with RIVM was launched in the shape of the CRADLE study (with PhD researcher Saskia Smits), which looks not only at technical challenges and aspects of implementation, but also at the ethical, legal and societal aspects of genome sequencing in the newborn screening programme. Through our research, we aim to make a valuable contribution to a newborn screening programme that is ready to face the challenges of the future. •

more information

The Community Genetics team

Dedicated to progress

CURGENE: Ex-vivo curative therapy for severe osteogenesis imperfecta

The CURGENE project, partly embedded in the research section Center for Connective Tissue, led by Dr. Dimitra Micha and part of the Human Genetics Department, is designed to bring about significant progress in developing advanced therapeutic medicinal products (ATMPs) for patients with osteogenesis imperfecta (OI). OI is a rare type of skeletal dysplasia that affects thousands of patients worldwide. ATMPs have now entered the clinical setting for several rare disorders but this is not yet the case for OI and hundreds of other skeletal dysplasia's; even clinical trials are completely non-existent at present.

CCT's dedication

CCT, the Centre for Connective Tissue research, is dedicated to addressing this clinical deficit by deploying a range of translational strategies that focus on bone tissue regeneration. In close collaboration with Prof. Vivi Heine's Stem Cell Lab at the Emma Children's Hospital and the section Functional Genomics of our Department of Human Genetics, run by Prof. Matthijs Verhage, CURGENE's efforts have generated a stem cell type that can be edited for gene therapy applications. This induced mesenchymal stem cell has shown positive outcomes in relation to osteogenic properties in bone-specific cell and animal models.

Financial support

The CURGENE project enables the expansion and testing of this stem cell strategy in additional genetic backgrounds and OI-based models, a prerequisite for proving its efficacy. Thanks to the generous financial support of the Care for Quality of Life Foundation and Dioraphte, € 417,000 has been made available to fund CURGENE's trajectory for the next three years. CURGENE is embedded in Amsterdam UMC OI Expert Centre and the Human Genetics Department, and aligned with the personalised medicine development theme that spans both research and clinical sections. •

financial support
€417.000
Care for Quality of Life Foundaiton

more information

CRISPR-Center team

Innovation

CRISPR Center 2024: A Year of Growth and Innovation

The Amsterdam UMC CRISPR Center, managed by Dr. Rodrigo Leite de Oliveira and hosted by the Human Genetics section of Oncogenetics & Oncogenomics, was founded in 2020 to advance CRISPR applications for Amsterdam UMC researchers and clinicians. The Center's initial aims focused on promoting expertise through innovation, outreach and education.

The CRISPR Facility

In 2024, support from our Department of Human Genetics and our funding partners resulted in a crucial addition to the Center: the CRISPR Facility. The CRISPR Facility has enhanced our ability to meet growing demand for CRISPR applications in »

research and clinical settings at Amsterdam UMC, while addressing societal questions surrounding their use. To date, the Facility has supported 30 projects, including 17 lab-based initiatives focused on CRISPR-modified cell lines and functional genetic screenings. We also provided consultancy and support to several research projects and grant applications, helping researchers secure vital funding.

Innovation

Innovation remains at the core of the CRISPR Center. We have expanded our protocol portfolio, developing FACS-based CRISPR screening, optimising adenoviral CRISPR delivery and refining a gene-tagging protocol. To facilitate data visualisation, we are developing a CRISPR screening analysis website. Our team has grown with the recruitment of a PhD researcher, and in 2025 we will be joined by a postdoctoral researcher funded by a TKI-KWF grant (in collaboration with LEXOR and iOnctura). We have also launched a CRISPR-iPSC research programme with the iPSC Center.

Outreach

Our outreach and education activities have raised our profile and strengthened collaborations: we have updated our website, engaged in high school education and shared our expertise with the media. The team has participated in academic mentorship, PhD committees, and supervising and evaluating Master's theses. We also organised national and international CRISPR courses (Cohesinet Marie Curie Doctoral Network, Oncology Graduate School Amsterdam) and represented the CRISPR Center at major conferences, including CRISPR Medicine 2024 (Copenhagen), EACR (Rotterdam), Oncode Institute Conference and Emma CPM Symposium (Amsterdam).

Emma Center for Personalized Medicine

A highlight was our collaboration with the Emma Center for Personalized Medicine. In March, we launched the CRISPR Q&A Clinic, advising nine patients and families on CRISPR-based treatments for genetic conditions.

Relocation

In December 2024, we relocated to the new, state-of-the-art CRISPR labs in the Research & Diagnostics Center ADORE building (at location VU University Medical Center). This major milestone enhances our research environment and fosters stronger collaborations in precision medicine. •

more information

Lifelong Vision

NWO Gravitation grant to combat vision loss

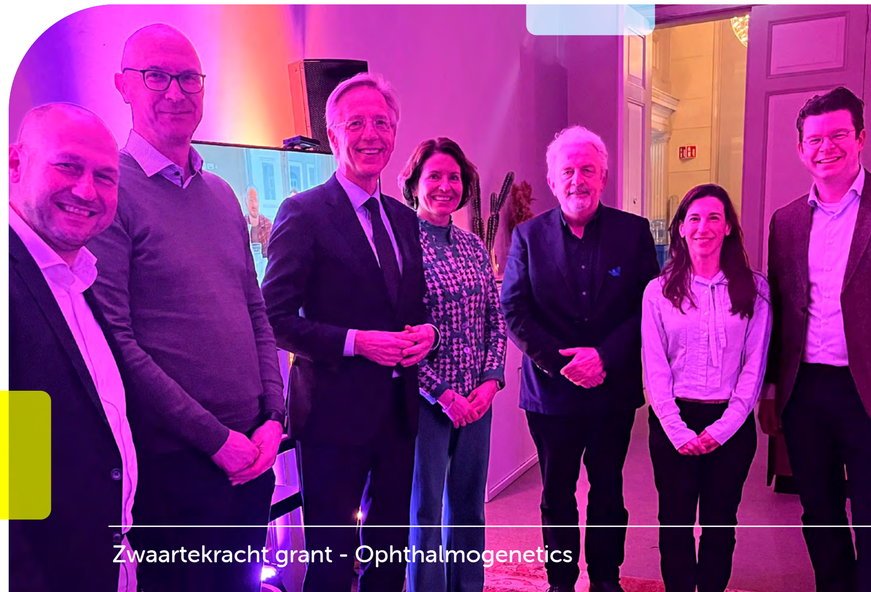
Vision loss is among the top 15 causes of disability. In close collaboration with partners in Amsterdam, Nijmegen, Rotterdam, Eindhoven, Utrecht and Enschede, the Ophthalmogenetics section of our Department of Human Genetics under the leadership of Prof. Arthur Bergen obtained a prestigious NWO Gravitation grant with the aim of combating vision loss.

Lifelong VISION programme

The resulting Lifelong VISION programme is designed to counter inherited retinal dystrophies (IRD) and age-related macular degeneration (AMD) by developing the next generation of treatment strategies. Its focus is on gene therapy, therapy targeting disease mechanisms and cell therapy, testing these approaches using robust model systems of the eye. The programme also deploys advances in artificial intelligence to optimise the match between patients, timing and treatment.

Prof. Bergen

Sadly, Prof. Bergen passed away unexpectedly in September 2024, after the grant had been obtained but before the official launch of the programme. With the help of Prof. Camiel Boon and Prof. Theo Smit and the full support of the Lifelong VISION consortium, Division 9 and Amsterdam UMC's Board of Directors, the decision was taken to build on Arthur's legacy and maintain our role within the consortium. The Ophthalmogenetics section is actively »



Zwaartekracht grant - Ophthalmogenetics

involved in Platform A, where Dr. Céline Koster will be responsible for developing animal models, and in Pillar 3, which deals with developing and validating cell-based therapies replacing lost retinal cells.

Collaboration

Collaboration is key to ensuring the project's success. Lifelong VISION not only incorporates collaboration with national partners, but also with other Departments within Amsterdam UMC, including the Department of Ophthalmology (Prof. Camiel Boon and Dr. Ingeborg Klaassen), Medical Biology (Prof. Theo Smit) and Medical Biochemistry, the Vascular Microenvironment and Integrity lab (Dr. Stephan Huveneers). Working with these amazing teams, we are convinced that we can make significant progress in preventing and curing blindness. •

more information

Humane Genetica
facts & figures

Finance
Human Genetics has realised all her activities in 2024 within available budget and resources.

Research
List of publications:
Human Genetics - Amsterdam UMC

13 Completed promotions in 2024

8

Education
doctors in training for Clinical Geneticist 2024

5

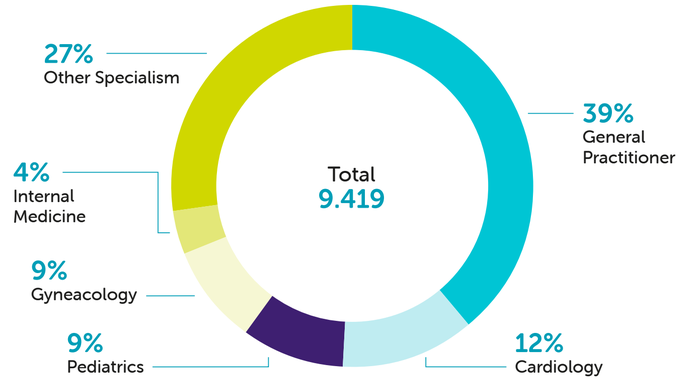
Education
staff in training for laboratorium specialist 2024

361

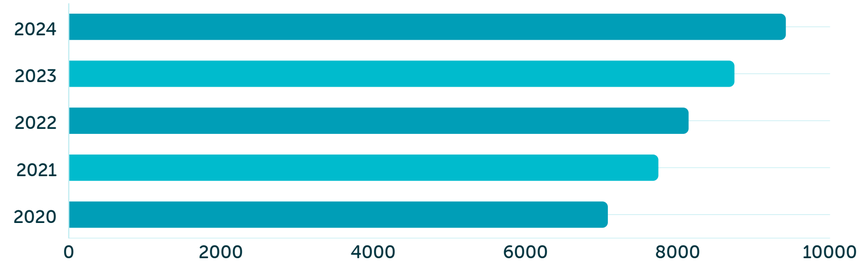
Personel
We have accomplished our goals and successes with the effort of 361 enthusiastic and driven colleagues

Patient Care

Referrers Patient Care 2024



Number of New Patients



Diagnostics

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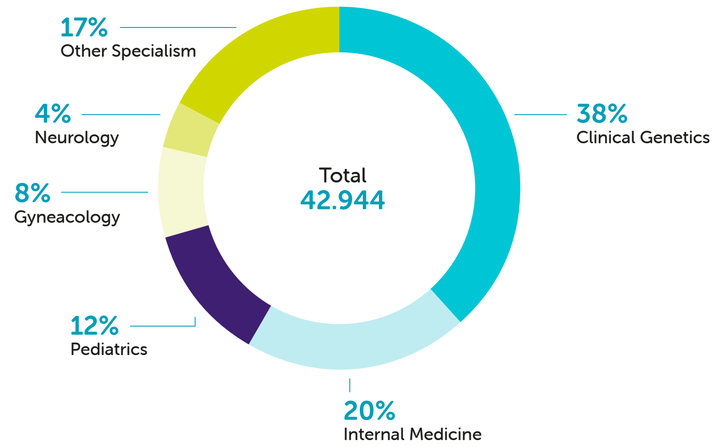
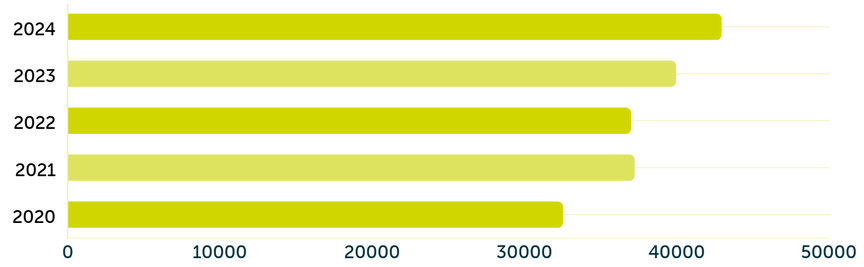
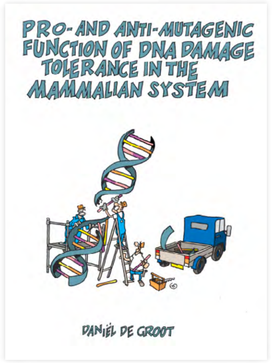


Number of Diagnostic Operations

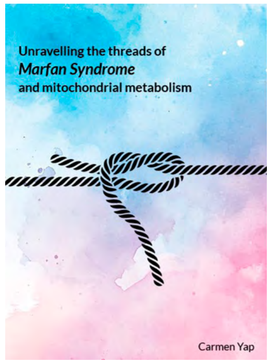


At a Glance
PhD Graduations

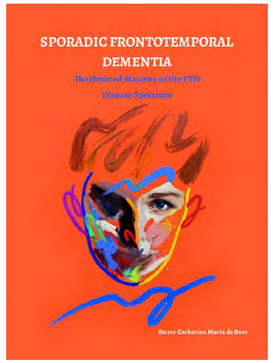
S.J.E. Verdonk



D.C. de Groot



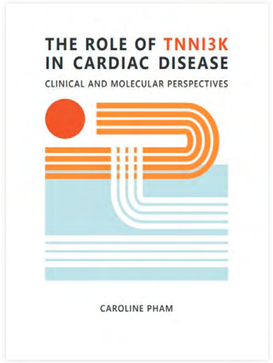
C. Yap



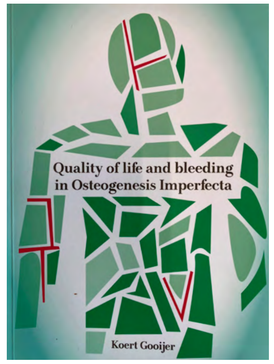
S.C.M. de Boer

L.J.M. Claeys

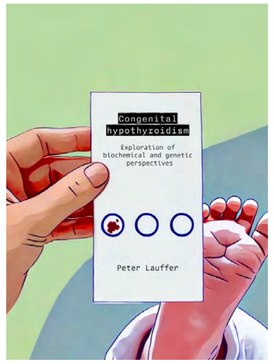
N. Landman



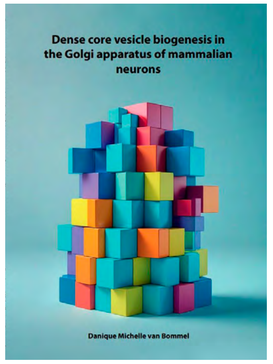
C. Pham



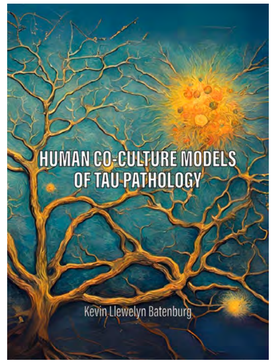
K. Gooijer



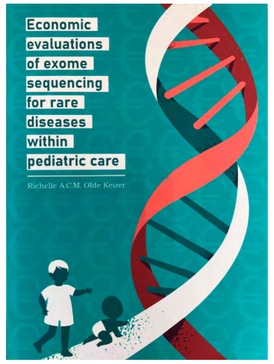
P. Lauffer



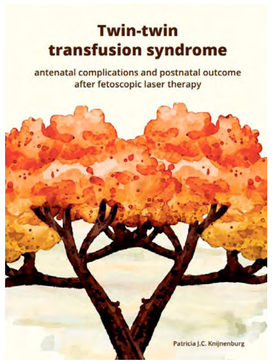
D.M. van Bommel



K. Batenburg



R. Olde Keizer



P.J.C. Knijnenburg

At a Glance 2024

In 2024, the NVHG (Netherlands Society for Human Genetics) marked its 75th anniversary. This was celebrated with a two-day symposium at th Tropen Museum in Amsterdam (September). An anniversary book was published for the occasion, to which Prof. Mieke van Haelst, former NVHG president, contributed

PhD theses

In 2024, 13 PhD candidates from the Department of Human Genetics successfully defended their theses and were awarded Doctor of Philosophy (PhD) degrees from the University of Amsterdam and Vrije Universiteit Amsterdam.

S.J.E. Verdonk

More than bones: Expanding the understanding of rare monogenic variants causing early-onset osteoporosis with emphasis on osteogenesis imperfecta.
Supervisors: Prof. E.M.W. Eekhoff, Prof. J.G. van den Aardweg, co-supervisor: Dr. D.Micha, Dr. L. Zhytnik.

D.C. de Groot

Pro and anti-mutagenic function of DNA damage tolerance in the mammalian system. Supervisor: Prof. H.P.J. te Riele, co-supervisor: Dr. H. Jacobs.

C. Yap

Unravelling the threads of Marfan syndrome and mitochondrial metabolism.
Supervisors: Dr. V. de Waard, Prof. C.J.M. de Vries, co-supervisors: Dr. M. Micha, A. Mieremet.

S.C.M. de Boer

Sporadic frontotemporal dementia: The omitted majority of the FTD disease spectrum.
Supervisors: Prof. Y.A.L. Pijnenburg, co-supervisors: Dr. S.J. van der Lee, Prof. O. Piguet.

L.J.M. Claeys

In Vitro and in Vivo approaches to modelling of Osteogenesis Imperfecta.
Supervisors: Prof. M. Verhage, Dr. N. Bravenboer, co-supervisors: Prof. V.M. Heine, Dr. D. Micha.

N. Landman

Identifying novel therapies against BAP1-deficient mesothelioma.
Supervisor: Prof. M.M.S. van Lohuizen, co-supervisor: Dr. J. Badhai.

C. Pham
The role of TNNI3K in cardiac disease: Clinical and molecular perspectives.
Supervisor: Prof. C.R. Bezzina, co-supervisor: Dr. E.M. Lodder.

K. Gooijer
Quality of life and bleeding in osteogenesis imperfecta.
Supervisor: Prof. M.M.A.M. Mannens, Prof. L. Henneman, co-supervisor: Dr. A.A.M. Franken, Dr. M. Elting.

P. Lauffer
Congenital hypothyroidism; Exploration of biochemical and genetic perspectives.
Supervisors: Prof. A.S.P. van Trotsenburg, Prof. A. Boelen, co-supervisors: Dr. Zwaveling-Soonawala, Dr. P. Henneman.

D.M. van Bommel
Dense core vesicle biogenesis in the Golgi apparatus of mammalian neurons.
Supervisor: Prof. M. Verhage, co-supervisor: Prof. R.F.G. Toonen.

K. Batenburg
Human co-culture models of tau pathology.
Supervisors: Prof. W. Scheper, Prof. M. Verhage, co-supervisor: Prof. V.M. Heine

PhD graduation University of Utrecht
Richelle Olde Keizer
Economic evaluations of exome sequencing for rare diseases within pediatric care.
Supervisor: Prof. H.K. Ploos van Amstel, Prof. L.E.L.M. Vissers, co-supervisors: Prof. L. Henneman, Dr. G. Frederix.

PhD graduation Leiden University
P.J.C. Knijnenburg
Twin-twin transfusion syndrome: antenatal complications and postnatal outcome after fetoscopic laser therapy.
Supervisor: Prof. E. Lopriore, co-supervisors: Dr. J.M.M. van Klink, Dr. F. Slaghekke.

Appointments

Dr. Petra Zwijnenburg was appointed associate professor.

Award Petra Zwijnenburg

Project Funding & Grants

- **Dr. Karuna van der Meij;** 'Using Artificial Intelligence to Support Counseling for Prenatal Screening' Starter Grant Amsterdam UMC, €150k
- **Dr. Karuna van der Meij;** Monitoring Counseling Prenatal Screening, RIVM, €50k
- **Dr. Céline Koster;** Venture challenge NWO - SupraVision: regenerative therapy for blinding retinal diseases, €60K
- **Dr. Céline Koster, Prof. Th. Smit, Anna El Kalaani, A. Lemaistre, S. van Huiden;** Biotech Booster 2024, BIOB24055, Supravision regenerative therapy for blinding retinal diseases, €200K
- **Prof. C. van Karnebeek, Dr D. Warmerdam;** Therapy development for Pyridoxine-Dependent Epilepsy and Gyrate Atrophy, €200K Metakids/Nasosris and €200K from Sector funds
- **Dr. Danai Riga,** Amsterdam UMC fellowship for, €750K
- **P. de Jonge/Prof. d'Haens, Dr. P. Henneman** WP2 leader, Henneman WP5 co-leader, METHYLOMIC - OMICROHN, HORIZON 2022, €400K and 1.0 FTE PhD candidate.
- **Prof. de Winther, Dr. P. Henneman** WP3 leader, MIRACLE, EU Marie-Curie action ITN, 1.0 FTE PhD candidate.
- **Dr. P. Henneman,** Exploring Nanopore sequencing applications in Forensics, NFI internal research budget, €60K.
- **Dr. Dimitra Micha,** Ex vivo CURative therapy for severe osteoGENEsis imperfecta, Stichting Care for Quality of Life (CURGENE), €417K
- **Dr. Lidiia Zhytnik,** Cure for Miniature Brittle Bones: Treatment of Osteogenesis Imperfecta patient-derived Bone organoids with Innovative AAV-mediated Ultimate Gene-editing System, Marie Skłodowska-Curie Actions (MSCA), €226K
- **Dr. Rodrigo Oliveira** 'Stroma Gerichte Therapie voor Fibrotische Tumoren', KWF, €367.725,-
- **Dr. Sven van der Lee & Dr. Alex Salazar,** grant to create and study the performance of a targeted long read sequencing panel. Study will be done in patients with dementia of the DemenTREE biobank

Awards & Prizes

- **Teacher Award,** Dr. Petra Zwijnenburg, for being the most engaged teacher by first year medical students (VU-Amsterdam)
- **High Performance Partner NOC*NSF,** Dr. Saskia van der Crabben received an honorary title: High Performance Partner of NOC*NSF. This is an official recognition for Saskia's work as a cardiogeneticist within the dedicated team of supervisors of our top Olympic athletes (teamNL).

Scientific Publications

Highlighted below are various scientific publications by our researchers from 2024, showcasing the extensive range and significant impact of our collective efforts to advance knowledge for human well-being.

Henneman L. Genetic Carrier Screening - Call for a Global Mission. N Engl J Med. 2024;391:1947-1948. doi: 10.1056/NEJMe2410086.

Cornel MC, van der Meij KRM, van El CG, Rigter T, Henneman L. Genetic screening – Emerging issues. Genes. 2024; 15(5):581. doi.org/10.3390/genes15050581

Kerkhof J, Rastin C, Levy MA, Relator R, McConkey H, Demain L, Dominguez-Garrido E, Kaat LD, Houge SD, DuPont BR, Fee T, Fletcher RS, Gokhale D, Haukanes BI, Henneman P, Hilton S, Hilton BA, Jenkinson S, Lee JA, Louie RJ, Motazacker MM, Rzasa J, Stevenson RE, Plomp A, van der Laan L, van der Smagt J, Walden KK, Banka S, Mannens M, Skinner SA, Friez MJ, Campbell C, Tedder ML, Alders M, Sadikovic Diagnostic utility and reporting recommendations for clinical DNA methylation episignature testing in genetically undiagnosed rare diseases. B.Genet Med. 2024 May;26(5):101075. doi: 10.1016/j.gim.2024.101075. Epub 2024 Jan 18.PMID: 38251460

Bergen AA, Buijs MJ, Ten Asbroek AL, Balfoort BM, Boon CJ; Dutch GACR "Bird's Eye View" Consortium; Brands MM, Wanders RJ, van Karnebeek CD, Houtkooper RH. Vision on gyrate atrophy: why treat the eye? EMBO Mol Med. 2024 Jan;16(1):4-7. doi: 10.1038/s44321-023-00001-1. Epub 2023 Dec 14. PMID: 38177529 Free PMC article.

van der Veen I, Heredero Berzal A, Koster C, Ten Asbroek ALMA, Bergen AA, Boon CJF. The Road towards Gene Therapy for X-Linked Juvenile Retinoschisis: A Systematic Review of Preclinical Gene Therapy in Cell-Based and Rodent Models of XLRS. Int J Mol Sci. 2024 Jan 19;25(2):1267. doi: 10.3390/ijms25021267. PMID: 38279267 Free PMC article. Review.

van der Laan L, Karimi K, Rooney K, Lauffer P, McConkey H, Caro P, Relator R, Levy MA, Bhai P, Mignot C, Keren B, Briuglia S, Sobering AK, Li D, Vissers LELM, Dingemans AJM, Valenzuela I, Verberne EA, Misra-Isrie M, Zwijnenburg PJG, Waisfisz Q, Alders M, Sailer S, Schaaf CP, Mannens MMAM, Sadikovic B, van Haelst MM, Henneman P. DNA methylation episignature, extension of the clinical features, and comparative epigenomic profiling of Hao-Fountain syndrome caused by variants in USP7. Genet Med. doi: 10.1016/j.gim.2023.101050

de Bruin DDSH, Haagmans MA, van der Gaag KJ, Hoogenboom J, Weiler NEC, Tesi N, Salazar A, Zhang Y, Holstege H, Reinders M, M'charek AA, Sijen T, Henneman P. Exploring nanopore direct sequencing performance of forensic STRs, SNPs, InDels, and DNA methylation markers in a single assay. Forensic Sci Int Genet. doi: 10.1016/j.fsigen.2024.103154.

Marieke Meijer, Tomosyns attenuate SNARE assembly and synaptic depression by binding to VAMP2-containing template complexes, Nature Communications, https://doi.org/10.1038/s41467-024-46828-1

Maaike van Boven, A de novo missense mutation in synaptotagmin-1 associated with neurodevelopmental disorder desynchronizes neurotransmitter release, Molecular Psychiatry, doi: 10.1038/s41380-024-02444-5
N. Tesi, Cognitively healthy centenarians are genetically protected against Alzheimer's disease, Alzheimers Dementia, doi: 10.1002/alz.13810.

N. Tesi and Y. Zhang, Characterizing tandem repeat complexities across long-read sequencing platforms with TREAT and otter, Genome Research, doi: 10.1101/gr.279351.124.

Celli L, Garrelfs MR, Sakkers RJB, Elting MW, Celli M, Bökenkamp A, Smits C, Goderie T, Smit JM, Schwarte LA, Schober PR, Lubbers WD, Visser MC, Kievit AJ, van Royen BJ, Gilijamse M, Schreuder WH, Rustemeyer T, Pramana A, Hendrickx JJ, Dahele MR, Saeed P, Moll AC, Curro-Tafili KR, Ghyczy EAE, Dickhoff C, de Leeuw RA, Bonjer JH, Nieuwenhuijzen JA, Konings TC, Engelsman AF, Eeckhout AM, van den Aardweg JG, Thoral PJ, Noske DP, Dubois L, Teunissen BP, Semler O, Wekre LL, Maasalu K, Märtson A, Sangiorgi L, Versacci P, Riminucci M, Grammatico P, Zambrano A, Martini L, Castori M, Botman E, Westerheim I, Zhytnik L, Micha

D, Eekhoff EMW. Adapting to Adulthood: A Review of Transition Strategies for Osteogenesis Imperfecta, Calcif Tissue Int. 2024 Dec;115(6):960-975. doi: 10.1007/s00223-024-01305-1.

Giubertoni G, Feng L, Klein K, Giannetti G, Rutten L, Choi Y, van der Net A, Castro-Linares G, Caporaletti F, Micha D, Hunger J, Deblais A, Bonn D, Sommerdijk N, Šarić A, Ilie IM, Koenderink GH, Woutersen S. Elucidating the role of water in collagen self-assembly by isotopically modulating collagen hydration, Proc Natl Acad Sci U S A. 2024 Mar 12;121(11):e2313162121.

Kohabir KAV et al; Synthetic mismatches enable specific CRISPR-Cas12a-based detection of genome-wide SNVs tracked by ARTEMIS Cell Reports Methods (4) p100912 ev (2024) - DOI: 10.1016/j.crmeth.2024.100912

Van den Heuvel D et al; STK19 facilitates the clearance of lesion-stalled RNAPII during transcription-coupled DNA repair Cell (187), p7107-7125 (2024) - DOI doi.org/10.1016/j.cell.2024.10.018

A spot on Early-Career Scientists

- Laura Ventura, ARD travel grant, €1000
- Laura Ventura, AMS symposium poster price, AMS, €250
- Kavish Kohabir, PhD student, Arthur Bergen Award 'Best Talk' HG Science Day 2024, €400
- Dr. Max Koppers, ERC Starting grant
- Dr. Amélie Freal, Vidi grant
- Dr. Danai Riga, Amsterdam UMC fellowship
- Dr. Isa van der Veen, Arthur Bergen Award, best poster, Human Genetics Science Meeting, November 2024
- Anna el Kalaan PhD student & Tessa Rouw PhD student, Biotech Days 2024, best poster
- Dr. Kim Wolzak, awarded with Alzheimer Nederland thesis prize 2024.
- Kavish Kohabir PhD student, OOA Retreat 2024 'Best Speaker Award'.

In the Media

Interview with Dr. Lotte Kleinendorst at Een Vandaag because of the possible cuts to universities, which will force important research into diseases to stop.

Clinical Genetics - explained (in Dutch) - **Dr. Philip Jansen.** Klinische genetica uitgelegd

Mariet Elting and Eva van Walree in ‘Arts in Spé, Mariet and Eva, as educators and intern clinical genetics, are featured in ‘Arts in Spé’ to promote their profession to the current generation of medical students. See link: Klinische genetica: een hoopvolle toekomst | medischcontact

World Sickle Cell Day 19 June; Prof Mieke van Haelst participated in the expert panel by invitation

Fundraising

On September 22nd, Dr. Sven van der Lee and his team took on the challenge of the Dam tot Damloop, running to raise funds for research on the genetics of Alzheimer’s disease. Through their participation, they not only generated financial support but also brought attention to research into families with a high incidence of dementia.

On November 2nd, 2024, Dr. Alexia Vermeer, Dr. Saskia van der Crabben and Prof. Lidewij Henneman laced up their walking shoes and undertook a 25-kilometer journey from Katwijk to Zandvoort in support of the Heart Foundation “11-Strandentocht”. Their walk aimed to raise awareness for the importance of scientific research for early detection and treatment of hereditary cardiovascular diseases.

Strandenloop

Colophon

Project management
Irene Kroon

Editorial Board
Irene Kroon, Mischa Hornman, Prof. Lidewij Henneman

Writing, editing & translation
Prof. Erik. Sistermans, Prof. Mieke. van Haelst, Prof. Lidewij Henneman, Dr. Peter Henneman, Dr. Henne Holstege, Willemijn Stoker, Prof. Matthijs Verhage, Kelsey Ax, Dr. Mariëlle van Gijn, Dr. Dimitra Micha, Dr. Rob Wolthuis, VU-vertaalbureau.

Design & Lay-Out
Hanneke Overhorst, Indy Hettema - Luumen

Photos
Department of Human Genetics, Adobe Stock

Date of Publication
5 June 2025

For more information and news about the Department of Human Genetics at Amsterdam UMC, visit our website

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