Research Agenda 2025 for a significant impact on healthcare

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We aim to create a scientific hotspot with the common goal of invigorating a collaborative, responsible and meticulous research culture, achieving cross-disciplinary and relevant translations to care and cure solutions.
High-quality research has always been a cornerstone of the Radboud university medical center (Radboudumc). We have concentrated our research in three excellent research institutes, each with a dedicated Graduate School, covering research from molecule to man to population. These research institutes interact closely and operate internationally to have a significant impact on healthcare across disciplines. Together, they cover eighteen focused and interactive research themes each aiming to develop tools for individualizing preventive, diagnostic and treatment strategies under the umbrella of “Personalized Healthcare”. If applicable, research programs are conducted in close cooperation with other faculties of the Radboud University.

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The mission of the Radboudumc is to have a significant impact on healthcare. I am sure this Research Agenda 2025 will align us for that.

The Executive Board
Prof. dr. Paul A.B.M. Smits
dean and vice chairman
The mission of the **Radboud Institute for Molecular Life Sciences** is to achieve a greater understanding of the molecular basis of disease. By integrating molecular and clinical research, the Institute obtains multifaceted knowledge of normal and pathological processes. Within the general concept of personalized healthcare, findings are translated into clinical applications, into the development of diagnostics and into the treatment of patients. In line with the Radboudumc’s strategic vision of having a *significant impact on healthcare*, research is clustered into clinically-orientated research themes from molecule to man plus a ‘mechanism-based’ theme, focusing on chemical biology and nanomedicine. The latter domain works in close alliance with the Faculty of Science. The Institute offers a challenging, enriching learning environment, where researchers of all levels are exposed to socially relevant multidisciplinary research questions along with our central theme of understanding the molecular basis of disease.

The mission of the **Radboud Institute for Health Sciences** is to improve clinical practice and public health. It does so by providing evidence of the efficacy and efficiency of existing and new tests, treatments and policies, by training young researchers in methodologies for obtaining such evidence and by developing new methodologies for improved research programs in this field. As evidence is typically obtained in probabilistic and qualitative rather than deterministic and mechanistic ways, research tends to be done among patients or the general population rather than through laboratory-based models. The Institute’s focus is on developing methodologies that optimize personalized healthcare and on the application of these tools in thirteen clinically-oriented research themes. In line with the Radboudumc’s mission of having a *significant impact on healthcare*, the Institute aims to bridge the gap between science and society, for example, by developing and evaluating guidelines and protocols. Societal impact is at the core of the Institute’s ambition.

**The Donders Institute for Brain, Cognition and Behavior** is devoted to understanding the mechanistic underpinnings of human cognition and behavior in health and disease. This cross-faculty institute is home to a large number of dedicated researchers, all of whom share the common goal of contributing to the advancement of brain, cognitive and behavioral sciences through investigator-driven research, and of improving health, education and technology by applying advances in this field. The Institute’s mission includes conducting interdis-
common goal of invigorating a collaborative, responsible and meticulous research culture, achieving cross-disciplinary and relevant translations to care and cure solutions. To support this transition, we will draw our scientists closer together in a global network so they can work with the most excellent infrastructure available in an open, transparent and interdisciplinary setting.

Inspired by the Radboud University invitation to change perspective, our **Research Agenda 2025** presents challenges and related objectives in improving the conceptual and practical impact of our research on healthcare and in advancing the global position of the Radboudumc as a leading academic institution. The aim of our plan is not modest: we aim to create a scientific hotspot with the interdisciplinary research of excellence at the unique interface between genetic, molecular and cellular processes, on the one hand, and clinical and system-level neuroscience, including cognitive and behavioral readouts, on the other. In doing so, we aim to have a significant impact on the prevention, diagnosis, staging and treatment of specific brain-based disorders.

**Scientific directors**
From left to right: Bart Kiemeney (Radboud Institute for Health Sciences), Guillén Fernández (Donders Institute for Brain, Cognition and Behaviour) and René Bindels (Radboud Institute for Molecular Life Sciences).
The strategic vision of the Radboudumc is based on four strategic foundations:

1. outstanding and proven quality, as scientific excellence is the basis of our research quality;
2. participatory and personalized healthcare, as involving patients in our research efforts will ultimately help to realize personalized and participatory healthcare from bench to bedside and vice versa;
3. operational excellence, with a focused research agenda, minimal administrative burden, optimal scientific training, and high standards of scientific integrity as essential ingredients;
4. sustainable networks, with scientists working across national and disciplinary borders and being embedded in clinical practice and education, which is indispensable for conceptual breakthroughs and their translation into patient care.

In this document, we have translated these strategic foundations into a ten-year research agenda, aiming to fulfill our shared goal of having a significant impact on personalized healthcare.
Excellence

We believe that scientific breakthroughs emerge when the most gifted researchers perform cutting-edge research to solve their curiosity-driven questions. This philosophy is embodied in our Principal Investigator structure, in our specific talent programs (Da Vinci challenge and Galilei track) and in our competitive Hypatia Fellowship Program for recruiting aspiring group leaders. The training of our students and young scientists is also governed by the pursuit of scientific excellence. We face stiff competition for talent and so we cannot afford to miss out on any source of talent. We are aware that scientific excellence is hard to measure and requires multidimensional assessment beyond quantitative measures.

Objectives

- We will implement a new coherent system for assessing scientific excellence in our training, promotion, and hiring activities as well as in our funding system. This assessment system will be based on multidimensional analysis beyond pure quantitative measures of excellence, thus acknowledging the contribution made by individuals or groups of researchers to conceptual or practical impact on healthcare.
- We will employ regular, rigorous and independent external assessment of our scientific excellence and its sustainability.
- We will work on our culture and structures in order to create a diverse workforce and broader talent source.
- We will develop a career path allowing talented junior researchers to combine international experience with local career perspectives.
- We will scout globally and provide flexible means of attracting the most creative and adventurous senior researchers in relevant strategic fields.
- We will provide systematic support and coaching for our researchers to gain prestigious personal grants and awards at all career stages and for us to obtain a top position in the Netherlands.
- We will reward researchers’ participation in education, as education has an impact on healthcare and stimulates young research talent.
Breakthroughs emerge when the most gifted researchers perform cutting-edge research to solve their curiosity-driven questions.
Patient as partner

Ultimately, we aim to improve disease prevention, diagnosis and prognosis as well as patient well-being. To achieve this goal, it is critical to actively involve patients, their relatives and support organizations as well as other private and public stakeholders in a discussion of our research agenda and its implementation. We are convinced that such a partnership is essential for the right perspective on priorities in health promotion and clinical care.
Objectives

• We will invite patients, relatives and other public stakeholders to participate actively as partners in our research activities.
• We will employ mechanisms of public outreach and advocacy, supporting and managing this partnership proactively and professionally.
• The most appropriate sites for substantiating this partnership are clinical expertise centers, where the translation of excellent research into highly specialized, complex patient care pre-eminently occurs. We will regard contributions to this partnership as an essential activity of our researchers.
• We will use these partnerships to identify possibilities for and develop disruptive innovations in healthcare.

Active involvement of patients, their relatives, support organizations and other private and public stakeholders is essential for the right perspective on priorities in health promotion and clinical care
Focus

As resources are limited, we can only excel if we work on a limited number of focused research themes. Each should have a core critical mass of excellent and interacting researchers, access to state-of-the-art facilities and optimal integration with excellent clinical care. Contemporary research should be patient-centered and integrated with biomedical research from the molecular to the human level, on the one hand, and with healthcare research from the community to the individual level, on the other. We will focus our research efforts, therefore, on a limited number of themes, most of which are targeting a specific disease or cluster of diseases. In addition, we have a few themes that focus on relevant methods that are distinctive of the research institute concerned.
Objectives

- We will improve the Radboudumc’s research focus by adapting our research agenda to a smaller number of clearly defined diseases or disease mechanisms.
- We will provide targeted support to the most excellent, interdisciplinary research that is integrated with patient care and has the most significant impact on healthcare in conceptual and practical terms.
- Within the chosen research themes, we will restrict ourselves to research that helps to individualize prevention, diagnostics or therapeutics.
- We will strengthen our workforce by supplementing expertise that is critical but currently unavailable at the Radboudumc.
- We will reduce the administrative burden on our researchers by professionalizing research support to achieve operational excellence.
- We will integrate research themes and clinical expert centers most optimally to enable seamless and bidirectional interaction between clinical care and research.

Improve our research focus by adapting our research agenda to a smaller number of clearly defined diseases and disease mechanisms
**Training**

Even the most talented individuals can only excel if they have been trained to the highest level. We regard our scientific education and training as the central aspect of our scientific work that provides us with novel perspectives, excellent colleagues and ambassadors of the Radboudumc in a worldwide setting. Our education and training programs optimally align with our research objectives.
Scientific education and training is the central aspect of our scientific work

Objectives

- We will take our students as closely as possible to scientific research.
- We will stimulate all students to gain international research experience.
- We will structure our scientific education and training programs in graduate schools to connect better master and doctoral training although the former is regarded as education and the latter the first step into professional scientific work.
- We will develop novel criteria for PhD thesis assessment, rebalancing the requirements for and duration of PhD projects to optimize training and accomplish ground-breaking, high-gain / high-risk projects.
- We will provide master stipends and PhD fellowships for the most gifted and motivated students.
- We will teach our students how to excel, to deal with patients as partners, to pursue operational excellence and to build sustainable networks.
- We will broaden our training programs to make our students, PhD candidates and postdoctoral fellows better prepared for possible careers outside academic research.
- We will establish an alumni network to put us at the center of a dense world-wide web of colleagues infected by the spirit of the Radboudumc.
Integrity

Taking responsibility is at the heart of the Radboud Way of Working, and following good scientific practice, therefore, is deeply rooted in our culture. We strongly believe that only research that produces reliable and meaningful data in a trustworthy process can have a significant impact on healthcare. Although poor quality science and malpractice cannot be fully prevented through training, rules and checks alone, the risk of violating principles of good scientific practice can nevertheless be substantially reduced in an appropriate culture with specific precautions.
Objectives

- We will install a training program on scientific integrity that is compulsory for all researchers.
- We will develop standard operation procedures and data management infrastructure to enable appropriate data stewardship.
- We will promote an open and interactive culture that is open to discourse and fosters scientific integrity.
- We will make all our publications accessible to everybody free of charge.
- We will publish negative findings and raw data in an open repository.
- We will reduce potential conflicts of interest arising at the intersection between research and ancillary activities and be transparent when they do occur.

Only research that produces reliable and meaningful data in a trustworthy process can have a significant impact on healthcare.
Infrastructure

World-class infrastructure and talented support staff are essential ingredients for high-quality research. Interaction between experienced and novice users is a prerequisite for research facilities to thrive. Though we have well-integrated laboratories, extramural research facilities and eighteen state-of-the-art Technology Centers, our research infrastructure can still improve in terms of access, quality and use. Furthermore, ever evolving and entirely new technologies are making substantial demands on our budgets and strategic planning objectives.

Objectives

- We will maintain and expand our research facilities and related ICT infrastructure to meet the demands of present and future research goals with optimal operational excellence safeguarding their sustainability.
- We will also make our research infrastructure and data available to external academic and commercial partners, especially in our region.
- We will create clusters of open and flexible office and lab spaces to support interdisciplinary interaction and availability for future activities that cannot currently be predicted.
- We will establish meeting and service spaces at critical positions between public spaces, laboratories and offices to foster the spirit of collaboration and interaction.
- We will provide conferencing and meeting facilities to support a conference and training program that ensures scientific vitality.
- We will lend direct support to efficient academic-private interactions that enable optimized access to research findings and that support commercial research and development.
- We will actively participate in and use external research infrastructure to increase efficiency, quality and collaboration.
Interaction between experienced and novice users is a prerequisite for research facilities to thrive.
Networks

Present-day science tackles the most complex problems, which usually cannot be solved by single researchers or even single institutions. These problems require collaborations across disciplines, interaction with other academics around the world and cooperation with public or private partners outside academia. There are many active networks linking researchers within the Radboudumc and with the outside world, but the pressure to work interactively is increasing further.
Objectives

- We will create an open and intellectual atmosphere for students and researchers.
- We will implement incentives and structures to make internal and local cross-campus collaborations more attractive and efficient.
- We will build and develop strategic academic partnerships with specific universities or institutes, both domestic and abroad.
- We will improve our proactive support in creating external collaborations with strong partners, domestic and abroad, with full use of the Radboud Excellence Initiative.
- We will invite our colleagues to join our existing networks to improve our embedding in dense collaborative networks.
- We will seek active collaborations with researchers and clinicians in the top clinical training hospitals in the region to broaden the scope of our mutual research efforts.
- We will follow our patients outside immediate clinical care settings, to realize a research network with greater participation and ecological validity.
- We will encourage researchers to be actively engaged in social debates to enable us to contribute to science policy.

Complex problems cannot be solved by single researchers or even single institutions. These problems require collaborations across disciplines.
Research themes

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Healthcare improvement science

High-quality healthcare has a significant impact on the health of individuals and the wealth of populations. The quality and affordability of healthcare, therefore, is a top priority on the social agenda. The healthcare system is in a state of transition as weaknesses in the current system of healthcare delivery as well as novel developments are urging the development and implementation of new concepts of healthcare delivery. This complex endeavor is only possible when a sound scientific base is in place. At present, patients are facing a large variation in healthcare quality, safety and costs. There is a wealth of literature to show that evidence-based medicine does not reach all patients in time or everywhere. Healthcare is predominantly delivered by local health systems, whose performance and outcomes should become transparent. Transparency opens the world of learning and improvement.

This theme’s research focus is on the structure, process and outcomes of healthcare in daily practice, aiming to improve its performance and delivery from the perspective of the patient. We study existing and new interventions at the micro and macro level. Our aim is to explore what interventions or structures work in what circumstances. The immediate value for the patient is paramount.

Objectives

- We aim to identify the facilitators and barriers to achieving improvements in patient care throughout the transmural care chain.
- We aim to support the concept of personalized healthcare from a non-biomedical perspective, by examining, for example, patient-oriented outcome measures (PROMs) and by investigating the value of integrative healthcare.
- We aim to further develop research methods tailored to answering complex questions in healthcare improvement science, such as the early and rapid evaluation of new medical technology, the impact of multimorbidity, the proper use of big data and patient participation in healthcare and research.
- We aim to provide other research themes with methodological innovations and support on the objectives mentioned above.
Nanomedicine

Nanomedicine is a rapidly developing area of research that aims to create functional units on the nanoscale to manipulate cellular processes for use in research and biomedicine. Understanding the functioning of living cells, particularly those processes that cause disease, requires a detailed molecular understanding of the biological processes that govern cellular behavior. This includes the analysis of omics data and the detailed study of molecular interactions, both inter- and intracellularly, with molecular probes that minimally affect the processes to be analyzed. Improved understanding, furthermore, will lead to better methods for amending biological processes that have become dysfunctional, and, hence, to the development of novel medicines.

Such an approach can only succeed in close collaboration between researchers in chemistry, biology and biomedicine with an affinity for molecular life sciences. The nanomedicine research theme thus encompasses a multidisciplinary research platform. It aims to study, design, synthesize and characterize molecules and molecular assemblies in order to elucidate the structure and function of biological systems and to unravel the molecular basis of disease. It seeks to translate improved understanding into novel and more effective diagnostics and therapeutics.

Objectives

- We aim to develop molecular probes and bio-orthogonal chemistry to label biomolecules in living cells with minimal invasiveness and optimal selectivity. Using state-of-the-art imaging methodologies, we study the fate of biomolecules in living cells and organisms.
- We study protein signaling pathways at the molecular level in living cells.
- We study mechanisms and approaches for cellular drug delivery.
- We will investigate the dynamic interactions of cells with their environment/extracellular matrix.
- We will identify and characterize molecular markers for disease-associated dysfunctional biological processes and develop methods for their detection.
- We will develop microfluidics platforms to study single-cell behavior in detail.
- We aim to develop bio- and chemo-informatics tools to analyze big data generated by omics platforms more effectively.
- We will develop targeted nanosized carrier systems for cargo transport, delivery and immune regulation.
- We seek to bring chemists, biologists and medical doctors together to create an open research environment in which medical challenges are translated into nanomedicine solutions.
Cancer development and immune defense

More than 100,000 people annually in the Netherlands, or one-third of the population, currently develop cancer at some point in their lives. About 40% of these patients will die within five years. For patients with a localized solid tumor, prospects are quite good, but for most patients with disseminated disease, unfortunately, prognosis is still poor. This also holds for some hematological cancers. In order to improve the success of treatment and to further individualize such treatment, we need to gain a better understanding of the molecular, (epi)genetic and immunological processes that are implicated in the transformation of normal (stem) cells to malignant cancer cells.

We investigate therapy resistance, the tumor micro-environment, cancer cell trafficking and the interaction between the immune system and cancer. We translate this basic knowledge into novel forms of therapy targeting tumor cells. We also develop strategies to expand and manipulate immune cells for clinical use, exploiting and boosting the power of the immune system. For the translational part, we are directing phase I, II and III clinical trials.

Objectives

- We aim to identify all genetic ‘driver’ lesions that underlie the pathogenesis of cancer.
- We study epigenetic mechanisms implicated in aberrant gene expression in cancer.
- We study immune cell and cancer cell trafficking.
- We investigate to what extent the immune system is capable of recognizing tumor cells.
- We study mechanisms to stimulate specific anti-tumor immune responses.
- We will perform clinical trials to test compounds that specifically target the molecular pathways that are disturbed.
- We will perform clinical trials in which manipulated immune cells are used to eradicate cancer cells.
- We direct prospective, population-based cancer registries to analyze prognosis, therapy response, quality of life and economic aspects.
Rare cancers

More than 4 million people in the European Union are affected by rare cancers. Despite the rarity of each of these 186 cancers, they represent a total of about 22% of all cancer cases. This is more than any single common cancer. Rare cancers are identified as those with an incidence of less than 6 per 100,000 persons per year and include head and neck cancer, sarcoma, thyroid cancer, neuro-endocrine cancer, brain tumors, lymphoma and pediatric cancer. Unfortunately, the average outcome for patients with rare cancers is inferior to those with more common cancers.

Due to their low frequency, rare cancers pose particular challenges. Our mission therefore is to improve diagnosis and prognosis and to perform personalized clinical studies and translational bench-to-bedside research in patients with rare cancers. This will be performed in relationship with patient advocacy groups, if applicable. Given the rarity of these tumors, collaboration with national and international centers and partners is vital for the success of this theme.

Objectives

- We aim to remedy late or incorrect diagnosis records.
- We aim to improve access to appropriate therapies and clinical expertise.
- We will raise the number of clinical trials in spite of the small number of patients.
- We will endeavor to raise market interests in the development of new therapies.
- We will seek to improve the number of available registries and tissue banks.
Tumors of the digestive tract

In this research theme, we aim to improve prognosis and treatment of patients with tumors of the digestive tract, with a focus on sporadic and hereditary forms of colorectal and pancreatic cancer. We aim to achieve better prevention of cancer in high-risk patients and develop and implement new diagnostic tools for staging and therapy response. In addition, we are working to create treatment innovations, ranging from improved surgical techniques to immunotherapy. Research into the etiology, epidemiology and genetics of these tumors will lead to improved primary, secondary and tertiary prevention.

Objectives

• We will identify new genes responsible for hereditary colorectal cancer syndromes.
• We will develop strategies for improving detection of hereditary forms of pancreatic cancer.
• We aim to prevent cancer in high-risk patients using vaccination and lifestyle interventions.
• We will develop new molecular diagnostic tools to predict tumor response to therapy.
• We will identify relevant biomarkers for the development of metastatic disease and implement these factors in daily practice.
• We will develop surgical techniques to optimize patient care.
Urological cancers

Every year, almost 20,000 people in the Netherlands are diagnosed with a urological tumor: 6,900 bladder cancers, 2,850 kidney and urethral cancers and 10,000 prostate cancers. Overall prognosis is quite good for patients diagnosed with a localized tumor, but prospects are still poor for patients with disseminated disease. Consequently, more than 5,000 people die from urological cancers annually.

In treating urological cancers, physicians are confronted with a number of unmet clinical needs: there are no markers that can accurately indicate patients with localized tumors who will ultimately develop progressive disease, and there are no pre-treatment markers that can identify patients expected to respond well or badly to specific therapies. It remains important to develop and evaluate new treatment modalities with better efficacy and less mutilating effects. Especially in the field of prostate cancer, there is also a clear need for a marker that can better distinguish insignificant from significant cancers so that population-based screening for this disease may become cost-efficient.

This theme focuses its research efforts on solving these diagnostic and treatment dilemmas. It has a strong track record in (molecular) imaging, biomarkers, molecular pathology, genetic epidemiology, immunotherapy and clinical trials. Integration of these efforts will produce concept-changing translational projects that can pave the way to more individualized urological cancer care.

Objectives

- We aim to identify novel high-penetrance susceptibility genes for bladder cancer.
- We aim to identify germline markers that may predict response to BCG treatment in bladder cancer and TKI treatment in renal cell cancer.
- We aim to quantify the effect of life-style factors on the prognosis of urological cancers.
- We aim to develop and validate new early detection and staging biomarkers in prostate cancer.
- We will evaluate and implement multi-parametric MRI for the detection and assessment of prostate cancer aggressiveness.
- We will validate and implement nano-MRI for the detection and treatment guidance of small lymph node metastases.
- We will evaluate the possibility of monitoring treatment response with hyperpolarized substrates.
- We will develop and validate per-operative imaging tools to improve cancer surgery outcomes.
- We will evaluate the efficacy of novel treatment modalities in RCTs including biomarkers.
- We will evaluate the cost effectiveness of new treatment paradigms in an early development phase.
- We will develop patient-derived models to individualize therapies.
Women’s cancers

The women’s cancer research theme is dedicated to the treatment of malignancies that specifically occur in women, such as breast cancer, ovarian cancer, cervical cancer, endometrial cancer and vulvar cancer. Our ultimate goal is to improve patient-centered quality of care in partnership with patients and relatives involved. We aim to improve care in the broad spectrum of prevention, early diagnosis, treatment and post-treatment follow-up. To develop better management strategies for every individual tumor type, we need a better understanding of carcinogenesis and tumor development with special attention for hereditary causes and preservation of fertility. Findings from basic research will be translated into clinical applications at a diagnostic and treatment level within the general concept of personalized healthcare.

Objectives

• We will study the oncogenesis of the various women’s cancers.
• We will improve screening strategies for the national screening program for breast and cervical cancer.
• We will optimize treatment strategies for women’s cancers.
• We will optimize diagnostic tools and introduce new tools for the detection of women’s cancers.
• We will develop and improve management strategies for hereditary cancers.
• We will introduce new immunotherapeutic treatment modalities in ovarian cancer.
• We will develop new fertility-sparing techniques to support the management of various malignancies.
• We will study patients’ distress levels and develop management strategies to improve quality of life.
Infectious diseases and global health

The theme of Infectious Diseases and Global Health (ID&GH) combines cutting-edge research in immunology, microbiology, pharmacology and novel omics methodology with translational and implementation research in immunology and infectious diseases. It is our mission to attain national and international leadership in research and research training in infectious diseases, immunity and global health. Working to improve the diagnosis, treatment and prognosis of patients with infections, therefore, our researchers aim to have a significant and global impact on the control, treatment and elimination of infectious diseases.

These aims will be accomplished through several complementary strategies. Basic research aiming to understand biological mechanisms will identify novel targets for diagnostics and therapy; translational research will explore relevant biological processes in patients; and epidemiological research will study infections, disease interventions and prevention at the population level. There are two research lines: infectious diseases & host defense, and poverty-related infectious diseases.

Objectives

- We aim to assess the pathophysiology of severe infections to identify novel diagnostic and therapeutic approaches.
- We aim to explore antibiotic resistance mechanisms to devise novel approaches to antibiotic therapy.
- Through public health approaches, we will investigate quality of care for patients with infectious diseases.
- We aim to explore malaria biology and contribute to the identification of novel drugs and vaccines, as well to optimize malaria elimination interventions at the community level.
- We will improve understanding of the interaction between arboviruses, human hosts and the mosquito vectors.
- We aim to identify genetic and other risk factors for mycobacterial infections and to optimize the diagnosis, prevention and treatment of tuberculosis.
- We will optimize infection prevention and control programs in low-resource settings, including HIV programs.
Inflammatory diseases

Inflammation is classically viewed as an acute response to tissue injury and more often than not resolves spontaneously. A well-controlled inflammatory response has several protective roles: it prevents the spread of infectious agents and damage to nearby tissues; it helps to remove damaged tissue and pathogens; and it assists the body’s repair processes. However, cellular stress and malfunction may trigger chronic inflammation, which, rather than benefiting health, contributes to disease and age-related deterioration. Chronic inflammation is currently among the leading causes of morbidity and mortality in the Western world.

Our aim is to translate results from the molecular and population level to the individual patient to improve diagnosis, disease management and treatment of (chronic) inflammatory disorders.

Objectives

- We aim to unravel the (immune)pathogenesis of inflammatory disease processes and the efficacy and side effects of current treatments.
- We will assess the role of tissue-specific factors in regulating local immunity and inflammation.
- We will identify druggable genes and develop anti-inflammatory drugs.
- We will identify biomarkers for personalized therapy and investigate treatment approaches using biomarkers as co-diagnostics.
- We aim to capture disease severity in validated outcome measures and assess side effects of treatments in real clinical practice.
- We will perform (pharmaco)genetic and epidemiological studies to identify risk factors associated with disease susceptibility, severity and treatment outcome.
Mitochondrial diseases

The Mitochondrial Diseases theme, which is closely associated with the Nijmegen Center for Mitochondrial Disorders (NCMD), aims to understand cellular bio-energetics in health and disease at all levels of complexity. This will enable the development of preventive measures and help to make substantial contributions to the development of rational treatment strategies for mitochondrial diseases. The theme’s strategy is founded on the understanding that true innovation in healthcare requires the full integration of unbiased fundamental research at all levels of complexity. Only then can we increase knowledge, accomplish innovation in personalized diagnostics, perform high-quality clinical research and realize applications to patient care.

The Mitochondrial Diseases theme concentrates on three research topics: the structure and function of molecules and complexes, cellular consequences, and clinical aspects of mitochondrial disorders.

Objectives

• We aim to identify new gene defects in the oxidative phosphorylation system and to characterize the cellular mechanisms involved.
• We aim to elucidate the molecular mechanism and regulation of mitochondrial complex I based on the atomic structure.
• We aim to resolve the complete assembly pathway of mitochondrial complex I and to identify and functionally characterize new components of the assembly machinery.
• We will study the dynamics of the mitochondrial complexome in health and disease.
• We will explore the tissue-specific inventory and regulation of the complexes of oxidative phosphorylation and their correlation with specific phenotypes.
• We will investigate the links and mechanisms connecting genetic defects with organ-specific disease phenotypes.
• We will further develop tools to monitor the metabolic state and bio-energetic status of mitochondria in living cells and tissues.
• We will study the influence of environmental factors on the progression of mitochondrial disease.
• We will develop a toolbox of biomarkers and relevant clinical outcome measures to monitor progression of mitochondrial disease and the effect of therapeutic interventions.
• We will perform long-term follow-up studies on defined patient cohorts.
• We will explore new therapeutic approaches to mitochondrial diseases.
Reconstructive and regenerative medicine

This theme focuses on the development and clinical translation of innovative diagnosis and therapies, including regenerative medicine and nano-medicine, for personalized care and cure of patients needing reconstructions of lost or damaged tissues. This will be achieved by transdisciplinary research by leading research groups in the fields of medicine, dentistry, biochemistry, chemistry, biology and materials science.

Reconstructive and Regenerative Medicine (RRM) is a center of excellence combining unique expertise present at the Radboudumc in the fields of cell biology, biochemistry, immunology, tissue engineering, molecular biology, biomaterials, chemistry, transplantation biology and clinical research. It is the leading research center in regenerative medicine in the Netherlands. The RRM bridges the bench-to-bedside gap by unifying a large number of renowned research groups focusing both on basic science and on clinical translation (such as tissue engineering, biomaterials and stem cell therapy). To this end, RRM participates in numerous leading national and international research programs funded by Dutch, European or American funding agencies.

The aim of RRM is to strengthen the already existing synergy between the participating laboratories by stimulating interaction between clinicians, basic scientists and private partners in the Nijmegen area. We seek to develop therapies that will improve the quality of healthcare.

**Objectives**

- We will investigate clinical applications for musculoskeletal diseases.
- We will investigate applications for kidney diseases.
- We are investigating applications for the urogenital tract.
- We are looking for applications for skin diseases.
- We are investigating reconstructive surgical procedures and TERM applications.

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Renal disorders

The mission of the renal disorders theme is to deliver excellent, efficient and innovative clinical care to our patients at the Radboudumc and beyond, and to be leading the field of kidney disease research in the world. The primary aim of the renal disorders theme is to understand the molecular mechanisms, physiology and pathogenesis of glomerular diseases and tubular transport disorders, including acquired and inherited forms of kidney diseases. To achieve this aim, we will increase knowledge of the molecular and immunological basis of glomerular and tubular disorders; develop biomarkers for optimal prediction of disease prognosis; and apply strategies for preventing and improving renal replacement therapy. The research projects are carried out at genetic, molecular, cellular and integrative levels, as well as on human subjects.

Objectives

- We will increase knowledge of the molecular and immunological basis of glomerular and tubular disorders and of graft performance.
- We will combine genetic and functional cutting-edge methodology to diagnose and identify novel renal diseases.
- We will identify novel therapeutic targets for renal disorders and kidney transplant survival.
- We aim to develop biomarkers for optimal diagnosis, prevention and prognosis of renal diseases, kidney injury and transplant survival.
- We aim to optimize treatment strategies for patients with renal diseases, focusing on patient-tailored treatment.
- We will apply strategies for preventing and improving renal replacement therapy.
Vascular damage

Despite major advances in acute management of ischemic events and treatment of atherosclerosis, cardiovascular disease is still the most important cause of morbidity and mortality worldwide. It is a major challenge to reverse the chronic process and to prevent acute events resulting from plaque rupture and atherothrombosis. New insights into the pathogenesis of atherosclerosis, particularly the role of inflammation, are providing potential new targets for therapy. In addition, organ damage resulting from ischemic events needs to be minimized. Preclinical research into the pathophysiology of ischemia-reperfusion injury has also provided important new insights.

Translation of these preclinical concepts into clinical realities is a major challenge for this theme, which has a strong track record in human in vivo translational research. In this effort, the impact of inflammation on atherosclerosis and plaque rupture will be an important focus in the years to come. Improving the implementation of evidence-based cardiovascular guidelines so as to prevent and treat cardiovascular disease is another major challenge.

Objectives

- We aim to unravel how traditional and novel cardiovascular risk factors induce a pro-atherogenic phenotype of these cells by performing in vitro and ex vivo studies on cells of the innate immune system.
- We plan to develop and improve noninvasive vascular imaging techniques to detect vulnerable plaques and vascular inflammation.
- We aim to develop and implement techniques to study inflammation and its impact on atherosclerosis in humans in vivo.
- Using animal models, we aim to develop and validate biomarkers to study the impact of inflammation on progression of atherosclerosis in humans in vivo.
- We aim to investigate the role of inflammation in the pathogenesis of the metabolic syndrome.
- We plan to study the mechanisms by which inactivity results in cardiovascular injury and evaluate interventions to prevent or reverse this.
- We want to improve diagnosis and treatment of the adrenal causes of hypertension and to explore mechanisms of vascular injury specifically related to these disorders.
- We aim to explore the role of gender differences in atherogenesis.
- We will study promising strategies to prevent ischemia-reperfusion injury, such as pharmacological and ischemic conditioning.
- We will study how current cardiovascular guidelines can be implemented most effectively.
Sensory disorders

The loss of our senses has a huge psychological and social impact on quality of life and poses a high burden on society. The number of blind and deaf individuals is expected to rise sharply over the next ten years as the global population is ageing. To limit the burden of sensory impairment, we need to develop tools that enable us to perform accurate diagnosis and prognosis of the disease, understand the underlying disease mechanisms and develop new treatments and rehabilitation strategies. Our mission is to have a significant impact on healthcare for sensory disorders, tailored to personalized needs.

Objectives

• We will implement advanced imaging technologies to improve diagnosis and monitor disease progression in the peripheral and central nervous system.
• We will develop diagnostic and prognostic tests based on clinical, behavioral, genetic and serum biomarkers.
• We will build large patient databases and biobanks for common and rare sensory disorders.
• We will use large-scale omics technologies to better understand the molecular mechanisms underlying disease onset and disease progression.
• We will identify novel targets for therapy to prevent disease onset or to slow disease progression.
• We will develop and characterize cellular model systems and animal models to study disease mechanisms and test novel therapies.
• We will design innovative molecular treatments, develop retinal, cochlear and vestibular implants using advanced technologies, and establish perceptual training protocols.
• We will perform clinical trials and implement novel treatments and rehabilitation strategies in the clinic.
• We will identify clinical, behavioral, genetic and serum biomarkers that can predict response to treatment.
• We will develop personalized treatment regimes for sensory disorders based on clinical, behavioral, genetic and serum biomarkers.
Alzheimer’s disease

Alzheimer’s disease is the leading cause of dementia worldwide. The number of people with dementia in the Netherlands will greatly increase over the next years, due to the ageing of our society. Seventy percent of patients live at home, supported by informal caregivers. Fifty percent of these caregivers work and care for their own children. More than any other disease, dementia negatively affects the lives and health not only of these patients but also of these caregivers. Years of intensive research have left us without an effective treatment for Alzheimer’s disease. Much of this research has been limited to monogenetic disease models that reflect the rare (<1%) familial forms of Alzheimer’s disease, with age of onset under 65 years. Treatments that have been developed on the basis of these models have repeatedly failed to show benefits in the common (>99%) form of Alzheimer’s disease, with age of onset over 65 years. At present, the heterogeneity in the etiology, clinical presentation and progression of this common form of Alzheimer’s disease remains largely unrecognized. Our mission is to have a significant impact on the personalization of dementia care by addressing these knowledge gaps.

Objectives

• We will study factors that have a clinically significant impact on the risk of developing Alzheimer’s disease. These factors include sleep deprivation, vascular disease, physical exercise, nutrition and psychosocial interaction.
• We aim to identify factors, such as multimorbidity, that are associated with fast and more benign disease progression and explain individual heterogeneity in disease progression. Behavioral problems have a strong negative impact on prognosis, quality of life and caregiver burden. We will improve early detection of these symptoms.
• We will develop personalized care for patients with dementia under 65 years of age.
• Driven by a social demand for earlier diagnosis, we will critically evaluate and improve diagnostic biomarkers, including cerebrospinal fluid and neuro-imaging.
• We will develop individualized care pathways in our memory clinic and in primary and long-term care settings, and we will initiate palliative care studies at all disease stages.
• We aim to improve support for caregivers by developing personalized psychosocial interventions and e-health tools.
Disorders of movement are common in patients with neurological abnormalities in the central or peripheral nervous system. A deeper understanding of these aberrations will help to improve and individualize the diagnostic, prognostic and therapeutic strategies for these patients. The emphasis lies on understanding the behavioral characteristics, the underlying pathophysiology and the associated neuroplasticity.

**Objectives**

- We will deepen our understanding of the nature and sources of variability in the clinical presentation of neurological patients presenting with disorders of movement. This includes a focus on environmental, behavioral and genetic determinants.
- We will develop and evaluate improved strategies aiming to establish timely diagnostic and prognostic evaluation of neurological patients presenting with disorders of movement.
- We aim to gain a better insight into the pathophysiological processes in the central and peripheral nervous system that lead to the clinical expression of disorders of movement. To achieve this aim, we will focus on both primary dysfunction and compensatory mechanisms as a basis for the future development of improved treatment strategies. Methods include state-of-the-art electrophysiology, biomechanics, structural and functional neuro-imaging and neurochemistry. A specific area of interest includes disorders of axial mobility.
- We will develop and evaluate new treatment strategies for neurological patients presenting with disorders of movement, including a focus on behavioral and self-management strategies. A specific new area relates to deep brain stimulation techniques, both as a novel treatment strategy and as an exploratory research tool for examining cerebral dysfunctions underlying disorders of movement.
- We will implement and develop an evidence basis for integrated care models for neurological patients presenting with disorders of movement, including a focus on allied health interventions and on innovative financial reimbursement systems.
- We endeavor to develop and evaluate personalized “precision” medicines for neurological patients presenting with disorders of movement.
Neurodevelopmental disorders

Neurodevelopmental disorders, especially intellectual disability, autism and Attention-Deficit/Hyperactivity Disorder (ADHD) are major causes of lifelong, chronic impairment. The etiology of these disorders is complex and barely understood. No effective treatments are available for autism and intellectual disability, and none of the neurodevelopmental disorders can be cured. We aim to improve our understanding of the causes and mechanisms underlying intellectual disability, autism and ADHD, seeking to improve the care for our patients by developing better diagnostics and better personalized treatment strategies.

Objectives

• We will identify the genetic and environmental risk factors and their interplay contributing to neurodevelopmental disorders, by leading and contributing to international collaborations.
• We will use computational modeling and bioinformatics to predict aberrant biological processes in the neurodevelopmental disorders.
• We will develop cell and animal model systems for the disorders and study them to understand the mechanisms leading from gene to disease phenotype and to test novel treatment options.
• We will identify the neural correlates of neurodevelopmental disorders through neuro-imaging-based research.
• By integrating findings at genetic, genomic and brain levels, we will identify biomarkers for diagnosis and prognosis of neurodevelopmental disorders and integrate this knowledge into clinical care.
• We will contribute to the development of more biologically-oriented diagnostic (sub)groups of neurodevelopmental disorders.
• Highly interdisciplinary research from molecule to man and population will help us to develop improved and personalized (non-)pharmacological treatments for neurodevelopmental disorders.
Stress-related disorders

Stress-related disorders such as depression, anxiety and addiction have an impact on mental and physical health worldwide. As closely collaborating interdisciplinary researchers, we aim to decrease the burden of these highly prevalent disorders by improving our understanding of their development, characteristics and consequences. We aim to develop both new biomarkers and individualized treatments. We will contribute to new strategies in personalized healthcare by determining individual sensitivity and optimally combining pharmacological, psychotherapeutic and neuromodulatory approaches.

Objectives

- We will study stress-related disorders throughout life by integrating child, adolescent, adult and old-age psychiatry and psychiatric research.
- We will study diverse brain functions by measuring and manipulating underlying cognitive, emotional, psychopharmacological, hormonal and neural mechanisms, both in animals and in humans.
- We will develop new biomarkers for diagnosis, prediction of treatment effects and assessment of treatment outcome in stress-related disorders.
- We will study the co-morbidity of stress-related disorders and develop innovative combined treatment approaches and algorithms to treat patients with both mental and physical stress-related disorders.
- We will identify factors that determine and strengthen resilience to stress aiming to prevent development and relapse of stress-related disorders.