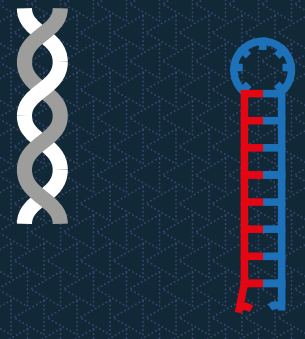
CARIM ANNUAL REPORT 2014

SCHOOL FOR CARDIOVASCULAR DISEASES



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CONTENTS

PREFACE
TALKING ABOUT STRATEGIES

CARIM, at present, features established research themes and structures of governance. In 2014, the school performed an extensive self-evaluation on paper, and in June of that year, hosted a site visit of the External Review Committee (ERC) evaluation group according to the criteria within the Standard Evaluation Protocol (SEP), which were drawn up by the Royal Netherlands Academy of Arts and Sciences (KNAW). During this procedure, the current strengths, weaknesses, opportunities and threats of an institution were displayed, analysed, discussed and rigorously evaluated. On the basis of four main criteria (quality, productivity, societal relevance and vitality, and feasibility), CARIM altogether scored quite well with an average of >4.5 of a possible highest score of 5 for excellence.

CARIM has gone through some exciting years, is now quite consolidated but is facing further years of financial austerity. At the same time, the research school has to cope constantly with actual scientific currents in biomedicine, integrate itself in local, national and international scientific networks and funding systems, fight for its place in European cardiovascular research institutions, and prepare for the future. In such periods, there is always a tendency to cry for "visions" as well as "strategic decisions" based on the former. By definition, without additional funding, these decisions have two sides: giving and taking. In other words, without additional resources, strengthening one aspect or topic of research can only be achieved by weakening another one. On first glance, this sounds pretty simple, but a second look reveals serious problems of such giving and taking strategies. These concern not only the selection of scientific topics to be addressed or abandoned, a usually very controversially discussed issue, but also numerous personal and legal aspects regarding the researchers themselves, their students and technical support, as well as the progress or termination of their individual and network research projects.

A major strategic instrument of CARIM has been and still is the institution of a Tenure Track System. Young, however already advanced researchers are eligible to be proposed by their Principal Investigators. If selected, they have to go through a strenuous five-year period in which they have to fulfill demanding requirements regarding grant income (self-financing), scientific output and academic education. If successful, they have the right of tenure, a permanent position provided by the school. CARIM creates these slots for tenure trackers by collecting all positions of CARIM which become free via retirement or for other reasons. This system, installed some years ago, has proven to be instrumental in securing a new generation of excellent researchers to the school. A potential drawback of this system is that it may limit capacities in the future and reduce the flexibility of strategic decision making in the presence. Thus, it appears wise to keep some of the budget resources free for the recruitment of scientific staff from external institutions. To decide on the question as to whom of these well-selected, highly qualified candidates to include in CARIM's tenure track program is one of the top strategic challenges CARIM is facing now and in the future.

Another strategic instrument of resources distribution consists of allocations of scientific staff including PhD students and/or technical assistance, sometimes also financial means, to successful individual researchers following the so-called Matthew principle ("For unto every one that hath shall be given, and he shall have abundance: but from him that hath not shall be taken even that which he hath." Matt 25,29). Nowadays, this principle is frequently executed in the allocation of funds to scientists and their

programmes. However, the other side of the coin is that, in the absence of additional funds, these resources have to be withdrawn from other, less successful colleagues. While this idea is quite popular with the more successful in the scientific community, decision-making is extremely difficult in a field of researchers with similar qualifications and comparable scientific quality. CARIM luckily boasts of a substantial number of highly qualified and successful scientists, especially in the ranks of the Principal Investigators (PIs), but this renders a clear distinction into the ones to be given and the ones to be taken a very difficult task.

Any research strategy needs to respond to the objectives and fields of interest of the main funding organisations. Of particular interest for CARIM in this context are the recently released research agenda of the Dutch Heart Foundation and the policy statements of the European Commission describing the main objectives of the Horizon 2020 framework program. The Dutch Heart Foundation in general continues the traditional policy of content-driven research program, although on a larger scale than before 2011 (CVON program). The main research topics defined by the foundation are earlier recognition of cardiovascular disease, cardiovascular disease in women, heart failure and arrhythmias, acute treatment of strokes and a healthy life style, many of these research fields being covered by CARIM investigators. Unlike the Dutch Heart Foundation, the European Commission has chosen for a selection procedure based on the research approach rather than its content. The main objectives within the health-related programs are sustainable health care systems, personalised medicine, ICT for health, healthy ageing and environmental factors as health challenges. CARIM has begun in 2014 to make major efforts in order to meet these new objectives and will continue in the years to come to create new European

research networks and strategically adapt its own research programmes as much as possible to the European calls.

In 2014, CARIM has made substantial progress in several important strategic fields. Complex Genetics, urgently requested for years by several members of cardiology and other groups, has been given a boost by CARIM with the appointment of a Professor of Genetic Epidemiology as Principal Investigator within CARIM (the first female PI after years), together with a visiting professorship to be advanced to a full professorship at Maastricht University. Her research group will also support a newly formed CARIM initiative on Systems Biology, which, in turn, will liaise with existing initiatives of Systems Biology at Maastricht University (MaCSBio).

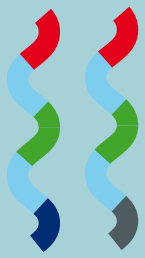
Further strategic topics which CARIM addressed or began to tackle in 2014 were: i) re-organisation of Theme III (Vascular Biology), ii) strengthening the interaction between basic- and clinical research groups in the sense of a translational approach which is increasingly required for (bio-)medical

research by grant givers, governments and society, iii) accommodation of new biomedical imaging techniques and procedures coming along with three recently appointed University Professors at Maastricht University, each concerned with another aspect of future-oriented analytic and regenerative medicine technologies, and iiii) expediting the cooperation of CARIM with the Heart-Vessel Centre (HVC) to an integrated Cardiovascular Centre (CVC) at Maastricht University Medical Centre (MUMC+).

Finally, efforts have been intensified to recruit promising students in CARIM's PhD program hoping that some of them will carry on the flag of high-quality biomedical research at CARIM and other institutions in the future.

Strategies, whether based on visions or not, are only as good as the people who implement them. I trust in CARIM with its excellent researchers, well-organised administration, highly motivated PhD students and competent technicians, continuously supported by the Dean of our Faculty. Together, in alliance and cooperation with the other schools at Maastricht University and a host of scientific institutions on a national and international level, we can face and meet the strategic challenges of the time and maintain CARIM at the high level of scientific and educational quality that has already been achieved.

Professor Thomas Unger
Scientific Director CARIM
School for Cardiovascular Diseases



PROFILE

01

PROFILE

Founded in 1988, the Cardiovascular Research Institute Maastricht (CARIM), School for Cardiovascular Diseases, has established itself as a leading research institute in the field of cardiovascular disease. At CARIM, basic mechanisms as well as early diagnosis and individual risk stratification of cardiovascular diseases are studied, allowing faster translation of new research concepts to clinical practice. New findings, products and techniques which can be applied in healthcare are evaluated, often in collaboration with private companies, and the results of scientific research are published in high-ranking international journals. Master's students, PhD students and MD students are trained to become independent researchers, and post-docs are trained to become leading scientists in the field of cardiovascular disease.

CARIM is built around three broader research themes, each led by a program leader: I) Thrombosis and Haemostasis, II) Cardiac function and failure and III) Vascular biology. These three themes comprise 26 basic and clinical programs, each led by a Principal Investigator (PI). The PIs are responsible for the scientific progress of their program, for linking activities and seeking collaborations between PIs and themes, for mentoring of PhD students and post-docs and, finally, for the financial basis of the program. All three themes involve basic and clinical programs. Cardiovascular scientists from around the world join CARIM because it values open communication, close cooperation, high ambitions, good facilities and a critical learning. CARIM is one of the six research schools of the Faculty of Health, Medicine and Life Sciences (FHML) of Maastricht University and is embedded within the Maastricht University Medical Centre+ (Maastricht UMC+). CARIM is recognised by the KNAW as a research school and as an international training site for Early Stage Researchers in the framework of the Marie Curie Program.

CARIM plays an important role in public-private research partnerships as main author and project manager of 6 out of 7 cardiovascular projects of the Centre for Translational Molecular Medicine (CTMM) in the Netherlands, CTMM is a public-private consortium that comprises universities, academic medical centres, medical technology enterprises and chemical and pharmaceutical companies. Some of the CTMM programs were expanded with valorisation grants in 2013. Other public-private research partnerships in which our researchers participate are: the BioMedical Material program (BMM) and Top Institute Pharma. In addition, CARIM is a member of several international networks, including the Horizon 2020 program in conjunction with other European institutions and the Leducq Transatlantic Network.

KEY FIGURES 2014

ANNUAL BUDGET: **21.407** K€

NEW CONTRACTS AND GRANTS: **8.106** K€

RESEARCHERS: **178** FTE

TECHNICAL AND SUPPORTING STAFF: **68** FTE

DEPARTMENTS/DISCIPLINES: **13**

SCIENTIFIC ARTICLES: **584** (Wi-1: 527)

PhD THESES: **35**

PATENTS: **3**

To translate research into clinical practice, CARIM, in close collaboration with the Heart-Vessel Centre (HVC) of the Academic Hospital Maastricht, under the name of the Cardiovascular Centre Maastricht (CVC) is aiming to develop into a unique internationally recognised centre of excellence in cardiovascular medicine in research (including translational research and medical care).

MONIKA STOLL
INTERVIEW

When Monika Stoll wanted to go to the States after obtaining her PhD, her supervisors decided she should work at a genomics lab. Until then, she had been working in cardiovascular research, where her mentors were Thomas Unger and Martin Paul. “They decided this for me and I just went along, very naively I must say.” It turned out to be a very good choice.

Not only because she published a paper in Science as first author that is as novel today as it was fifteen years ago, which got her a professorship at the University of Münster, but especially because she discovered a way of working there that fuels her curiosity to this day. In 2014, CARIM started the process of changing her status from ‘visiting professor’ to ‘professor/Principal Investigator’.

Monika Stoll likes flat hierarchies, like those that exist in the US and the Netherlands. At the Westfälische Wilhelms-Universität Münster, she leads a research group on genetic epidemiology, consisting of mathematicians, biologists, informatics experts and others. “I always call it my personal zoo, and I’m one of the zoo animals in it. It’s a challenge every day, working with all these different people with different ideas about research. But we’re all equal. I’ll never say: I’m doing the research. We are.” Besides leading her group of nine researchers she is also the scientific director of the genomics core facility. “We do the next generation sequencing for the entire medical faculty, so it’s quite an operation. I love it.”

“GENOMICS RESEARCH FUELS MY CURIOSITY”

BEAUTY

Her main research interest is how chronic inflammation relates to the onset and progression of cardiovascular disease. But with her expertise in genetics she could just as easily work in another field. “That’s the beauty of genetics: the fundamental principles apply to everything which is heritable. It doesn’t matter what phenotype you’re looking at; whether it’s tomatoes or heart disease or something else.” The research methods that she learned at the genetics lab of Prof. Howard Jacob, and that she still applies, initially shook her up. “The first three months I was so stressed out! It was a completely different concept of working. Instead of working on one molecule or pathway, Jacob said: ‘We’re going in there completely hypothesis-free. We’re asking the genome and the genome is giving us the answer.’ After six months I realised it was exactly the way I wanted to work.”

GENOMICS BASICS

She explains the basic concept of genomics. Every person has about three million different markers in his or her genome, which define the difference between two individuals. With the current technology, a person’s genotype can be assayed on a tiny chip overnight. “Then you ask the question whether this person, who has, for example, heart failure, differs at these markers from someone who doesn’t, and you do that in large populations. So you genotype anonymous markers in the genome, compare lots of samples, then run statistics and the genome throws back at you: there’s something on chromosome 5, for example. On this chromosome there are ten genes, so you’ve now narrowed down your search from 28 000 genes to 10.” The big difference with other research is going in there without a prior hypothesis.

NEXT GENERATION SEQUENCING

One of the most exciting technological advances in her field is “next generation sequencing”. The Human Genome Project, in which Stoll was involved from 1996, took almost fifteen years, involved 400 laboratories and cost about 300 million dollars. “Technological innovation now allows us to sequence the human genome in eleven days for 3000 dollars. This is what makes it so much fun. The biggest obstacle, and this is one of the things I try to address at CARIM, is that the technology is way ahead of our understanding of what to do with all these data. In many instances we don’t know how to analyse them and to translate them into clinical benefits, which has always been a top priority in the genome field.” In genetics, she knows, everything has changed in the past decade, due to the rapid advancement in technology. “It’s all about sharing data, working in large consortia where walls between different fields of life sciences crumble, in an international environment; that really fits my personality.”

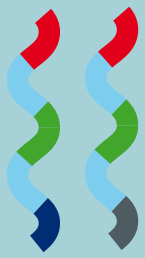
PERFECT MATCH

She was very pleased with Thomas Unger’s invitation two and a half years ago to work at CARIM on a part-time basis. The University of Münster is one of the biggest in Germany, very innovative, but unfortunately the strong cardiovascular emphasis has somewhat faded in the past ten years. The request from Maastricht was exactly what she was looking for. And CARIM in its turn found a perfect match in Monika Stoll as well. “CARIM is a very strong institute, particularly when it comes to the functional work. The people are very good at describing cardiovascular phenotypes. Researchers like Paul Volders, Leon de Windt and Uli Schotten had some research questions they wanted to address and were looking for someone to help with the genetics and genomics too get to another dimension of research. They saw how genomics and genetics are creeping into clinical research and practice. Think of individualized medicine. We turned out to be a good match; we’ve worked together ever since and the plan is for me to be a Professor of Genetic Epidemiology and Statistical Genetics from July 2015.”

WORM COHORT

She is also impressed by some clinical cohorts that CARIM researchers have. “I’m working with Paul Volders, who has this fantastic large family of 3000 people, living near the Worm river. This ‘Worm cohort’ has a founder mutation, but the family members represent differently in their cardiology. We try to disentangle how much is genetics. I’ve not come across such a unique population in Europe before, with so much information. That makes it really interesting for a geneticist. I’m wondering, for example, how a mutation that causes people to die from cardiac disease can still be maintained in a population? It should be eradicated.” With Uli Schotten she has been working on atrial fibrillation, and they have already managed to get two grants enabling them to appoint two PhD students at Maastricht. “I will primarily be working on heart phenotypes in the restricted time I have in Maastricht.”

She will continue to live in Münster, working in her “zoo”, and will be in Maastricht one week a month. She is very eager to discover new genes or mutations that can be used to find a cure. “Those are the best days and they’re very rare. Fortunately I have a high tolerance for frustration and I like to laugh a lot.”



ORGANISATION

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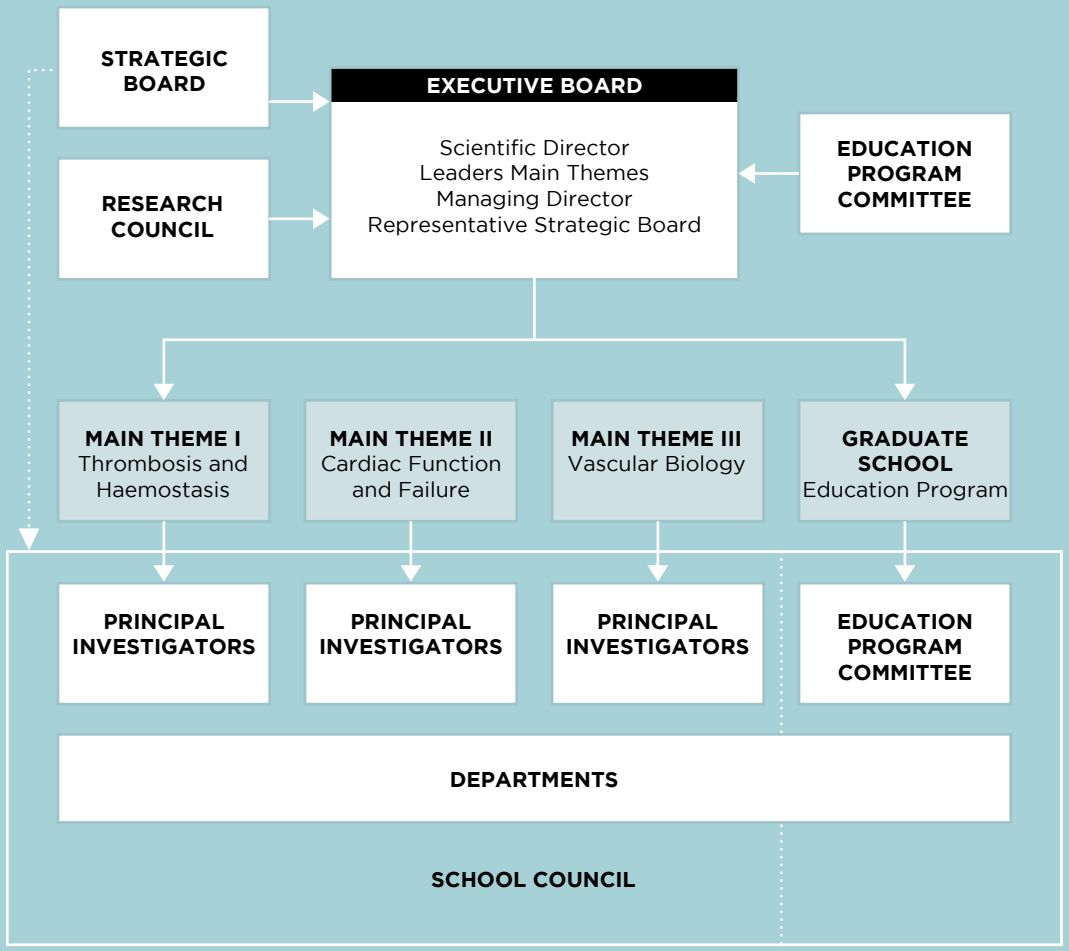
ORGANISATION



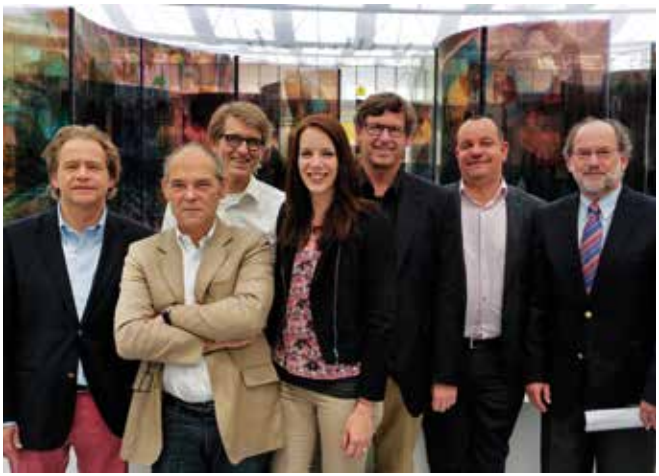
CARIM's Scientific Director, Professor Thomas Unger, has the final responsibility for the research institute, including the organisation and management of the research program, the scientific output, the training of Master's and graduate students and post-doctoral fellows, and the financial management and the public relations of the institute. At the end of 2012, the Strategic Board (SB) was formed to advise and support the Scientific Director in managing long term policy. The board is also a discussion forum and generates written visions of the future of CARIM and its survival in an increasingly competitive European scientific environment. The SB meets regularly to discuss issues such as grant applications, national and international collaboration networks, interdisciplinary communication and CARIM's visibility in the national and international cardiovascular fields.

The Scientific Director is assisted by the Managing Director, Rob van der Zander, who takes care of the financial and human resource management. Together with the three leaders of the main themes and a representative from the SB, the Scientific and Managing directors make up the Executive Board (EB) of the institute. The EB meets monthly to discuss and decide upon issues at strategic and operational level. The EB is advised by three councils/committees: the SB, the Education Program Committee and the CARIM Research Council. The Educational Committee coordinates both the PhD- and Master's training programs and consists of the PhD Program Coordinator, the Master Program coordinator, 4 CARIM staff members (of which 2 clinical) and 3 PhD students. The committee advises the EB on all issues regarding the PhD and Master's programs. At the end of 2009 the EB established the Research Council (RC). The RC advises the EB and PIs on the quality of all research proposals and meets regularly to discuss grant applications.

Finally, the School Council consists of the principal investigators (PIs) and department heads and meets four times a year.

EXECUTIVE BOARD

- Professor Thomas Unger, Scientific Director
- Professor Tilman Hackeng, Leader Main Theme I
- Professor Harry Crijns, Leader Main Theme II
- Professor Coen Stehouwer, Leader Main Theme III
- Professor Leon de Windt, representative Strategic Board (until June 2014)
- Professor Uli Schotten, representative Strategic Board (from September 2014)
- Rob van der Zander, Managing Director



STRATEGIC BOARD

- Professor Uli Schotten, chairman
- Professor Hugo ten Cate
- Professor Leon de Windt
- Professor Chris Reutelingsperger
- Professor Robert van Oostenbrugge
- Dr Judith Sluimer

PRINCIPAL INVESTIGATORS

- Professor Erik Biessen, Dept. of Pathology
- Dr Matthijs Blankesteijn, Dept. of Pharmacology
- Professor Hans Peter Brunner-La Rocca, Dept. of Cardiology
- Professor Harry Crijns, Dept. of Cardiology
- Professor Hugo ten Cate, Dept. of Internal Medicine
- Professor Tammo Delhaas, Dept. of Biomedical Engineering
- Professor Tilman Hackeng, Dept. of Biochemistry
- Professor Johan Heemskerk, Dept. of Biochemistry
- Professor Stephane Heymans, Dept. of Cardiology
- Professor Jan Glatz, Dept. of Genetics and Cell Biology
- Professor Leo Koole, Dept. of Biomedical Engineering
- Dr Bram Kroon, Dept. of Internal Medicine (interim)
- Professor Jos Maessen, Dept. of Cardiothoracic Surgery
- Professor Robert van Oostenbrugge, Dept. of Neurology
- Professor Mark Post, Dept. of Physiology
- Professor Frits Prinzen, Dept. of Physiology
- Professor Chris Reutelingsperger, Dept. of Biochemistry
- Professor Harald Schmidt, Dept. of Pharmacology
- Professor Uli Schotten, Dept. of Physiology
- Professor Bert Smeets, Dept. of Genetics and Cell Biology
- Professor Coen Stehouwer, Dept. of Internal Medicine
- Professor Harry Struijker Boudier, Dept. of Pharmacology
- Dr Hans Vink, Dept. of Physiology
- Professor Paul Volders, Dept. of Cardiology
- Professor Christian Weber, Dept. of Pathology
- Professor Joachim Wildberger, Dept. of Radiology
- Professor Leon de Windt, Dept. of Cardiology

RESEARCH COUNCIL

- Professor Frits Prinzen, chairman
- Dr Kristiaan Wouters, secretary
- Professor Erik Biessen
- Dr Matthijs Blankesteijn
- Professor Jan Glatz
- Professor Chris Reutelingsperger
- Dr Henri Spronk
- Professor Thomas Unger

EDUCATION PROGRAM COMMITTEE

- Dr Marc van Bilsen, chairman, PhD Coordinator
- Dr Adriaan Duijvestijn, Coordinator Biomedical Sciences Master
- Dr Matthijs Blankesteijn, staff member
- Dr Eline Kooi, staff member
- Dr Hans Vink, staff member
- Dr Simone Sep, staff member
- Yvonne Olischläger, PhD student
- Siamack Sabrkhany, PhD student (until January 2015)
- Emiel van der Vorst, PhD student (until December 2014)
- Tom Mastenbroek, PhD student (from September 2014)
- Elke Marsch (from September 2014)
- Armand Jaminon (from January 2015)

CARIM OFFICE

The CARIM office consists of Riet Daamen, Tara de Koster and Esther Willigers. The controller is Sietske Satijn.

HR-SUPPORT

Patrick Janssen and Yves Engelen of the Human Resources Department of Maastricht University are related to CARIM.

ADMINISTRATIVE SUPPORT

The Finance Department of Maastricht University provides support on accounting the CARIM research projects on a part-time basis. At this moment the Finance employees are Henny Kerckhoffs, Esther van Heel, Joost von Weersch (until October 2014), Jan Willem Janssen (until July 2014), Patrick van Schoubroeck (from August 2014), Dayenna Bakker (from October 2014) and Mark van Gisteren (from November 2014)

PARTICIPATING DEPARTMENTS AND DISCIPLINES

The research in the three main themes involves the research activities of people working in several basic and clinical departments/disciplines of Maastricht Medical Centre+.

BASIC RESEARCH DEPARTMENTS

- BIOCHEMISTRY
- BIOMEDICAL ENGINEERING
- GENETICS AND CELL BIOLOGY
- PHARMACOLOGY
- PHYSIOLOGY

CLINICAL DEPARTMENTS

- CARDIOLOGY
- CARDIO-THORACIC SURGERY
- CLINICAL CHEMISTRY
- INTERNAL MEDICINE
- NEUROLOGY
- PATHOLOGY
- RADIOLOGY
- SURGERY

INTERVIEW

ERIK BIESSEN

PUTTING CARIM IMMUNOLOGY ON THE MAP

FRAMING THE PLAQUE IN ITS CONTEXT

If atherosclerosis turns out not to be a local phenomenon, but to be part of the overall context/environment in the body and influenced by a multitude of all kinds of factors, then gaining a deeper insight into the problem also involves taking this environment into account. “Immunology is a very powerful/ ideal approach to understanding the relation between a plaque and its environment”, says Prof. Erik Biessen, “precisely because immunity should not be seen merely as a defence mechanism, but just as much as a communication channel between cells.”

It provides an excellent opportunity for a better understanding of the comorbidities associated with atherosclerosis. So there is every reason to invest in establishing a centre for cardiovascular immunology over the next few years.

Erik Biessen has been working at Maastricht since 2007, where he heads CARIM's Experimental Vascular Pathology group. Before moving to Maastricht, he had spent sixteen years working at Leiden University, where he also did research into atherosclerosis. "I was, and still am, interested in the immunological aspects, that is, the inflammatory processes, which play a part especially in the late, clinical stage of atherosclerosis, when plaques may cause a cardiac infarction." He used to work mainly with in-vitro and mouse models, and had little contact with clinical staff. When CARIM invited him to come to Maastricht, this meant a unique opportunity to work in a clinical setting, using human plaque samples.

"The first time I saw a human plaque, I was shocked. Its structure and composition were completely different from the characteristics that I was familiar with from my work with mice." That was when Erik Biessen realised he might have been on the wrong track altogether. "I think many research groups are backing the wrong horse by focusing on resolving plaques in mice. So far, the process of translating the findings of mouse studies to humans has not been very successful, particularly as regards immunological processes. So I then realised we should reverse the research process; not start by exploring mouse models and then try to translate the findings to humans, but include humans in our hypotheses from the beginning. We should examine human materials, as any dedicated pathologist does."

CONCENTRATING EXPERTISE

Another slightly painful realisation followed. "I thought: if immunology is such an important factor, maybe Maastricht isn't the right place for me. Although some immunological research is being done at CARIM, and in a wider sense also in the Faculty, it is scattered across various departments, like Pathology, Biochemistry, Cardiology and Internal Medicine. What might be even more worrying is that the infrastructure required to concentrate all available expertise is not easy to find, or even lacking altogether, and that there doesn't appear to be enough critical mass. As a result, everyone is individually spending a lot of effort on things like introducing new models."

He finds that whereas the interest in immunology from various departments in Maastricht is clearly growing, the discipline unfortunately has actually been somewhat neglected in recent years. "A number of excellent immunologists have moved elsewhere, leaving a kind of vacuum. There was a feeling that there was insufficient justification for cardiovascular immunology at Maastricht, that it didn't offer enough added value. In fact, we're about the only university medical centre in the Netherlands that doesn't have its own dedicated immunology department. That seems to me a missed opportunity."

"WHAT WE NEED IS MORE VISIBILITY"

A FINE CLUSTER

The UM management agreed with Biessen's view. When he suggested to them at the end of 2014 to support the initiative to establish a cardiovascular immunology centre, they readily appreciated its importance. And so Biessen will be spending all his energy over the next twelve to eighteen months assessing what is feasible at CARIM and beyond. "We need to carefully identify the gaps in our knowledge and technology. If we want to achieve the necessary critical mass, we will also have to involve people at Hasselt and Aachen, where they have excellent translational research groups, like those led by Professors Trautwein and Pabst at the Institute of Molecular Medicine of RWTH Aachen. Together we might form a strong cluster." The fact that he has been given a part-time position at RWTH Aachen may also be helpful.

It is not clear yet what exactly the centre will look like. "At first it might just be a virtual platform for collaboration, with a website and an annual conference. The biannual Maastricht Immunology Meeting, organised by Marjo Donners and Kristiaan Wouters, is a good starting point, but more can be done to raise the profile and impact of this platform. And CARIM has agreed to make a tenure available to make this happen. We want to find a top immunology researcher to fill this post, as I'm really more of a self-proclaimed immunologist", smiles Biessen. "I'm more of a generalist, which as I realize is at once my strength and my weakness."

He is very enthusiastic about the upcoming developments. "Immunology is a complex and therefore intellectually challenging field. There are so many new developments, especially in molecular immunology, so I'm really excited to work on those. And when the intended reinforcement at Maastricht materialises, I think we'll definitely have more than enough quality in Maastricht and the Euregion to be competitive. But we have to concentrate our efforts, and raise our profile in the outside world."

JOINING FORCES

In the near future, his energy will therefore be focused partly on instilling the same kind of enthusiasm in his CARIM colleagues. "People have to realise that there is an added value in joining forces in this discipline. And not only in a virtual sense, but also, for example, in developing technology together, so that we're not each of us inventing the same wheel. They have to acknowledge the importance of long-term thinking. The second challenge in these 'times of financial cholera' is to convince the CARIM management, and perhaps also the Faculty, that they should make a few targeted some capital-intensive investments."

He is eager to turn it into a success. "I don't think our ambition should be to compete with the molecular biology research that is already established at other universities. What I'm thinking about is especially the translational immunology, an area in which we not only have a right to exist, but can actually compete with the top institutes. And in a few areas, such as cardiovascular immunology, we even have a broader research base than other Dutch universities. What we need is more visibility."

HIGHLIGHT THEME I

JUDITH COSEMANS

DEPARTMENT OF BIOCHEMISTRY

Acute and persistent platelet and coagulant activities in atherothrombosis

Atherothrombosis results from rupture or erosion of an atherosclerotic plaque, by which plaque-derived constituents are exposed to the blood stream. Platelets adhere to sites of plaque disruption, become activated, and secrete secondary mediators that recruit other circulating platelets to form a thrombus (Figure 1). In addition, platelets support coagulant activity by forming a procoagulant surface with exposed phosphatidylserine and by providing sites for thrombin and fibrin formation.[1] Extensive thrombus growth can result in occlusion at the site where the thrombus is formed, or in downstream vessels, by emboli. These events are the most common cause of acute ischaemic conditions such as heart attack and stroke. Although the currently used antiplatelet and anticoagulant therapies effectively reduce premature deaths from atherothrombotic events, patients are still at risk of bleeding or recurrent thrombotic events.[2]

NOVEL INSIGHTS INTO THE CLASSICAL MODEL OF COLLAGEN-INDUCED PLATELET ACTIVATION AND ACUTE THROMBUS FORMATION

There is considerable evidence that fibrillar type I collagen starts to activate platelets upon exposure to the blood stream. Previously we have shown that blockage of the platelet collagen receptor glycoprotein VI (GPVI) greatly suppressed the thrombotic process in Apoe$^{-/-}$ mice both *in vivo*, triggered by ultrasound-induced plaque rupture,[3,4] and *in vitro*, using a flow chamber.[5] The classical concept, in brief, is that at high arterial wall shear rates, initial platelet rolling is regulated by the interaction of platelet glycoprotein Ib-V-IX (GPIb) with von Willebrand factor (vWF), which is bound to collagen. Platelet adhesion and activation by vWF/collagen is then enforced by GPVI, with an assisting role for integrin $\alpha 2\beta 1$.[1] However, in the perturbed atherosclerotic vessel wall, platelets will be in contact with many other adhesive ligands than collagen and vWF. Knowing that platelets express adhesive receptors for a range of vascular and plasma proteins, we made a systematic comparison of 52 adhesive surfaces with components activating the main platelet-adhesive receptors, and of eight output parameters reflecting distinct stages of thrombus formation. Using systems biology approaches, we employed the test outcomes in a model predicting the roles of various receptors in thrombus formation at high and low wall shear rates. We found that not only the traditional model, consisting of surfaces

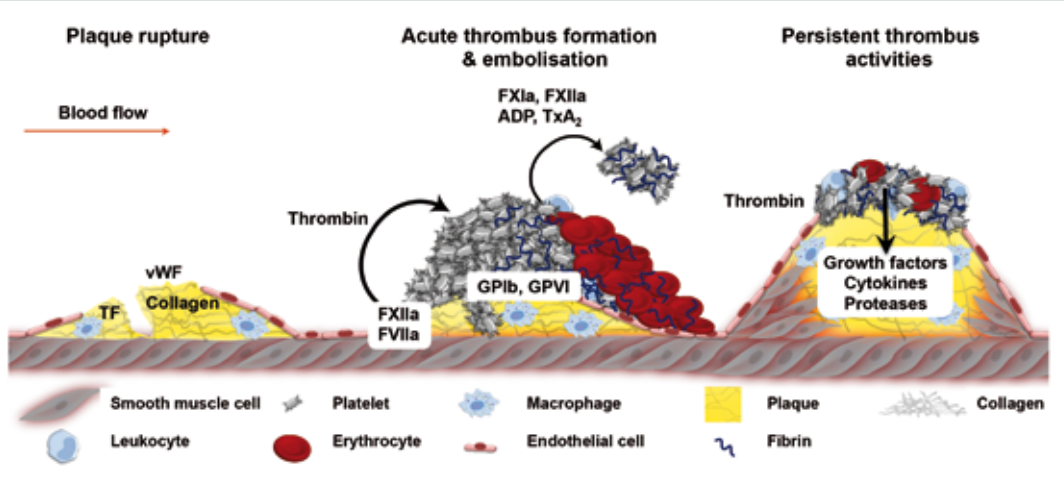


FIGURE 1
Schematic overview of factors involved in thrombus formation at a site of plaque disruption. Adapted from.[11]

binding GPIb (vWF) in combination with integrins α2β1 and GPVI, but also surfaces binding GPIb with α6β1 (laminin) and CLEC-2 (podoplanin) resulted in the formation of large thrombi.6 Together, the results of this multi-parameter assessment of thrombus formation have enabled us to design a substrate array assay involving all main platelet receptors, and investigate the value of such a test in predicting the risk of bleeding.[6] The next step will be to use this multi-parameter test to study groups of patients who have reduced platelet function and patients in whom we expect an increase in platelet function. In this way, we hope to be able to establish the most predictive combination of parameters for the clinical outcome.

DISTINCT BUT COMPLEMENTARY ROLES OF THE EXTRINSIC AND INTRINSIC COAGULATION PATHWAYS IN ACUTE ATHEROTHROMBOSIS

In the atherosclerotic vessel wall, several cell types express tissue factor (TF), especially the macrophages and smooth muscle cells. Upon exposure to the blood stream, de-encrypted TF forms a complex with coagulation factor VII(a), which activates factor IX (FIX), factor X (FX) and prothrombin.[1] Using Apoe$^{-/-}$ mice subjected to ultrasound plaque rupture or photochemical injury, we and others have shown that inhibition of the TF/FVIIa complex suppresses the process of thrombus formation, pointing to a key role of the extrinsic coagulation pathway in experimental atherothrombosis.[4,7]

Collagen type I not only binds and activates platelet GPVI, but has also been shown to activate coagulation factor XII (FXII),[8] which triggers the intrinsic pathway of coagulation. In contrast to the extrinsic (TF and FVIIa) and common pathways (FXa and thrombin), factors of the intrinsic pathway of coagulation (FXIIa, FXIa, and FIXa) are not essential for haemostasis. Several

observations point to a unique role of the intrinsic pathway in experimental atherothrombosis (Figure 1). Using an *in vivo* model of ultrasound-induced plaque rupture, we recently demonstrated that inhibition of FXIIa or treatment with FXI antisense oligonucleotides caused a substantial suppression of thrombus formation.[9,10] In *in vitro* studies where blood was flowed over plaque material, inhibition of FXII with corn trypsin inhibitor (human) or the absence of FXII or FXI (mouse) led to unstable thrombus formation.[9] Together, this suggests that TF–FVIIa and FXIIa-triggered coagulation pathways have distinct but complementary roles in atherothrombus formation. The TF–FVIIa pathway contributes to initial thrombus build-up, whereas FXIIa bound to fibrin-containing thrombi ensures thrombus stability. Since the majority of this work points to a clear role of the FXII pathway in atherothrombus formation without affecting haemostasis, the intrinsic coagulation pathway may be an attractive target for antithrombotic drugs, with low risk of bleeding.

EMERGING EVIDENCE FOR PERSISTENT PLATELET AND COAGULANT ACTIVITIES IN ATHEROTHROMBOSIS

In addition to the acute process of thrombus formation, there is increasing clinical evidence for a more persistent activity of thrombi.[11] For instance, there are strong indications that arterial thrombi, obtained by aspiration from patients with acute myocardial infarction, often remain present and active for a prolonged time and that the age of these thrombi is an independent risk factor for long-term mortality.[12] In addition atherosclerotic plaques are frequently multilayered with intraplaque fibrin patches. Together, this is suggestive for repeated episodes of (clinically silent) thrombotic activities followed by lesion growth. The mechanisms underlying these persistent thrombus activities are only slowly emerging and point so far to a role for both activated platelets and ongoing thrombin generation (Figure 1).[11] I aim to elucidate (i) which platelet and coagulation processes are continuously active after a thrombus is formed; (ii) how these processes affect vascular remodelling, and (iii) what intervention could suppress these processes. I currently hold a personal grant from the Dutch Heart Foundation to study the role of platelet-derived matrix metalloproteinases in vascular remodelling.

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FACTS AND FIGURES

03

FUNDING AND EXPENDITURE AT INSTITUTIONAL LEVEL 2009-2014

	2009	2010	2011	2012	2013	2014
	K€	K€	K€	K€	K€	K€
FUNDING						
Direct Funding structural	8.653	8.411	8.242	7.391	7.419	7.500
Direct Funding specific programs	3.606	3.603	2.830	2.717	2.272	1.309
Total Direct Funding (1)	**12.259**	**12.014**	**11.072**	**10.108**	**9.691**	**8.809**
Research grants (2)	1.201	2.140	1.284	1.566	1.730	1.481
Contract research (3)	9.385	9.900	13.202	13.464	13.456	11.117
	10.586	**12.040**	**14.486**	**15.030**	**15.186**	**12.598**
Total funding	**22.845**	**24.054**	**25.558**	**25.138**	**24.877**	**21.407**
EXPENDITURE						
Personnel costs	14.656	15.024	15.984	16.492	17.501	16.343
Other costs	6.469	7.474	7.855	8.475	8.379	6.392
Total Expenditure	**21.125**	**22.498**	**23.839**	**24.967**	**25.880**	**22.736**
RESULT	**1.720**	**1.556**	**1.719**	**171**	**-1.003**	**-1.328**

(1) Direct funding originating from the University as provided by the Dutch government

(2) Research funds received in competition from national science foundations and governmental organisations e.g. NWO, ZonMW, STW, KNAW

(3) Third party funding received in competition from European Union, Netherlands Heart Foundation, Dutch Kidney Foundation, Industry

RESEARCH OUTPUT IN 2009-2014

	2009	2010	2011	2012	2013	2014
SCHOOL LEVEL						
Scientific publications	514	544	571	635	605	584
Other publications	45	37	53	80	50	70
PhD theses	32	35	39	50	34	35
Total* (I)	**591**	**616**	**666**	**765**	**689**	**689**
Academic staff** (II)	37,0	38,3	34,3	33,1	32,4	33,4
Ratio I and II	16,0	16,1	19,4	23,1	21,3	20,6
THEME I						
Scientific publications	89	95	107	108	111	109
Other publications	9	6	12	12	13	19
PhD theses	9	5	8	8	7	10
Total	**107**	**106**	**127**	**128**	**131**	**138**
THEME II						
Scientific publications	153	190	214	246	240	239
Other publications	11	6	13	25	20	34
PhD theses	8	9	14	20	17	10
Total	**172**	**205**	**241**	**291**	**277**	**283**
THEME III						
Scientific publications	321	312	309	353	331	313
Other publications	26	25	28	45	22	32
PhD theses	15	21	17	22	12	17
Total	**362**	**358**	**354**	**420**	**365**	**362**

* Please note that the sum of the publications in Themes I, II and III exceeds the total number of publications at School level, due to a double counting of publications with authors from different themes ** Academic staff: PhD students and post-docs not included

PhD theses: including PhD theses externally prepared

Scientific publications: Wi-1 publications in refereed SCI-SSCI indexed journal, excluding abstracts, Wi-2 publications in refereed non SCI-SSCI indexed journals, and Letters to the Editor

Other publications: Wn (publications in national journals), Wb (book, or contribution to book, conference papers/proceedings), Vp (professional publications in national or international periodical)

NEW CONTRACTS AND GRANTS CONCLUDED IN 2014

FUNDING	THEME I	THEME II	THEME III	TOTAL SUPPORT
	K€	K€	K€	K€
Type 2	953	1.307	676	2.936
Type 3	1.267	1.638	512	3.418
Type 4	116	151	1.115	1.382
Type 5	250	250	250	750
Total	**2.586**	**3.347**	**2.553**	**8.486**

Type 2 Grants received in competition from national and international science foundations (NWO/ZonMw, STW, KNAW)

Type 3 Grants received from third parties for specific research activities and from charities (NHS, EU Framework, CTMM, BMM, etc.)

Type 4 Industry, excl. CTCM (turn over in 2014: 1,848 K€)

Type 5 Annual support (750 K€) Cardiovascular Center-CARIM “Pieken vanuit de Breedte”

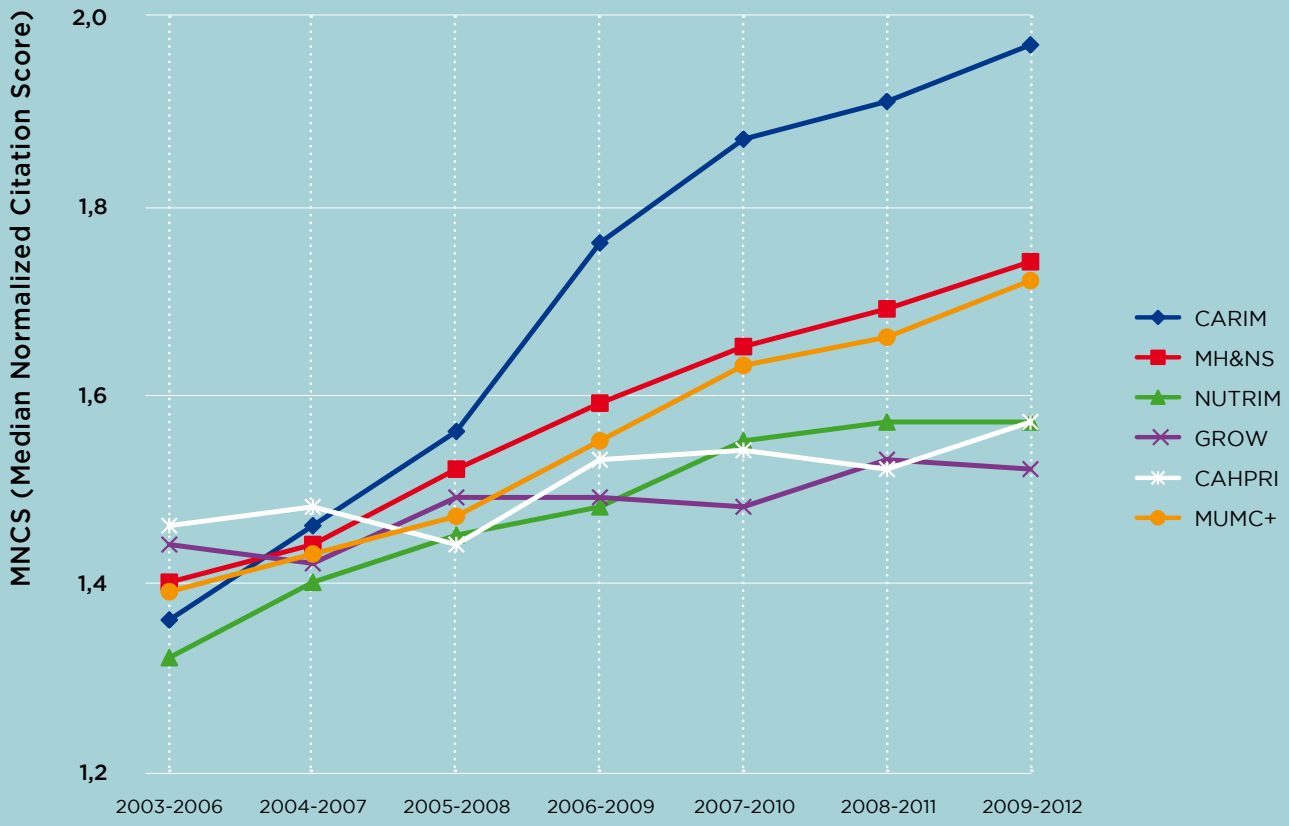
SUMMARY OF SCIENTIFIC AND TECHNICAL STAFF CARIM 2014 (IN FTE)

RESEARCH AREA	WP1			WP2			WP3			WP4			azM	TOTAL
	Faculty	PhD-stud	Post-doc	WP	PhD-stud	Post-doc	WP	PhD-stud	Post-doc	WP	PhD-stud	Post-doc	WP	FTE
Thrombosis and haemostasis	7,5	3,9	0,6	-	1,0	2,6	-	10,7	2,5	1,3	4,3	4,9	1,6	40,9
Cardiac function and failure	13,2	4,7	0,9	1,0	8,0	2,3	-	18,5	13,3	-	2,0	-	4,2	68,1
Vascular biology	12,8	4,9	2,9	0,4	0,6	2,3	0,9	23,9	15,6	-	1,5	0,3	3,4	69,4
TOTAL	**33,5**	**13,5**	**4,4**	**1,4**	**9,6**	**7,2**	**0,9**	**53,1**	**31,4**	**1,3**	**7,8**	**5,2**	**9,2**	**178,4**

RESEARCH AREA	OBP 1	OBP 2	OBP 3	OBP 4	azM	TOTAL
Thrombosis and haemostasis	5,0	0,7	2,3	2,7	2,1	12,9
Cardiac function and failure	14,4	2,0	3,6	-	-	20,0
Vacular biology	11,9	0,2	18,0	1,4	3,5	35,0
TOTAL	**31,3**	**2,9**	**23,9**	**4,1**	**5,6**	**67,9**

WP scientific staff
OBP technical staff
1 University
2 NWO/KNAW
3 non-profit organisations
4 industry
azM University Hospital Maastricht

LOCAL PERFORMANCE CARIM



Source: Bibliometric study on Dutch academic medical centers 1998-2012/2013 – enter for Science & Technology Studies (WTS) and Dutch Federation of University Medical enters (NFU)

INTERVIEW
BLANCHE SCHROEN

She spent years researching heart failure due to high blood pressure. “But very few people that develop heart failure only have high blood pressure. Life is not as simple as that. I’m now at the stage where I can look for mechanisms using more complex models, in collaboration with the clinical people.”

In 2014, Blanche Schroen (1980) was given a Vidi grant by the Netherlands Organisation for Scientific Research (NWO) and a Dekker Senior Postdoc grant by the Netherlands Heart Foundation. “I’m still just as ambitious as I used to be.”

When Blanche Schroen was told at primary school that university was the highest possible type of education she could end up in, she immediately decided that was where she was going to go. “I’ve always been eager and inquisitive.” So as a research scientist, she feels like she is working on her hobby all day. “You’re exploring a completely virgin territory, working with a team of young, very bright people. In most cases, your hypothesis turns out to be incorrect, which means you have to have a lot of stamina, but occasionally something wonderful emerges, which you could never have imagined. Sometimes it’s difficult to organise enough support at the lab, but as far as the research is concerned, I never despair. It gives me new energy every day.”

molecules from human “junk DNA” which might contribute to the development of heart failure. If the levels of these long RNA molecules could be manipulated, it might lead to more targeted drugs than the ones that are available now.

AMBITIOUS

After she had successfully concluded her tenure track and had obtained a permanent position, she was invited to join the *“Toptalenten”* program at the UM Faculty of Health, Medicine and Life Sciences in 2014. This group is basically being prepared for a professorship over a five-year period. “I’m still just as ambitious as I used to be, so in five years’ time I hope to be able to collaborate even more with other research groups, do even more clinically relevant research,

“YOU LEARN MORE IF YOU ALLOW YOURSELF TO BE VULNERABLE”

PUBERTY

Just before she received the two grants in 2014, she had reached a critical stage in her career. “I had to raise funds to be able to continue my own research, and I was going through some sort of puberty, which I think every tenure tracker at CARIM goes through at some stage. It’s the stage where you have to find your own course, and let go of your mentor. I had great drive, and I perceived that stage as a real fight with myself and with the system.” But then the grants came, so her research effort on early detection of heart failure and the possible development of medication is safe for the time being. Her Vidi-sponsored research focuses on

and secure other grants. And indeed perhaps become a professor. One of the course instructors in the talent class often talks about ‘Peter’s Principle’, which says that people often get promoted to a level above what they’re capable of. I hope I’ll recognise in time what the limits of my abilities are, rather than just aiming to go higher and higher to a level that I can’t handle.”

SNAPPISH

She emphasises that she can still learn a lot from her bright PhD students and from her mentor, Prof. Stephane Heymans, who is able to see the big picture and the clinical relevance.

She is especially proud of her four PhD students and the technicians, who present her on a daily basis with new data she can use to practise her "hobby". "I think people probably call me passionate. I always want to get the most out of everything, and I don't have a lot of patience for people with an indifferent work attitude. And I can be snappish: where my research area is concerned, I think I'm entitled to have my say as an expert." What worries her most is professional jealousy from fellow researchers who also apply for grants and may just fail to get them. "You know who's on the same career path in the same university, and things can get a little awkward if you manage to obtain two major grants in one year. I try to come across as someone who's accessible and doesn't live in an ivory tower where I'm invulnerable. I think you can get more done and learn more if you allow yourself to be vulnerable."

NICHE

Whereas at the start of her research career she had to deliberately focus on finding and occupying her own niche, she now thinks it is high time to start collaborating with the clinicians. "I find it incredible that neither researchers nor clinicians until recently paid much attention to the relations between things like heart failure, obesity and diabetes. We're currently working on a model that combines these three disorders, which of course means more complex and more expensive research. But as a researcher I'm now ready to tackle the more complex matters."

INTERVIEW INGRID DIJKGRAAF

Until a few years ago, Ingrid Dijkgraaf (1979) tried to plan ahead in her career.

"I was always busy planning where I wanted to be in five years' time. But I've found out that doesn't really work. If I hadn't got this Vidi grant, things would have been very different now." But she did get the grant, at a time when she was working in the US for eight months on a Fulbright scholarship. Her decision in 2011 to change from oncological research to cardiovascular diseases worked out very well.

"FORTUNATELY, PATIENCE IS ONE OF MY CHARACTER TRAITS"

Ingrid Dijkgraaf had an eventful year in 2014. She had just settled into her work at the Scripps Research Institute in California, on a Fulbright scholarship, when she was invited for the interview round for the Vidi grants. She flew back to the Netherlands for a week, and then it was a matter of waiting. "I knew I would get the decision on a particular day in May. I thought to myself I'll leave reading the email until the end of the working day, as I was nervous the news would be bad and it would ruin my mood." But the email brought good news. "I was over the moon. I immediately went to the supermarket to buy a bottle of wine for myself and some beer for my husband, who was with me in America. I saw a homeless person sitting by the supermarket and I offered him a beer too," she laughs. "Such a grant really motivates you." She had a "super time" in the US: "I learned a lot, not only professionally but also personally. My view of Americans has become much more favourable; they are welcoming and take an optimistic view of life."

PARASITE

Whereas before her stay in America she was mostly working on her own as a postdoc in the research group led by Prof. Tilman Hackeng, after her return she was able to start setting up her own group. She has already engaged one PhD student, and hopes to engage another one soon. "Suddenly you're a very busy person." Her research concerns plaques, the fatty deposits in blood vessels. When two of the body's large proteins interact, it accelerates the formation of plaques. "I'm studying which parts of the proteins actually interact. In addition, I'm studying whether it's possible to bind a protein obtained from ticks, these blood-sucking parasites, to one of these two human proteins, called RANTES, in such a way that it prevents the interaction that accelerates the plaque formation." She is currently synthesising the proteins *in vitro*. "We build them using chemical synthesis, so we can modulate them just as we want to."

SYNTHESIS

This technique of synthesising molecules is exactly the reason why she came to Maastricht University in 2011. Having studied molecular sciences at Wageningen University, she got her PhD from the Universities of Utrecht and Nijmegen for her work synthesizing molecules that bind to the new blood vessels growing in tumours. The subject fascinated her so much that she went to the Munich University of Technology for a postdoc position in the group led by Hans-Jürgen Wester. "At the time that was the best group in the world for radiochemistry and radiopharmacy. I learned a lot of new techniques there, for instance radioactive labelling of molecules so you can visualise what happens to them in vivo by means of imaging techniques." She returned to Nijmegen in 2009 to join her partner, but since the work there was more biological than chemical, she applied for a position in Maastricht in 2011.

PATIENCE

After her job interview she was invited to join the staff for drinks, and was immediately introduced to the joie de vivre culture in the southern provinces. “I was used to drinks with just some crisps and nuts, but here they had stuff like olives and French cheeses and bread laid out on the table.” When she started working at CARIM she had to brush up on her cardiovascular knowledge. “But that’s what I like about research. That and the unexpected things you encounter from time to time.” In her view, the presence of so many disciplines and research techniques at CARIM, and the proximity of the clinic, are major advantages. “It offers many opportunities to collaborate, which I do.”

When asked what she finds difficult about research, she answers: “Sometimes something you’re trying to do appears to be very simple, and yet it doesn’t work. That’s frustrating. But fortunately, patience is one of my character traits. I’m usually able to leave my work behind me when I return home.” By that time, she has usually had a nine-hour working day, and that five days a week. And after work, she often goes for a run. From time to time there’s a marathon to be run, like the one in London the previous weekend. “Once I’ve done a couple of miles, all thoughts of my work are gone.”

HIGHLIGHT THEME II

SANDRO GELSOMINO

DEPARTMENT OF CARDIAC SURGERY

From a two-step towards a one-step hybrid ablation of atrial fibrillation: the evolution continues

Improving the treatment of atrial fibrillation (AF) is one of the major challenges in cardiovascular disease for the next decades. For AF patients refractory to drug treatment and cardioversion, catheter-based interventions have been developed to restore sinus rhythm and to prevent secondary embolic complications such as cerebrovascular accidents. So far, two main types of interventional approaches have been used, one endocardial catheter based approach, applied by an electrophysiologist, and one epicardial surgical approach, applied by a cardiothoracic surgeon. In both of these interventions, scars are created by ablating atrial tissue, in order to prevent the occurrence of AF or, if it does occur, its persistence. The lesions affect the arrhythmia by either isolating arrhythmogenic foci or reducing the substrate for AF. Scars in the atrial tissue can be created by several tools, using a number of different energy sources like radiofrequency, cryoenergy, ultrasound and laser. The ultimate goal in creating a scar is to obtain a transmural lesion in the wall of the atrium. This is difficult to achieve with the current tools, however, as the thickness of the wall may vary. In addition, the cooling effect of the blood may prevent the ablation tool from delivering sufficient energy across the full thickness of the wall.

Bipolar ablation tools have been shown to be able to create continuous transmural lesions. When used on the beating heart, however, these bipolar tools are limited to the epicardium and to atrial tissue that can be clamped in between its jaws. This limits the use of such tools to certain parts of the atrium.

With the development of new tools and advanced techniques, the treatment of atrial AF has been moving towards a multidisciplinary approach which increasingly involves cardiac surgeons and electrophysiologists working together. Our group has introduced and developed the so-called hybrid approach, which combines thoracoscopic epicardial ablation with a percutaneous trans-septal procedure, the two being carried out in sequence in a single surgery session. Although clinical studies have confirmed the potential of this approach, what we have learnt from our clinical experience is that to raise the success rate of this procedure, especially in patients with long-standing and persistent AF, we have to increase our understanding of the limitations of the current energy sources and ablation catheters, and we have to develop new surgical tools enabling us to reliably create the transmural atrial

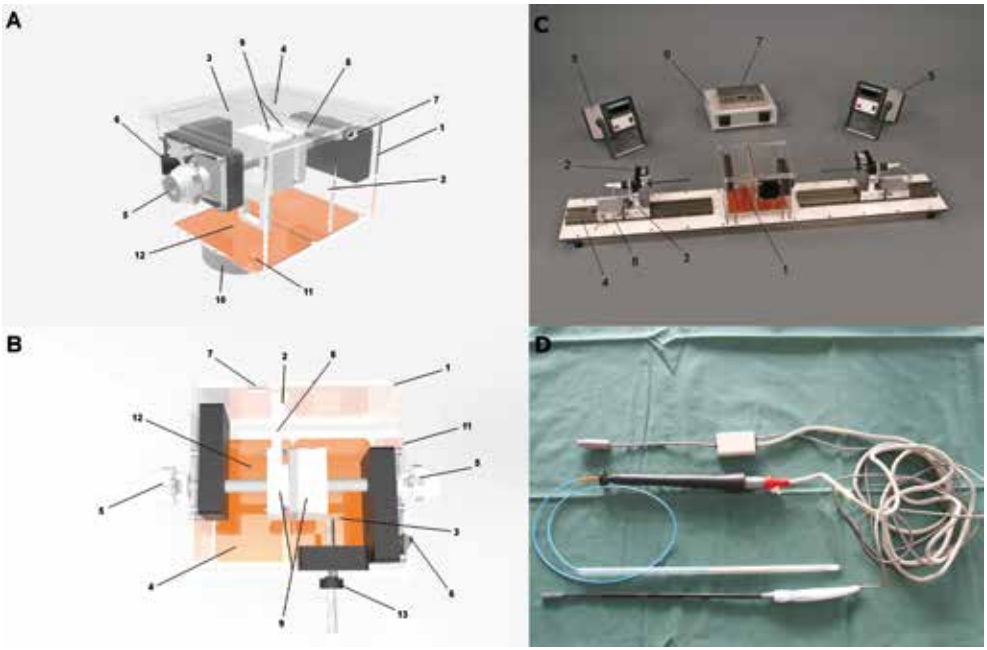


FIGURE 1
A-B. The ABLA-BOX (1) Plexiglas box; (2) Plexiglas septum; (3) Endocardial compartment; (4) Epicardial compartment; (5) 12-mm trocar; (6) Linear lesion entrance; (7) Thermocouples entrance; (8) Rail for thermocouples; (9) Magnetic tissue holder; (10) Stirring motor; (11) Outlet; (12) Heating mat; (13) Inlet. **C.** The ABLA-BOX (1) Plexiglas box (2) Force transducer; (3) Catheter holder; (4) Catheter holder rail; (5) Digital force monitor; (6) Heating mat temperature controller; (7) Stirring motor controller; (8) Catheter holder fine-tuning system **D.** Prototype of the "truly bipolar" catheter.

linear lesions which are often essential to diminish the left and right atrial triggers and substrate, especially in long-standing and persistent AF.

These tools should allow bipolar ablation of the atrial wall as well as electrophysiological mapping of the electrical activity in the tissue. Addition of direct thoracoscopic vision and virtual mapping will provide a complete framework for producing and controlling any lesion in the atrial tissue that may be needed.

With the support of the Triton Foundation and in cooperation with IDEE Instrument Development Engineering & Evaluation, Maastricht University, NL, we have developed a prototype of a new "truly bipolar" catheter. Indeed, whereas the bipolar clamp acts only on the tissue between the jaws (poles) during the ablation, this is not the case with pens used to create linear lesions. This might result in non-transmural scars, leading to AF recurrence. In our new catheter, the atrial tissue is comprised between the epicardial pole placed by the surgeon and the endocardial

one positioned by the electrophysiologist. The tips of these two catheters are coupled so they can be moved consensually and allow a real one-step epi-endocardial ablation.

The new catheter has been first tested in the ABLA-BOX, an in-vitro module for hybrid atrial fibrillation ablation (Figure 1).

The system consists of two chambers that mimic the epicardial and endocardial sides of the heart. The septum between the chambers provides catheter access on both sides of the cardiac tissue. A circuit, including a pump, an oxygenator and a heating device, circulates porcine blood inside the system; left atrial fresh tissue is mounted on a tissue holder and magnetically fixed. Epicardial and endocardial catheters are mounted onto an external railing system, allowing controlled catheter positioning with a geared mechanism, while a force transducer secured on the catheter holders gives real-time feedback on contact forces during the ablation procedures.

The issue of contact forces is a significant concern to explore for the correct design of the catheter. Indeed, hybrid ablation in which energy is applied from both the endocardium and epicardium may increase the likelihood of tissue damage, whereas insufficient contact pressure may not result in full-thickness lesions, thereby abolishing potential advantages of the new approach.

We used the ABLA-BOX to histologically assess different combinations of epi-endocardial radiofrequency ablation contact forces using porcine atria, evaluating diameters, area and volume of the ablation. We found that a minimal endocardial force of 30 grams combined with an epicardial force of 100 grams is the best combination to achieve transmural lesions.

This one-step procedure should optimise the hybrid ablation approach for AF. As a result, more patients may be treated with lower risks, at lower costs and with a high success rate. For the physicians, both electrophysiologists and surgeons, it means that these procedures might become less complex. The opportunity to get information about the AF mechanisms simultaneously from both sides of the atrial wall may potentially bring a patient-tailored ablation approach within our reach.

ONGOING AND UPCOMING RESEARCH OF THE GROUP:

- New short intra-aortic balloon pump to avoid visceral ischemia, tested in-vivo.
- New pulmonary artery cannula for A-V and V-V ECMO, tested in-vivo.
- Minimally invasive cell-based nano-fibrillar scaffold for cardiac regeneration.
- Storage-navigation-simulation computing system for patient-targeted mitral valve surgery and results prediction.
- Minimally invasive atrial patch for atrial fibrillation.

EVENTS AND HIGHLIGHTS

04

SCIENTIFIC HIGHLIGHTS

In 2014 the hard work of our researchers paid off in **584 scientific publications*** in peer refereed journals (527 WI-1 publications, excluding abstracts, and 23 Letters to the editor), **35 PhD theses**, **3 patents**, 2.9 million Euros funding received in competition from national and international science foundations and 4.8 million Euros funding from third parties, charities, EU-framework programs, industry, etc. In 2014, the overall average Impact Factor is 4.6.

* Please take notice that the numbers regarding the output are not yet confirmed by the Faculty Office. The final numbers will be presented in next year's annual report.

TOP PUBLICATIONS

WITH THE HIGHEST IMPACT FACTOR IN 2014 (with CARIM researcher as first and/or last author)

Schober A, Nazari-Jahantigh M, Wei YY, Bidzhekov K, Gremse F, Grommes J, **Megens RTA**, Heyll K, Noels H, Hristov M, Wang SS, Kiessling F, Olson EN, **Weber C** –
MicroRNA-126-5p promotes endothelial proliferation and limits atherosclerosis by suppressing Dlk1.
Nature Medicine 2014; 20: 368-376 IF 28.054

El Aidi H, Adams A, Moons KGM, Den Ruijter HM, Mali W, Doevendans PA, Nagel E, **Schalla S**, Bots ML, **Leiner T** –
Cardiac Magnetic Resonance Imaging Findings and the Risk of Cardiovascular Events in Patients With Recent Myocardial Infarction or Suspected or Known Coronary Artery Disease.
Journal of the American College of Cardiology 2014; 63: 1031-1045 IF 15.343

Klinkenberg LJJ, van Dijk JW, Tan FES, van Loon LJC, **van Dieijen-Visser MP**, **Meex SJR** -
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SCIENTIFIC GRANTS, AWARDS, HONORS

In this part we present most of the CARIM researchers that were successful in obtaining projects and personal grants.

NWO VIDI

In May 2014, the Netherlands Organization for Scientific Research (NWO) granted a Vidi fellowship (with a maximum of 800 K€) to Dr **Ingrid Dijkgraaf** (Dept. of Biochemistry) and Dr **Blanche Schroen** (Dept. of Cardiology). Ingrid receives this grant to conduct her research project "Parasitisation during a gradual disease process: artherosclerosis". Artherosclerosis is a chronic disease in which the interaction between two inflammatory proteins plays a causative role. The researchers will study this interaction at the molecular level and try to break it with the help of a recently discovered tick protein. Blanche receives the grant for her project on immune cells in the heart. Despite the presence of immune cells in healthy and diseased hearts, their contribution to the functioning and dysfunctioning of the heart muscle has received too little attention. The researchers have found that recently discovered, non-coding genes such as "mascRNA" control immune cell behaviour. It will be investigated whether mascRNA in immune cells contributes to heart failure. Vidi is aimed at excellent researchers who have carried out successful research for a period of several years after gaining a PhD. They belong to the best ten to twenty percent in their discipline. (Read full interviews with Blanche and Ingrid on pages 34 and 38).

NWO VENI

Dr **Ellen Dirkx** (Dept. of Cardiology) received a Veni grant for her project "Listen to the genes in your heart" from the Netherlands Organization for Scientific Research (NWO). High blood pressure leads to the growth of heart muscle cells, which causes a decrease in pump function and eventually heart failure. With the current pharmacological therapies, the prognosis of affected heart failure patients remains poor and there is a dire need to develop new therapeutic approaches. In order to develop these new medications, we need to obtain a better understanding of the molecular processes leading to heart failure. In this context, the researcher aims to identify and investigate new gene programs involved in pathological growth of the cardiac muscle and subsequently heart failure. Furthermore, the therapeutic potential of these newly identified genes will be tested, using a gene therapeutic approach in a model for heart failure, which might be translatable to human clinical trials. For the execution of her Veni grant, Ellen Dirkx will closely collaborate with the ICGEB in Italy.

NHS DR E. DEKKER PROGRAM

In the framework of the Dr E. Dekker program of the Dutch Heart Foundation, Dr **Blanche Schroen** received a Senior Postdoc grant for the project "MenRNA is a noval structural DNA molecule involved in the development of heart failure". Long non-coding RNAs (lncRNAs) have recently started to attract attention for their involvement in development and disease. Though their conservation is poor, their diverse roles in regulating gene expression and other molecular biological functions are becoming clear. The goal of this NHS Dekker Senior Postdoc grant is to investigate the molecular involvement of lncRNAs in heart failure, and to assess their potential as clinical biomarkers.

Dr **Martijn Smulders** (Dept. of Cardiology) received a Arts vóór aanvang specialistenopleiding grant of € 100,000. The

financial support helps him to complete the CARMENTA trial (Smulders et al. American Heart Journal 2013; 166: 968-75). The CARMENTA trial investigates whether the implementation of cardiovascular magnetic resonance imaging (CMR) or computed tomography angiography (CTA) early in the diagnostic process in patients suspected for non–ST-elevation myocardial infarction (MI) leads to an early alternative diagnosis than MI (eg, myocarditis, pulmonary embolism) as compared with routine clinical management (eg invasive coronary angiography). Consequently, this could prevent unnecessary invasive evaluation and associated complications and reduce length of hospitalization and costs. Especially in the current era of high sensitivity troponin assays that have very high sensitivity but lower specificity for acute MI, this trial may have important implications for the future diagnostic workup of patients with suspected but not yet proven non–ST-elevation MI.

KOOTSTRA FELLOWSHIPS

During the first round of the Kootstra Talent Fellowships 2014, **Susanne de Witt** and **Jelle Posthuma** (post docs Dept. of Biochemistry) were granted a fellowship and **Maarten Heusinkveld** (post doc Dept. of Biomedical Engineering) received the grant in the second round. The Kootstra Talent Fellowships are granted to young scientific talents by the Board of Maastricht UMC+ with the aim to support developing their scientific career. The fellowship is meant to provide financial support for young researchers to bridge the time between graduation in Medicine, Health or Life Sciences and the start of a PhD, between the graduation of the PhD student and the start of an official contract as a post doc or enable them to combine their studies in Medicine, Health or Life Sciences with an active involvement in scientific research.

OTHER AWARDS, PRIZES AND GRANTS

In 2014 many CARIM researchers were awarded with prizes, awards and other grants. Below, some of them are highlighted.

UM AWARD ROEL SPÄTJENS

At the New Year's reception of Maastricht University, **Roel Spätjens** (Dept. of Cardiology) received the 2014 UM award of special merit for his work at the University. The UM award is given to employees in recognition of their distinctive performance in administrative or academic services, in the provision of services, or for commendable social work based at Maastricht University. Roel was praised for his professionalism and loyalty. "You never come up empty handed when you ask him for something" was one of the comments made by his colleagues. (read a full interview with Roel on page 62).

EDMOND HUSTINX PRIZE FOR SCIENCE FOR JUDITH COSEMANS

On behalf of the Edmond Hustinx Foundation the 2014 Edmond Hustinx Prize for Science was awarded to

Dr **Judith Cosemans** (Dept. of Biochemistry). The prize comprises € 15,000 to be used for research purposes. She receives the award for her research proposal on developing techniques to measure thrombosis tendency in small volumes of blood, which reduces the need for animal testing. The jury, that unanimously elected Judith, believes that her research is very applicable and has a valuable social impact. Her leading publications, her acquisition of significant grants and awards, and the fact that she is vice-chairman of the Scientific Subcommittee on Biorheology illustrate the outstanding qualities of this researcher.

YOUNG INVESTIGATOR AWARD SFRR-EUROPE FOR PAMELA KLEIKERS

On September 7, **Pamela Kleikers** (Dept. of Pharmacology) received the Young Investigator Award sponsored by the Society for Free Radical Research Europe in recognition of extraordinary scientific achievements in this field.

MATTHIJS CLUITMANS RECEIVES YOUNG INVESTIGATOR AWARD CINC 2014

Matthijs Cluitmans (PhD Dept. of Cardiology) has won the Young Investigator Award at the Computing in Cardiology (CinC) 2014 Conference in Cambridge, USA. Cluitmans was awarded for giving the best oral and written presentation of the Rosanna Degani Young Investigators Competition, for his research in which he developed and validated a new method that incorporates knowledge about the electrical conduction system of the heart in its reconstruction.

SCIENTIFIC PRIZE CLINICAL CHEMISTRY FOR MUMC+

The article "Circulating cardiac troponin T exhibits a diurnal rhythm" of L.J. Klinkenberg, J.W. van Dijk, F.E. Tan, L.J. van Loon, M.P. van Dieijen-Visser and S.J. Meex, published in Journal of the American College of Cardiology, has won the Scientific Prize Clinical Chemistry granted by the NVKC (Dutch Society for Clinical Chemistry) for highest valued publication in 2014.

AWARD OF EXCELLENCE FARIDA OMAROVA

Farida Omarova (PhD student Dept. of Biochemistry received an Award of Excellence at the Annual Symposium of the Dutch Society on Thrombosis and Haemostasis (Koudekerke, The Netherlands, 9-10th April 2014) for the abstract: "Fibrinogen γ' increases the sensitivity to activated protein C in normal and factor V Leiden plasma".

LIFETIME ACHIEVEMENT AWARD ARTERY SOCIETY FOR ROB RENEMAN ARNOLD HOEKS

During the Artery Conference 2014, which was performed from October 9 and October 11, Prof. **Rob Reneman** (Dept. of Physiology) and Prof. **Arnold Hoeks** (Dept. of Biomedical Engineering) received the Lifetime Achievement Award for their outstanding contributions to ultrasound based studies of the arterial wall.

The local organising committee of the conference consisted of Prof. **Harry Struijker Boudier**, Prof. **Coen Stehouwer**, Dr **Koen Reesink**, Dr **Isabel Ferreira**, Prof. Luc van Bortel (Ghent, Belgium) and **Rob van der Zander.**

EVENTS AND HIGHLIGHTS

ERC VISIT

In 2014, the evaluation of the scientific research within CARIM over the years 2007 until 2012 was performed. Besides a self-evaluation document which was prepared in the first few months of 2014, an External Review Committee (ERC), consisting of Prof. Pim van Aken (chairman), Prof. Pieter Reitsma, Prof. Stéphane Laurent, Prof. Eugene Barrett,

Prof. Stefan Engelhardt, Prof. Dirk Brutsaert and Erik Drenthe (secretary) visited CARIM from June 4 until June 6. During this visit, the ERC members were provided with a program which pursued to cover all important aspects of CARIM: the School in general, presentations per theme, a poster session, meetings with tenure tracks, top talents and post docs, the PhD program (including the CARIM Course Week) and site visits to the different facilities of CARIM.

TILMAN HACKENG APPOINTED AS VICE SCIENTIFIC DIRECTOR

As of November 1, 2014, Professor **Tilman Hackeng** has been appointed as Vice Scientific Director of CARIM. Tilman Hackeng is Professor and chairman of Biochemistry, Principal Investigator and leader of Theme I Thrombosis and Haemostasis, of CARIM. He is past president of the Netherlands Society on Thrombosis and Haemostasis. Professor Hackeng will focus on improving CARIM's visibility and position in the Dutch and international scientific and R&D environment.

COOPERATION UNIVERSITY MEDICAL CENTER MAINZ WITH CVC/CARIM MAASTRICHT

The Center for Thrombosis and Hemostasis at the University Medical Center Mainz (CTH) and the Thrombosis Expertise Center within CVC/CARIM decided to join efforts on mutual projects, grand applications, exchange of personnel and teaching activities. The Cooperation agreement was signed on February 20, 2014. From the left to the right: Prof. Ulrich Walter, Scientific Director CTH, Prof. Michael Jacobs, Director Cardiovascular Center, Prof. Thomas Unger, Scientific Director CARIM, Prof. Johan Heemskerk, CARIM, Prof. Wolfram

Ruf, CTH, and Professor Hugo ten Cate, Gutenberg Forschungskolleg (GFK) University Mainz/CARIM

VASCULAR NETWORK GROUP INITIATIVE

The Vascular Network Group (VNG) is a semi-open organisational structure led by Dr **Koen Reesink** (Dept. of Biomedical Engineering), Prof. **Chris Reutelingsperger** (Dept. of Biochemistry), Prof. **Robert van Oostenbrugge** (Dept. of Neurology) and Dr **Hans Vink** (Dept. of Physiology). Initiated in 2013, the Vascular Network Group is fostering translational research in Vascular Biology and Medicine in two ways. The VNG created a draft to re-establish the Vascular Biology program within CARIM, based on a thorough review of leading investigators and their research lines and resources. Furthermore, the VNG organised 5 Vascular Networkshops in 2014 where both clinical and basic research groups presented and interacted, sparking new initiatives e.g. on post-thrombotic syndrome in deep vein thrombosis and on arterial calcification.

CARIM-MH&NS WORKSHOPS

Interaction between CARIM and MH&NS has resulted in the newly-formed collaborative group 'Cardiovascular Research meets Neuroscience', led by Prof. **Harry Steinbusch** and Prof. **Thomas Unger**, together with Prof. **Robert van Oostenbrugge** (Chief of the Neurology Department), and Dr **Pawel Namsolleck** (pharmacologist). In recognition of the need to combine forces on vascular, microvascular and neurological research in the field of cerebral small vessel disease with its consequences of cognition deficits and dementia, this group was formed by two research schools to create synergies and optimally exploit existing resources. In 2014, two successful CARIM-MH&NS workshops took place.

CARIM IN THE MIDDLE EAST

The board of CARIM appointed Drs **Mehrdad Omidvar**, MBA, CEO of R&D Group Vitak, as Director Business Development CARIM in the Middle East, to guide CARIM in their pursuit of collaboration with Universities and Governments in the Middle East in the field of PhD trajectories, biobank initiatives, and research & development activities.

As a first step, a delegation of CARIM with its spin off R&D Group Vitak visited the United Arab Emirates at which a meeting was held at the University of Sharjah (UOS) with Professor Hamid M.K. Al Naimiy, Chancellor of the University of Sharjah, Professor Maamar Bettayeb, UOS Vice Chancellor of Research and Graduate Studies at the University of Sharjah, Dr. Salah Taher Al Haj, UOS Vice Chancellor of Community Affairs, and a number of deans and faculty members from the UOS colleges. During the meeting, the two parties discussed a collaboration between the two universities in general, and especially in the fields of research in cardiovascular health and disease, computer aided drug design and chemical biology.
An agreement was reached to open the channels of communication between members of faculty from the two universities in order to exchange information and research ideas in the abovementioned fields.

INTERVIEW

PIM VAN AKEN
PIETER REITSMA

In June 2014, CARIM was evaluated by an External Review Committee (ERC), chaired by Pim van Aken, emeritus Professor of Internal Medicine.

Pieter Reitsma, Professor of Experimental Molecular Medicine at Leiden University was one of the other committee members, to take part in the ERC's task of thoroughly evaluating the work of CARIM.

MEMBERS OF THE EXTERNAL REVIEW COMMITTEE REFLECT ON CARIM'S EVALUATION

Based on the Standard Evaluation Protocol (SEP), which was drawn up by the Royal Netherlands Academy of Arts and Sciences (KNAW), the seven committee members spent two days interviewing many researchers, listening to presentations and examining data on aspects like publications and citations. Pieter Reitsma: "On such days, the entire staff of the research school put their best foot forward. Not that it helps cover up any existing problem, though. The committee is too well-informed not to see through that."

CLEVER

Reitsma has been researching blood coagulation since 1985, so he is no stranger to CARIM. "CARIM is the only really well-organised cardiovascular research school in the Netherlands. You can tell from the way they present themselves, but also from the fact that they were ahead of the other University Medical Centres in setting up a graduate school for PhD students. And as regards the quality of their research, it's just all really clever work, of course." Van Aken adds: "The research in all three of the themes is very good to excellent. It's a highly ambitious, productive organisation, where top-level researchers are engaged in all kinds of science, from basic to applied. The pioneers from CARIM's early days, Reneman, Hemker and Wellens, built up a very solid reputation, so it's a matter of keeping it up."

CHALLENGE

If you look only at the figures, this doesn't appear to have been a problem in recent years. As Van Aken puts it: "CARIM's budget has nearly doubled between 2008 and 2014. They've gone from 176 researchers to 200; from 400 publications a year to 650 and from 23 PhD theses to 40. A huge growth. If they want to keep this up in the future, they'll need not only dedicated staff, but also sufficient funding, and I think that will be the challenge for the coming years." Reitsma agrees: "What matters is the future. I always say: true science policy is staff policy. You have to engage the right talents for the institute, and the CARIM management are actively involved in doing this. Today's young talents will partly determine the quality of the institute in ten years' time. It's useful to have a tightly organised PhD program, like the tenure tracks CARIM uses for young talented researchers; about half of the 'top talent' class instituted by the Faculty to prepare future professors consists of CARIM researchers."

CHORE

The grants that CARIM researchers manage to secure also impact positively on the quality of the institute. Or is it the other way about? Reitsma: "Young researchers, including those at other institutes, often fail to see it that way. To them it's just time-consuming, it feels like a kind of chore, and they don't realise that such an institute is a kind of showcase that can be used to impress the world of serious sponsorship." Van Aken can imagine CARIM appointing a "dedicated fundraiser" at some stage, as some universities have already done. Another focal point they both completely agree on is that of the facility for animal experiments at Maastricht. "That really needs to be improved. We've been saying that for years. It's crucial for the type of research done at CARIM; you can't do cardiovascular research without large test animals." Reitsma agrees: "It's detrimental to CARIM's standing if they fail to set it up adequately."

TRANSITIONS

One of the things the ERC was impressed by was the Cardiovascular Centre Maastricht (CVC), where researchers and clinicians interact directly, in order to raise the translational level of both research and clinical care. Reitsma calls this an excellent way to raise the profile of the top-level tertiary care in a university hospital. "Without that, you'll lose the government's support." "Very important", agrees Van Aken. Other transitions the chair saw in recent years were of course the arrival of a new director and two new main theme leaders, as well as the merger between the two faculties and the university hospital. In their view, an important future development to invest in is systems biology, and the planned appointment of a Professor of Genetic Epidemiology (see page 10) is an important step in that direction.

MOTIVATION

Reitsma and Van Aken differ little in their personal motivations for accepting the membership of the ERC. Van Aken: "I had some time available and I have found it very interesting to help further the cause of CARIM this way." Reitsma: "After you've retired, you're no longer a competitor, so you can take a completely independent position. You meet interesting people in the field of cardiovascular research, which is close to my heart and which I want to promote. And after all", he laughs, "Isn't all of life a fight against boredom?"

INTERVIEW
ROEL SPÄTJENS

He began working as a technician at Maastricht University in 1996, and all the knowledge and expertise he has gained since then has earned him the title “senior technician”. It means that at the lab led by one of the Principal Investigators for cardiology, Prof. Paul Volders, he is the first person to whom fellow analysts, PhD students and postdocs turn with questions. In 2014, Roel was first author of a publication in the journal Cardiovascular Research. It was his organisational talent, his sense of social commitment, his loyalty and his professionalism that inspired his colleagues to nominate him for the 2014 UM Employee Award.
And Roel Spätjens won.

“I WAS GIVEN THE OPPORTUNITY TO DEVELOP AS A RESEARCHER”

"I've always preferred to do what I wanted to do, and not necessarily what I was best at", says Roel Spätjens. So even though he was better at languages in school, he found biology and biochemistry much more of a challenge. As part of his studies at a training college for lab technicians, he did a placement at the UM laboratory of neuropsychology. Paul Volders, who at the time was still a PhD student, recognised his talents and recommended him to Marc Vos, whose department had a vacancy at the time. And that is how his career at Maastricht University started.

GROWTH

"Some years later, Marc Vos left for Utrecht with his group, but the move would have been inconvenient for me and my wife at that time. Fortunately, Paul Volders stayed on in Maastricht, and together we expanded his lab." The fact that Volders is not only a researcher but also a cardiologist at MUMC+ means that, in practice, Spätjens is often the first person that young researchers turn to for advice. "I've been given the opportunity to develop as a researcher too. Paul encourages that; he thinks it's important to keep people motivated. And if that means you're able to complete a research study and be the first author of a publication, and you get to present it at a conference in San Francisco, that's great of course."

NEW YORK

The study in question, about electric currents in the hearts of patients with ECG abnormalities, brought Spätjens to New York, where he visited the laboratory of Prof. Robert Kass at Columbia University. He learned to set up an in-vitro stress test to simulate the beta-adrenergic stimulation of potassium channels with faulty conductance. "We're now using this technique at our lab almost every day."
In recent years he has seen about 13 students of the research group get their PhD degree, and many postdocs have come and gone. "I'm sharing an office with researchers from Belgium, Spain and Italy, and I really enjoy the international character of our group. It's the contacts with my colleagues that I enjoy most. I'm still in contact with people who have moved elsewhere, and I always get on well with new colleagues. It means I still enjoy coming to work every day, even when the results are perhaps not always as good as you'd like them to be."

HIGHLIGHT THEME III

MARJO DONNERS

DEPARTMENT OF PATHOLOGY

ADAMs Revisited

Atherosclerosis continues to be a major source of morbidity in Western society, and accordingly a central theme in cardiovascular research. The Experimental Vascular Research group at the Department of Pathology has a long track record in atherosclerosis research. Based at this Department and having access to human tissue, it is combining the investigation of human end-stage atherosclerosis to generate hypotheses, and *in vitro* and mouse transgenic studies to test the hypotheses. The emphasis in the group is on a hallmark process in end-stage atherosclerosis, i.e. inflammation, which we consider to be instrumental in the conversion of a stable into an unstable, rupture-prone plaque. Within Experimental Vascular Pathology, Erik Biessen is pursuing a systems medicine approach to link plaque and peripheral inflammation, while Judith Sluimer's group is studying the impact of hypoxia on macrophage status and inflammation, and Marjo Donners' group focuses on proteases as inflammatory effectors, more specifically on the role of A Disintegrin And Metalloproteases (ADAMs), in atherosclerosis. The present overview outlines the recent progress achieved by Donners' group.

ADAMs have emerged as key regulators of various cell functions by acting as molecular scissors, cleaving (shedding) various cell surface molecules, including adhesion molecules, chemotactic factors, growth factors and cytokine receptors. This pleiotropic activity implicates especially ADAM10 and ADAM17 (also known as TNF-converting enzyme) in various critical processes in atherosclerosis (Fig 1). Whereas protein shedding is a rather novel topic in cardiovascular research, it has been embraced as a major target for therapeutic intervention in cancer and Alzheimer's disease.

CELL-TYPE SPECIFIC EFFECTS OF ADAM10 ON ATHEROSCLEROSIS

Marjo Donners was the first to show ADAM10 expression in endothelial cells and macrophages in human atherosclerosis, which was associated with plaque progression and neovascularization. Considering the embryonic lethality of ADAM10$^{-/-}$ mice, she decided to opt for a cell-specific conditional knockout approach to study the causal role of this enzyme in atherosclerosis. By transplanting ADAM10-deficient bone marrow into atherogenic LDLr$^{-/-}$ mice, she was able to show that

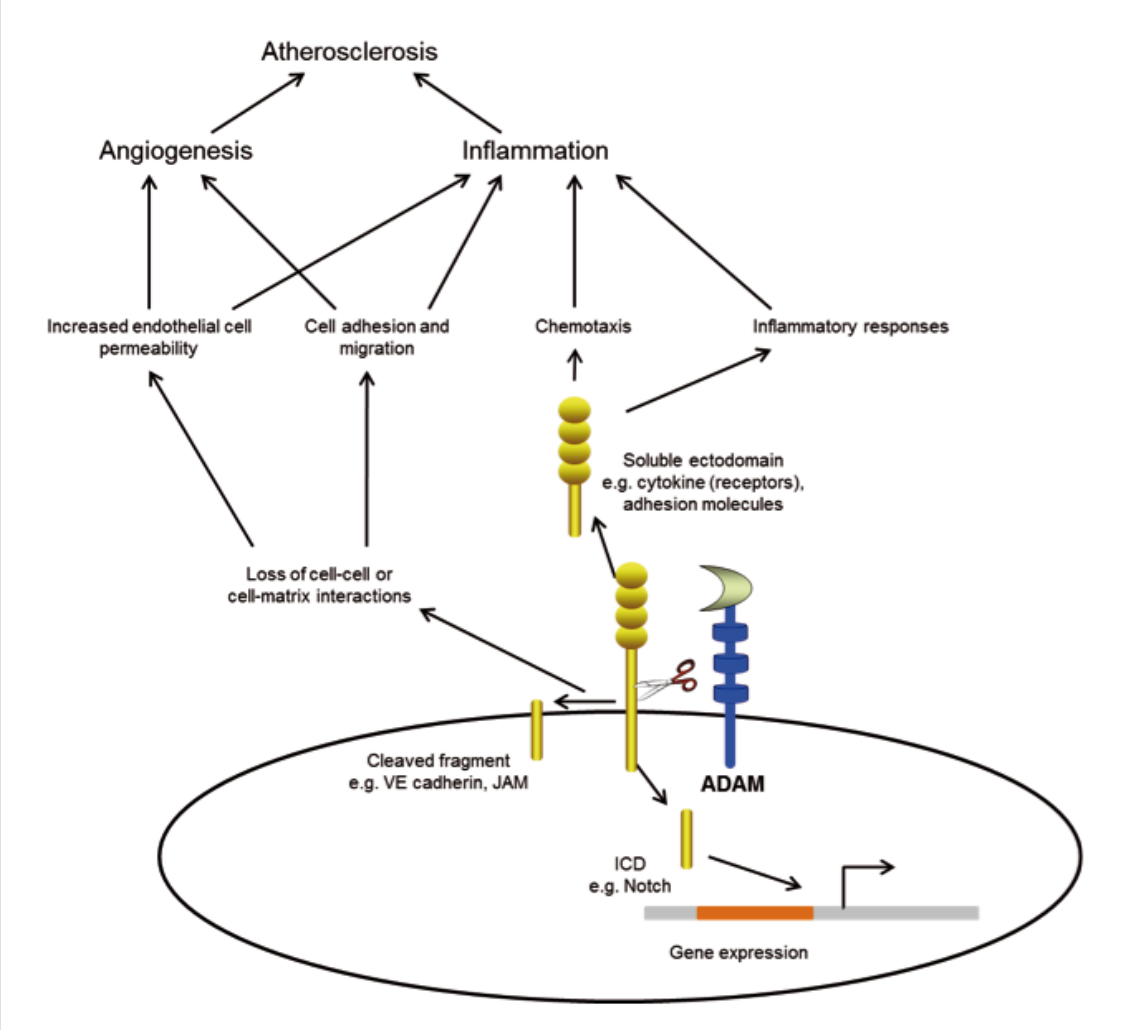

FIGURE 1

Diagram depicting the mode of action of, and the biological processes impacted by, ADAMs.

conditional deletion of ADAM10 in **myeloid cells** did not affect plaque size, but affected plaque stability by increasing fibrosis. The collagen content in the atherosclerotic lesion is determined by both collagen production (predominantly by vascular smooth muscle cells) and collagen degradation. The research showed that myeloid ADAM10 deficiency did not alter the production of pro-fibrotic factors by primary bone marrow-derived macrophages, which could in turn stimulate collagen production by smooth muscle cells. However, bone marrow-derived macrophages from myeloid ADAM10$^{-/-}$ mice did produce less matrix-degrading metalloproteases, which could explain the elevated collagen content in the atherosclerotic lesions.

In view of the key role of ADAM10 in controlling leukocyte adhesion and transmigration in endothelium, a logical next step was that two of her PhD students, Emiel van der Vorst and Kosta Theodorou, set out to study the role of **endothelial** ADAM10 in atherosclerosis development. In collaboration with Dr. Jacob Bentzon (Aarhus University, Denmark), the team employed a very elegant new method to induce atherosclerosis in endothelial-ADAM10 deficient mice without the need for laborious backcrossing to atherosclerosis-prone mice (LDLr$^{-/-}$ or ApoE$^{-/-}$). Just a single i.v. injection with an adeno-associated virus construct carrying the PCSK9 gene was enough to achieve persistent overexpression of this gene in liver, which rendered the mice functionally deficient of the LDL receptor and thus hyperlipidaemic and atherogenic. Contrary to expectations, we found that endothelial-ADAM10 deficient mice had severely augmented atherosclerosis. These data indicate that, in contrast to our *in vitro* findings in leukocyte transmigration assays and the in vivo results obtained in other inflammatory diseases, ADAM10 expressed by plaque endothelium exerts strongly protective effects under hyperlipidaemic conditions. We are now digging further into the underlying mechanisms of these thrilling but counterintuitive findings.

HIGH-DENSITY LIPOPROTEIN HAS PRO-INFLAMMATORY EFFECTS IN MACROPHAGES

Earlier studies have shown that environmental cholesterol levels are very important for the regulation of ADAM activity. This is probably related to the fact that ADAMs are localized and proteolytically active in dedicated regions within the cell membrane, which are rich in cholesterol (the so-called lipid rafts). Indeed, cholesterol depletion, e.g. by a major cholesterol transporting particle (high density lipoprotein or HDL) has been shown to increase the activity of the related enzyme ADAM17, leading to increased TNF release in endothelial cells.

HDL is considered to be the “good cholesterol”, mainly by mediating reverse cholesterol transport from the periphery (e.g. coronary arteries) to the liver. In addition to this, several other atheroprotective effects have been reported, mainly focusing on HDL’s effects on endothelium, ranging from anti-thrombotic to anti-inflammatory. The anti-inflammatory effects of HDL in endothelium predominantly encompass reduced expression of cytokines, chemokines and adhesion molecules, i.e. limiting leukocyte recruitment. Nevertheless, though various experimental models do indeed show reduced atherosclerosis development after HDL-raising interventions, the clinical efficacy of such treatments remains limited.

With this in mind, Donners’ team (as part of Emiel van der Vorst’s CARIM PhD award studies) zoomed in on the effects of HDL on another vital cell in atherosclerosis, the macrophage. Van der Vorst’s findings, which are currently under revision in a prestigious journal, surprisingly showed **pro-inflammatory** effects of HDL in this cell type. Cholesterol

depletion increased the production of pro-inflammatory mediators (TNF,IL-12, IL-1b, IL-6, NO) and reduced the release of the anti-inflammatory cytokine IL-10 by both human and murine macrophages, a pattern generally considered to be associated with aggravated cardiovascular disease. Moreover, the team has been able to confirm our *in vitro* findings in vivo using transgenic mice that overexpress human ApoA-I, the major protein component of HDL, and therefore have high HDL levels. As expected, ADAM17 inhibition blocked TNF release, though this could not explain the transcriptional upregulation of inflammatory mediators. Gene expression and ChIP-PCR analyses revealed a major role for interferon and NFkB signalling pathways, a notion confirmed by targeted pharmacological and knockout intervention approaches (Fig 2). On the one hand, the findings could provide an explanation for the rather disappointing results of clinical studies aimed at raising HDL levels in cardiovascular disease patients. On the other hand, they have more far-reaching implications, as they could illustrate HDL's capacity to improve intrinsic functions of a range of cell types relevant to cardiovascular diseases, such as smooth muscle cells, endothelial cells and innate immune cells. Indeed, in collaboration with Prof. Touqui of Inserm Institute, Paris, Marjo Donners was able to show that HDL levels are important for the proper clearance of P. aeruginosa bacterial infection in the lung.

FUTURE DIRECTIONS

Supported by personal fellowships from the Netherlands Heart Foundation (Dekker junior and senior grants), Marjo Donners and coworkers have so far been able to reveal important new cell-specific functions of both ADAMs and cholesterol depletion by HDL in atherosclerosis. Obviously, these findings will have considerable impact on our perception of ADAM/HDL as regulators of inflammatory processes in atherosclerosis. Inspired by these results, Donners' group will embark on a new challenge, which is to address the interaction between lipid homeostasis and ADAMs-mediated shedding in this disease. Knowledge of the regulation of ADAMs localization and shedding activity under hyper- versus normolipidaemic conditions will be very important issues that need to be addressed before we can consider therapeutic intervention (and gauge potential side-effects) in lipid-driven disorders like atherosclerosis and Alzheimer's disease or other chronic inflammatory conditions. Special attention will be given to the role of the HDL/ADAM axis on exosomes and their shedding, an exciting new research area which Donners aims to explore in the near future, hopefully supported by a landmark paper on HDL and/or future grants.

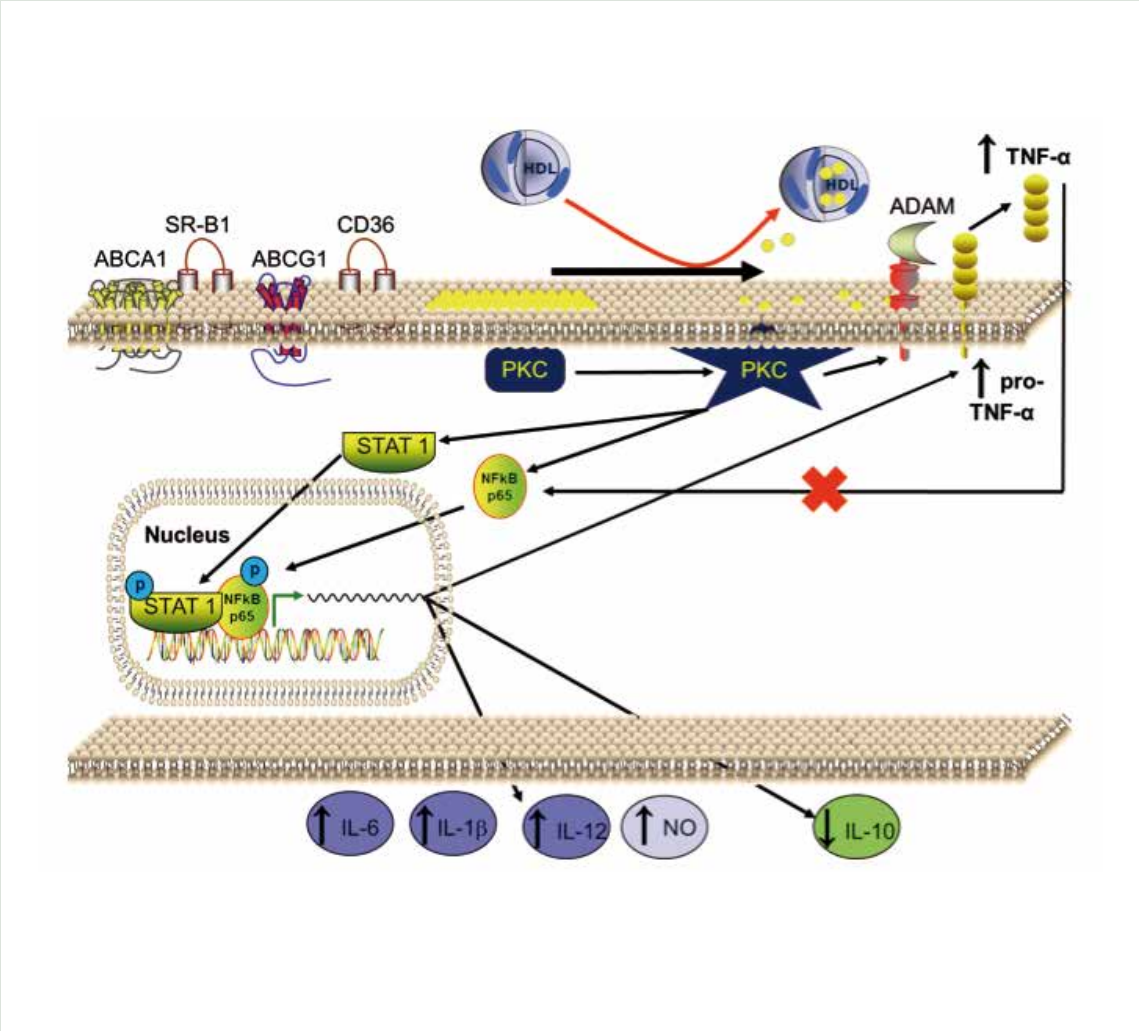

FIGURE 2

Schematic representation of HDL-modulated inflammatory pathways in macrophages

TRAINING AND EDUCATION

05

INTRODUCTION

CARIM School for Cardiovascular Diseases offers a flexible and integrated education and training program that suits individual ambitions of our students. The education program consists of a specialisation within the FHML Master of Biomedical Sciences and a Physician-Clinical Investigator Program (MSc/MD) and a contiguous PhD (doctoral) training program. The content of the education program has been developed by CARIM's top researchers, while its framework has been created by senior educators of Maastricht University, who have earned an excellent international reputation for their didactical system that is based on problem-based learning.

RESEARCH MASTER

In the Biomedical Sciences program, Master's students are informed about the FHML Research School programs in the first half year by attending school-specific lectures and parallel programs organised by School researchers. In the second half year, students may get acquainted in more detail with school-specific practical research. In this phase CARIM offers students the opportunity to participate in the CARIM course week program and to do a CARIM junior research internship at one of CARIM's laboratories. This allows students to make up their mind about the school of choice in which to receive their practical research training. When students choose CARIM, they can follow a CARIM senior research internship in their second year. This will lead to a notification of cardiovascular specialisation on their Master's certificate.

PHD PROGRAM

Our PhD program is accessible for talented and motivated students graduated from national and international Medical and Biomedical Masters. At the end of 2014, 129 PhD students attended our PhD program. Almost 50% of our PhD candidates come from foreign countries, guaranteeing an international atmosphere. The principal goal of the 4-year PhD training program is to support PhD candidates in developing themselves into independent and productive researchers in the cardiovascular field. To ensure high quality PhD training, CARIM offers frequent interaction of PhD candidates with a skilled and experienced supervisory team, thereby providing a stimulating and critical environment to further develop one's research skills. We also offer our PhD candidates a broad range of possibilities to attend seminars, master classes, and symposia to present their own research on national and international podiums.

NUMBER OF PHD STUDENTS
(at 31.12.2014)

FUNDING SOURCE	2011	2012	2013	2014
UNIVERSITY	48	42	41	34
NWO	14	13	12	13
NON-PROFIT AND INDUSTRY	79	81	74	82
TOTAL	**141**	**136**	**127**	**129**

PHD DELIVERABLES

In 2014 32 PhD students finished their theses within our institute, and 3 theses were externally prepared. The table below illustrates the numbers of PhD students in the years 2009-2014, related to the period in which they obtained their degree. The graphics on pages 30 present the number of PhD theses on the level of our research themes.

PHD STUDENT CAREERS
(date set 01.01.2014)

YEAR INTAKE	2009	2010	2011	2012	2013	2014
COHORT VOLUME (annual intake)	41	40	42	21	16	29
MALE	23	17	22	9	7	13
FEMALE	18	23	20	12	9	16
PHD FROM ABROAD	19	16	18	8	4	11
DROP OUT	5	3	2	4	1	-
DROP OUT > 1 YEAR	2	2	1	1	1	1
THESIS COMPLETED	18	8	3	-	1	-
AVERAGE DURATION (in months)	59	50	39	-	14	-
ONGOING	18	28	39	17	13	28

CARIM THESES 2014

Van Kruchten R -
Platelet procoagulant acitivity: focus on calcium entry and phospholipid scrambling
Promotor: Prof. J Heemskerk
Co-promotor: Dr E Bevers
Maastricht University, January 17, 2014

Konings J -
The role of coagulation factor XII in fibrin clot formation and fibrinolysis
Promotor: Prof. H ten Cate
Co-promotor: Dr J Govers-Riemslag
Maastricht University, January 24, 2014

Huijts M -
Cognitive function in patients with cerebral small vessel disease
Promotor: Prof. R van Oostenbrugge
Co-promotor: Dr A Duits, Dr J Staals
Maastricht University, January 24, 2014

Nietlispach F -
Structural Interventions in Invasive Cardiology
Promotor: Prof. H Brunner-La Rocca
Maastricht University, April 17, 2014

Gladka-de Vries M -
(Post) transcriptional regulation of heart failure
Promotor: Prof. L de Windt
Co-promotor: Dr P da Costa Martins
Maastricht University, April 17, 2014

Jetten N -
Macrophage heterogeneity in neovascularization
Promotores: Prof. M Post, Prof. M de Winther
Co-promotor: Dr M Donners
Maastricht University, May 9, 2014

Wlazlo N -
Novel aspects of insulin resistance and type 2 diabetes mellitus: Iron metabolism, the complement system, and liver cirrhosis
Promotor: Prof. C Stehouwer
Co-promotores: Dr M van Greevenbroek, Dr B Bravenboer, Dr B Halle
Maastricht University, May 14, 2014

Ninivaggi M -
Thrombin generation: innovations and clinical applications
Promotor: Prof. H ten Cate
Co-promotores: Dr T Lindhout, Dr B de Laat
Maastricht University, May 23, 2014

Eskens B -
Role or the endothelial glycocalyx in regulation of insulin sensitivity in muscle
Promotor: Prof. Th Unger
Co-promotores: Dr H Vink, Dr J van Teeffelen
Maastricht University, May 23, 2014

Pounis G -
The impact of dietary habits on cardiovascular risk factors and other metabolic parameters of free-living populations: methodological approaches to dietary analyses
Promotores: Prof. H ten Cate, Prof. G de Gaetano, Prof. L Iacovielle
Maastricht University, June 11, 2014

Houthuizen P -
Left Bundle Branch Block; Controversies in Aortic Valve Interventions and Cardiac Resynchoronization Therapy
Promotores: Prof. F Prinzen, Prof. P de Jaegere
Co-promotor: Dr L van Gelder
Maastricht University, June 11, 2014

Geenen I -
Endothelial Cell function from a tissue engineering perspective
Promotores: Prof. M Post, Prof. G Schurink
Co-promotor: Dr D Molin
Maastricht University, June 20, 2014

Michel S -
Flax as a bio-based biomedical textile material
Promotor: Prof. L Koole
Co-promotores: Dr M Knetsch, Dr D Molin
Maastricht University, June 26, 2014

CARIM THESES 2014

Schmitt M -
JAM-A: Junctional Adhesion Molecule-A or Janus Acting Mediator in atherosclerosis
Promotores: Prof. T Hackeng, Prof. C.Weber
Co-promotor: Dr R Koenen
Maastricht University, June 30, 2014

Versluis B -
Quantitative morphologic and functional MRI of peripheral arterial disease
Promotores: Prof. W Backes; Prof. J Wildberger
Co-promotores: Dr T Leiner; Dr P Nelemans
Maastricht University, July 3, 2014

Jaarsma C -
Cardiovascular magnetic resonance imaging of myocardial ischemia and infarction
Promotores: Prof. H Crijns; Prof. J Wildberger
Co-promotor: Dr S Schalla
Maastricht University, July 3, 2014

Wolfs I -
Macrophage polarization in atherosclerosis; from a black and white paradigm to a multicolored view
Promotores: Prof. E Biessen, Prof. M de Winther
Co-promotor: Dr M Donners
Maastricht University, September 10, 2014

Van Deursen C -
Cardiac Resynchornization therapy: maximizing benefits with minimal efforts
Promotor: Prof. F Prinzen
Co-promotores: Dr K Vernooy, Dr L Wecke
Maastricht University, September 12, 2014

Du J -
Application of in-silico approaches to cardiovascular Disease
Promotor: Prof. T Hackeng
Co-promotor: Dr G Nicolaes
Maastricht University, October 8, 2014

Steegh F -
The role of early peritubular capillary loss in the development of chronic kidney disease
Promotores: Prof. M Daemen, Prof. L van Heurn
Co-promotores: Dr C Peutz-Kootstra, Dr M Christiaans
Maastricht University, October 31, 2014

Lemmert M -
Predicting the unpredictable; electrocardiographic parameters associated with ischemic ventricular fibrillation
Promotores: Prof. A Gorgels, Prof. M Krucoff
Maastricht University, November 6, 2014

Wildhagen K -
Biomolecular engineering in the design of novel therapies to treat coagulation disorders and inflammatory diseases
Promotores: Prof. T Hackeng, Prof. C Reutelingsperger
Co-promotor: Dr G Nicolaes
Maastricht University, November 25, 2014

De Witt S -
The entanglement of thrombus formation: systems biology as a novel key – **CUM LAUDE**
Promotor: Prof. J Heemskerk
Co-promotor: Dr J Cosemans
Maastricht University, November 27, 2014

Nagler M -
Validity and diagnostic value of tests used in thediagnostic work up of haemostatic disorders!
Promotor: Prof. H ten Cate
Co-promotores: Prof. W Wuillemin, Prof. L Bachmann
Maastricht University, December 3, 2014

Alnima T -
Carotid baroreflex activation therapy. Potential mechanisms in resistant hypertension
Promotor: Prof. P de Leeuw
Co-promotor: Dr A Kroon
Maastricht University, December 5, 2014

CARIM THESES 2014

Kleikers P -
NOXious oxidative stress: from head to toe and back
Promotores: Prof. H Schmidt, Prof. H Steinbusch
Co-promotor: Dr B Janssen
Maastricht University, December 8, 2014

Wijnands J -
Gout, uric acid, and cardiovascular disease; know your enemy
Promotores: Prof. A Boonen, Prof. I Arts, Prof. C Stehouwer
Maastricht University, December 11, 2014

De Vos C -
Clinical and echocardiographic parameters to characterize atrial fibrillation
Promotor: Prof. H Crijns
Co-promotor: Dr K Tieleman
Maastricht University, December 17, 2014

Rahimi N -
Electro-Responsive Hydrogels for vascular tissue engineering
Promotor: Prof. M Post
Co-promotor: Dr D Molin
Maastricht University, December 18, 2014

Bloemen S -
Managing anticoagulant therapies using innovative thrombin generation assays
Promotores: Prof. T Hackeng, Prof. H Hemker
Co-promotores: Dr R Al Dieri, Dr B de Laat
Maastricht University, December 19, 2014

Van Breugel N -
Add-on ablation surgery in patients with atrial fibrillation; Drivers for Intervention
Promotor: Prof. J Maessen
Co-promotor: Prof. S Gelsomino
Maastricht University, December 23, 2014

Zandbergen R -
Mechanisms and Imaging of myocardial injury and repair
Promotores: Prof. J Maessen, Prof. L Hofstra, Prof. S Gelsomino
Maastricht University, December 24, 2014

PHD THESES externally prepared

Medina Rodriguez I -
Modulation of leukocyte homeostasis in atherosclerosis
Promotores: Prof. E Biessen, Prof. T van Berkel
Leiden University, May 13, 2014

Stöger J -
Atherosclerosis & inflammation: Macrophage heterogeneity in focus
Promotores: Prof. M de Winther, Prof. E. Lutgens
Co-promotor: Dr M Gijbels
University of Amsterdam, May 15, 2014

Van Bussel B -
Endothelial dysfunction and low-grade inflammation: Determined by diet and cause of arterial stiffness
Promotores: Prof. C Stehouwer, Prof. C Schalkwijk
Co-promotor: Dr R Henry
Maastricht University, May 28, 2014

DISSERTATION PRIZE 2013

Dr **Heleen Bouman** receives the Dissertation Prize 2013 on January 10, 2014, during the 38th Dies Natalis at the MECC Maastricht. Heleen received the award, which was presented this year for the first time on behalf of the 'Hooglerarenfonds' (part of Limburg University Fund), for her PhD thesis entitled 'Towards personalized antiplatelet therapy' (promotor Prof. Hugo ten Cate). In her thesis Heleen studied different aspects of the prevention of thrombosis. She illustrated the mechanism behind the effect of clopidogrel (blood coagulation prohibitor), with a special focus on genetic and personal factors in the farmacokinetic determinants of the response to clopidogrel. "Since this mechanism is rather complex, it was necessary to develop several new research techniques. The jury is convinced that the studies really forwarded knowledge and have contributed to a solution to the thrombosis problem in medical care."

KNOWLEDGE TRANSFER

CARIM COURSE WEEK

In parallel to the ERC visit, the CARIM Course week took place from June 2 until June 6. The course week consisted of parallel courses, covering several aspects of CARIM's research, alternated with a combined scientific program and a social program organised by I'M CARIM, the organisation of CARIM's PhD's. In 2014, four courses were organised by CARIM researchers: Drug Discovery and Development, Heart Failure Research: Getting to Excellence, Non-Invasive Biomedical Imaging and Advanced Microscopy and Vital Imaging. Almost 45 PhD and Master students participated.

CARDIOVASCULAR GRAND ROUNDS

The Cardiovascular Grand Rounds Maastricht and the yearly CARIM Symposium are means to update the knowledge of our graduate students, our researchers and other external people with interest in the field of cardiovascular research. In the framework of the Cardiovascular Grand Rounds Maastricht, three successful lecture series were organised in 2014 by Dr **Blanche Schroen** and Dr **Paula da Costa Martins** (Dept. of Cardiology), with cardiovascular lectures given by national and international experts, on a weekly basis. For the current programs please visit www.carimmaastricht.nl, 'CARIM lectures' in the 'Education' section.

CARDIOVASCULAR GRAND ROUNDS MAASTRICHT

CARIM SYMPOSIUM 2014

CARIM's annual scientific symposium was held in Maastricht on November 26. As in previous years, a substantial part of the program was a poster session, in which scientists of the institute presented their recent research findings. The lecture program existed of three sessions including current and future developments and discussions within the cardiovascular research field. The first session consisted of the presentation of Vidi laureate **Blanche Schroen**, the second session contained five short presentations around the theme "systems biology" and the last session was focused on experimental approaches in cardiovascular research with lectures of Prof. **Harry Struijker Boudier** and Prof. **Jos Kleinjans**. The traditional Robert Reneman lecture was presented by Prof. Pieter Reitsma, professor and head of the Department of Thrombosis and Hemostasis and the Einthoven Laboratory for Experimental Vascular Medicine at Leiden University Medical Center. The main purpose of Prof. Reitsma's present research is to develop diagnostic tests for the identification of individuals who are at risk of bleeding or thrombosis. Furthermore Prof. Reitsma is member of the Council of the International Society for Thrombosis and Haemostasis (ISTH) and co-Editor in Chief of the Journal of Thrombosis and Haemostasis.
The symposium was successfully completed with a festive evening in Grand Café Maastricht.

OTHER CARIM LECTURES SEMINARS AND SYMPOSIA 2014

Complementary to the regular lecture series and CARIM symposium, several lectures, seminars and conferences were organised by our research staff in 2014. Some of them are presented below.

The **MIMSA (Maastricht Inflammation in the Metabolic Syndrome and Atherosclerosis)** mini-symposium, organised by Dr **Marjo Donners** (Dept. of Pathology) and Dr **Kristiaan Wouters** (Dept. of Internal Medicine) took place twice in 2014, in March and October. The topic of the mini-symposium is focused on inflammation related to the metabolic syndrome and atherosclerosis. The aim is to provide a platform for young researchers (post docs and PhD students) to present and discuss their data in an informal meeting (i.e. unfinished projects, plans or problems encountered) and to get acquainted with each other's research to stimulate collaborations. Each time a senior researcher from another university is invited to give a keynote lecture.

From September 20 until September 22 the **38th Meeting of the European Working Group on Cardiac Cellular Electrophysiology,** organised by Prof. **Paul Volders** (Dept. of Cardiology), Prof. **Uli Schotten** (Dept. of Physiology), Dr **Cristina Morena**, **Rachel ter Bekke** and **Roel Spätjens** (all Dept. of Cardiology), took place in Maastricht. As a tradition, this meeting is the perfect combination of the best of lectures given by very high level of international experts and an incredible friendly and stimulating spirit. Over 170


CARIM
SYMPOSIUM
2014

scientists, coming from 18 different countries visited the annual Meeting to present and discuss their latest research in an informal and pleasant way.

On November 14, **the second scientific meeting of the Maastricht Study** took place, where the new results were presented by PhD students. Additionally a brief update on the progression of the study was given. The keynote lecture "The role of psychological factors in the development of type 2 diabetes and the long-term complications" was given by Frans Pouwer, Prof. of Pyschosomatic Research in Diabetes Mellitus, Tilburg University.

On November 25, the mini-symposium **Blood Coagulation and Inflammation: two double-edged swords to safeguard homeostasis** on the occasion of the PhD defense by **Karin Wildhagen** (Dept. of Biochemistry) took place.

Furthermore several (internationally) high profile scientists were invited to present a lecture at CARIM, a.o. Prof. Stevo Julius, Prof. Joachim Jankowski, Prof. Peter Peters, Prof.Stephane Richard and Prof. Nigel Mackman.

INTERVIEW

MARC VAN BILSEN YVONNE OLIGSCHLÄGER

The Education Program Committee (EPC) advises the CARIM Board on matters regarding its policy on PhD students, whether in response to a request or at its own initiative. Staff and representatives of the PhD students meet once a month to discuss how the working climate for the 120 PhD students at CARIM can be optimised.

One of these PhD representatives is Yvonne Oligschläger. The chair of the committee is Dr Marc van Bilsen, who is also the PhD coordinator at the research school: “It remains a big challenge to convince PhD supervisors that it may be useful for a PhD student to look beyond the boundaries of their own research project.”

GOING ALL-OUT FOR THE BEST PHD CLIMATE

The EPC consists of six staff members and five PhD representatives, who basically remain a member until the end of their PhD project. Yvonne Oligschläger joined the EPC in January 2012, a few months after she had started her PhD. "I think it's important to get an opportunity to network during your PhD project, and to be in regular contact with your fellow PhD students. So I think it's really valuable that we've set up a bimonthly 'Young Investigator Rounds' meeting for PhD students in recent years. These are interactive meetings where two of the colleagues present their research. The meetings are only attended by PhD students as we want to ensure an informal and relaxed atmosphere."

ENTHUSIASTIC

Yvonne's eagerness to become a member of the committee does not stem only from her personality. Marc Van Bilsen thinks membership is also encouraged by the atmosphere in the EPC. "These are highly motivated people, and that also has a positive effect on the others. I'm happy to say we have no problems finding new EPC members." Marc himself was asked to write down his views on CARIM's PhD program, after which he was appointed chair of the committee and PhD coordinator. "I enjoyed examining the existing PhD policy and seeing what could be changed or improved."
This led to a new CARIM Research Education and Supervision (CaRES) plan, which involves, among other things, asking each PhD student to write their own research plan during the first few months of their project. "We also updated the courses program, and formalised the attendance procedure, as things had lately become a little slack", says Van Bilsen.

COURSE WEEK

Currently, the PhD students can choose from a very wide range of courses, including five CARIM courses. Since 2014, each PhD student is obliged to attend at least two of them. Oligschläger attended the courses on "Drug Discovery" and "Advanced Microscopy". "It's very useful to look beyond the boundaries of your own discipline; it's also good for your network." Van Bilsen: "The course week is in June, and I sometimes get an email from a PhD student who claims to find nothing suitable among the courses. That's impossible, really. Of course a PhD project requires a very specific focus, but at the same time it would be a shame not to use the opportunity to broaden your scope at this stage of your career. After all, what are the chances that you'll be working on almost the same research subject after you've got your PhD?"

Van Bilsen and the EPC are also trying to convince the PhD supervisors of the need to look beyond boundaries. “When I was doing my PhD, we weren’t doing any courses at all, and that’s the culture in which most of the supervisors have been ‘raised’. Some regard anything that distracts you from the research work for your PhD thesis as a waste of time. But I think we have a moral duty to prepare the youngest generation of CARIM researchers for post-degree life.”

AWARD

In 2014, the EPC laid the foundation for a success it scored in the spring of 2015: the establishment of the CARIM Talent Fellowship Award. This grant is intended for talented PhD students who have nearly completed their PhD project, and will enable them to do research at an institute abroad for a year. “That’s good for their CV”, says Van Bilsen, “as such an experience is very important when you’re applying for prestigious grants, such as a Veni grant. And we also try to get them to return to Maastricht to share and further expand their knowledge and expertise.” What needs to be done now is to specify the plan and to scout and select these talents. The introduction of the Faculty’s PhD-TRACK system also led to much debate in the EPC. The purpose of this system is to ensure that most PhD students are able to complete their PhD project in time. “Some of the elements of the system were copied from our own CaRES plan, such as the obligation to write a research plan in the first few months. But it also forced us to adapt our course program to some extent to be in line with that of the other schools, which is unfortunate”, says Van Bilsen. The EPC also evaluates sponsoring applications, organises PR activities particularly among Masters students and discusses other practical issues that CARIM PhD students are concerned about.

PARTICIPATION

Yvonne Oligschläger is working hard to complete her PhD thesis by 31 July, as her contract expires in August 2015. She does not rule out that she will take part in another participation council. “This experience has taught me how exactly a research school works, and that’s interesting, especially if you intend to go on working in academia. I wouldn’t have missed it for the world.”

For the Education Program Committee members, see page 17.

COLOPHON

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