

Graduate School Life Sciences (GS-LS), Utrecht University
PhD programme Cardiovascular Research (CVR)

- 1. Name of the programme:** Cardiovascular Research (CVR)
Programme director: Prof. G. Pasterkamp (Dept. Exp. Cardiology, UMCU)
Programme coordinator: M.L. Zonderland, PhD (Dept. Med. Physiology, UMCU)
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Website: <http://www.cardiovascres-utrecht.nl>

2. Research area

In the western world, cardiovascular diseases still are one of the most prevalent causes for morbidity and overall mortality. Our research programme aims to enhance our knowledge concerning atherothrombosis and heart failure in order to improve therapeutic options for these disorders.

The two lines of research (atherothrombosis and heart failure) include the whole spectrum from basic to clinical activities. The research is done at various levels of complexity ranging from health care in general, to population and prevention, patient care, experimental work on animals, cell biology and using molecular techniques as proteomics and genomics. Within the theme *Atherothrombosis*, research is aimed to enhance knowledge concerning vascular remodeling, plaque vulnerability, relevance of toll-like receptors, coagulation, arteriogenesis, thrombogenicity of platelets and protein misfolding. The theme *Heart Failure* focuses on understanding the pathophysiology of and signals responsible for cardiac adaptation processes leading to ventricular hypertrophy, heart failure, arrhythmias and sudden cardiac death. Complementary integrative research is conducted on inherited and acquired diseases related to heart and kidney with an emphasis on the consequences of aging for the progression of the disease.

3. Profile of prospective PhD candidates

The CVR programme is open for PhD students with a master education in Life Sciences, Medicine or Veterinary Medicine (Fig. 1). In addition, PhD students with a master education of other programmes are admitted provided that the PhD research relates to cardiovascular topics.

PhD education in cardiovascular research already starts in the Bachelor studies at Utrecht University. In that phase, students follow or choose courses that are relevant for their training as researcher in cardiovascular sciences (Fig. 1): e.g. Organ systems ("Orgaansystemen"), Conceptual Pathophysiology ("Conceptuele Pathofysiologie"), Circulation ("Circulatie"), Heart and vessel diseases ("Hart- en vaatziekten"), and Haemostasis and Thrombosis ("Hemostase en Thrombose"). These courses are mostly advanced courses, organized by the Bachelor programmes Biomedische Wetenschappen, Medicine and Pharmaceutical Sciences. The course Organ systems and the course general Pathology are required in order to be admitted to the master programme Biology of Disease of the Biomedical Sciences education.

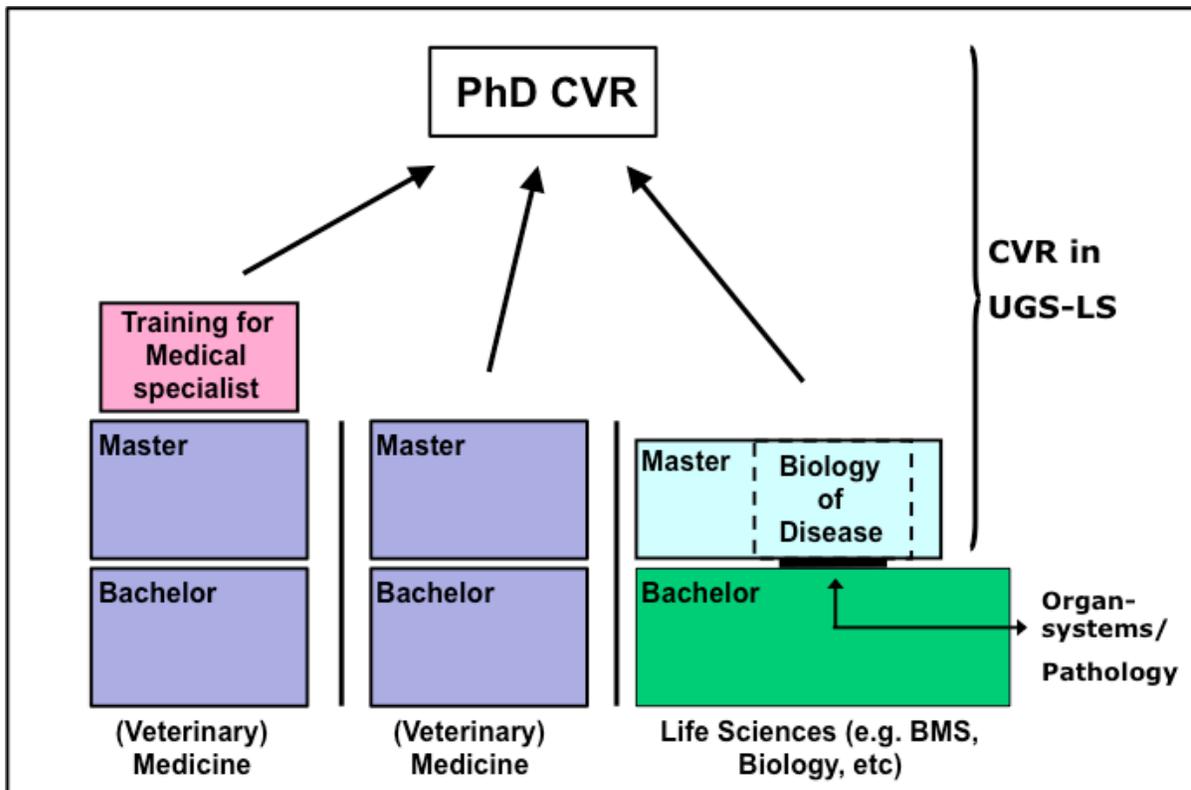


Fig 1. Origin of PhD students in the CVR programme

The master programme Biology of Disease includes a line of study that focuses on cardiovascular items. The study programme consists of the following elements (credits assigned according to the *European Credit Transfer System, ECTS*):

- major research project: 9 months (51 EC)
- minor research project : 6 months (33 EC)
- writing assignment (master thesis) (7.5 EC)
- master courses (15 EC):
 - Mechanisms of disease (3 EC)
 - Biomolecular and cellular cardiology (3 EC)
 - Cardiovascular immunology (formerly: Vascular biology and innate immunity) (3 EC)
 - Metabolic disorders (3 EC)
 - Thrombosis and haemostasis (3 EC)
- Electives: 12 EC
- Life Sciences seminars (10 abstracts; 1.5 EC).
- Total: 120 EC

4. Mission of the training programme

The programme wants to challenge PhD students to gain more in-depth knowledge of cardiovascular research. In a multidisciplinary setting the students participate in research, meetings, symposia and courses, a.o. on the (patho) physiology of heart and vessels. Subjects include thrombotic aspects, methodology including animal models, valorization and regenerative medicine. Via this, the students are offered the opportunity to explore the area from the level of molecular biology to patient care. Besides theoretical education the programme aims to train academic researchers who are familiar with exceeding the limits of their own project.

After completion of the programme, the PhD student:

- has profound knowledge of cardiac and vascular diseases and disease mechanisms;
- is able to communicate and collaborate with peers and other scientists in the Netherlands and abroad;
- can operate independently;
- can formulate new research questions and write grant proposals;
- is able to communicate with the broad scientific community on an academic level, and with the general public;
- will have insight into the various possibilities to develop his/her career according to personal interests.

To ascertain its high quality and actuality, the admission to and mission of the CVR programme is continuously monitored by the programme committee consisting of:

Prof. G. Pasterkamp (chair), Exp. Cardiology, UMCU
S.A.J. Chamuleau, MD, PhD, Cardiology, UMCU
Prof. M.L. Bots, Julius Center, UMCU
M. Roest, PhD, Clinical Chemistry, UMCU
J.A. Post, PhD, Cell Biology, Department Biology, Utrecht University
M.L. Zonderland, PhD, Medical Physiology, UMCU
M.F.A. Bierhuizen, PhD, Medical Physiology, UMCU
PhD candidate representative(s)

5. Areas of research at the Utrecht University

Within the UMC Utrecht the CVR programme comprises the research activities of eight divisions (Heart and Lungs; Internal Medicine and Dermatology; Laboratory and Pharmacy; Surgical Specialties; Radiation, Radiology and Nuclear Medicine including Imaging; Julius Center; Neuroscience; Pediatrics); within Utrecht University extensive collaborations exist with Veterinary Medicine (A. de Bruin, Pathology), Pharmacy (A. de Boer, Pharmaco-epidemiology and Pharmacotherapy), Biology (J.A. Post, Cell Biology) and the Proteomics Center (A. Heck).

6. Specifics of the CVR training programme

Programme selection and admission

Within 3 months after starting the PhD, students have to select a PhD programme that fits their research project or interest, register in Metis and have to complete a Training and Supervision Agreement (TSA), this in consultation with the (co)promoter. The general description of these procedures can be found on the following website of the Graduate School of Life Sciences:

<http://www.uu.nl/university/education/EN/graduateschools/gsls/phdcandidates/Pages/Admission.aspx> (Graduate School of Life Sciences/ PhD candidates/ Admission)

Upon choosing the CVR PhD programme, the TSA should reflect this programme selection and contain a provisional educational programme (i.e. planning of courses etc.) according to CVR programme regulations. However, it is still possible to change this original planning during the PhD-track. Moreover, a Supervisory Committee ("aiobegeleidingscommissie") should be installed that will monitor the progress of the PhD-track on a yearly basis.

Finally, The TSA should be signed by both the PhD student and supervisors, and approved by either the Head of the Department (Faculty of Science), the Director of the Institute of Veterinary Research (Faculty of Veterinary Medicine) or the Division Manager Research (UMCU). After that, it is sent to the coordinator of the programme. The TSA is then discussed by the Programme Committee and if approved, signed by the Programme Director. The original is sent to the dean, copies are sent to the student and kept by the programme coordinator.

Monitoring

The progress (rate, direction) of the PhD-track is monitored on a yearly basis in two ways. First, PhD student and supervisors conduct the annual assessment interview. The outcome of the interview is reported to both the personnel department and the programme coordinator. In case of disagreement, the coordinator and/or the chair of the programme are available for consultation and advice. Second, the Supervisory Committee will discuss the PhD-track with the PhD candidate every year and provide independent advice on its progress to both supervisors and PhD candidate. For this, the PhD candidate needs to provide the Supervisory Committee with an annual progress report that will serve as the basis for the discussion.

Educational programme

The CVR educational programme consists of various elements with a total of 5 EC/year of appointment (20 EC total for a 4-year PhD-track) (1 EC = 28 hr; 1 day = 0.3 EC):

- | | |
|---------------------------|--|
| a. Generic courses | minimal 20% of total (4 EC for a 4-year PhD-track) |
| b. Cardiovascular courses | minimal 40% of total (8 EC for a 4-year PhD-track) |
| c. Elective courses | appr. 40% of total (8 EC for a 4-year PhD-track) |

a. Generic courses

Students can choose generic courses from the list of the GS-LS or externally organized courses. The courses that have a large interest are:

- Presenting in English (Babel; <http://www.babel.nl>)
- Writing in English for publications (Babel; <http://www.babel.nl>)
- Biostatistics (Julius Center)
- Laboratory animal science (art. 9)
- Management for PhD students and postdocs (NIBI; <http://www.nibi.nl>)
- That thing called science (UMC Utrecht)

The CVR programme itself also organizes one generic course:

- Entrepreneurship and innovation in life sciences & health seminars (3 EC; see Appendix 1).

Alternative courses, if well-founded, can be followed after consultation and approval of the programme committee (via the programme coordinator).

b. Cardiovascular courses

Cardiovascular-specific education is offered in:

- **SEMINARS**
 - Jongbloed seminars (monthly from September-June; 5 seminars = 0.5 EC; max. 1.5 EC total; registration via attendance list)(**compulsory**)
 - Regenerative Medicine meetings (1.5 EC for a 4-year PhD track)
 - Research Colloquia Cardiology (weekly from September-June; 10 seminars = 0.5 EC; max. 3.0 EC total; registration via attendance list)
 - Other seminars after consultation of the coordinator
- **(INTERNATIONAL) CONGRESSES**
 - Scientific meetings of professional associations
 - Symposia during scientific congresses
- **PhD RETREATS**
 - 1 day per retreat, 0.3 EC per day (**at least 1 compulsory**)
- **COURSES ORGANIZED BY THE CVR PROGRAMME (at least 1 compulsory; see Appendix 1)**
 - Cardiovascular animal models (3 EC)
 - Sophisticated laboratory techniques in cardiovascular research (3 EC)
 - Innovations in clinical cardiovascular medicine (3 EC)
- **EXTERNAL COURSES BY THE DUTCH HEART FOUNDATION ((at least 1 compulsory; see Appendix 2)**

c. Elective courses

PhD students CVR may choose courses organized by other PhD programmes of the GS-LS, or by other universities in the Netherlands or abroad. Choice is made in consultation with supervisors and programme coordinator.

d. Courses to repair deficiencies

After consultation with supervisors and programme coordinator, deficiencies may be repaired by participating in courses of master programmes (see Appendix 3).

Participation of PhD students of other GS-LS programmes

PhD students of other GS-LS programmes are welcome to participate in the courses of the CVR PhD programme provided that the capacity of the course is not exceeded.

APPENDIX 1: COURSES ORGANIZED BY THE CVR PROGRAMME

1. ENTREPRENEURSHIP AND INNOVATION IN LIFE SCIENCES & HEALTH SEMINARS (3 EC)

Goal

Many Master or PhD students who are active in biomedical sciences will not pursue a career in an academic institute. Many will become involved in R&D or management in the private sector. Some may even be working in a recently established biotech company, a start-up. This course will provide insight how your current knowledge will be utilised into practice in a non-academic setting or in public-private partnerships.

Content

Seminars are given by academic experts and practitioners from industry and government who share their insights on entrepreneurship and innovation in the life sciences and health domain. The seminar series covers a broad range of topics, including new ventures in life sciences, growth of ventures, collaboration for innovation, marketing new products, intrapreneurship, intellectual property, finance, university-industry interaction, innovation policy, and science policy.

At the end of the course the student is:

1. acquainted with processes of new value creation, and more particularly the interaction between science, industry and policy in the domain of Life Sciences & Health.
2. prepared for interacting with business and policy, and to create new value as a professional in the Life Sciences & Health domain.

Format

The Entrepreneurship and Innovation in Life Sciences & Health Seminars is organized on a monthly basis. More specific information about dates, speakers and topics can be found on the website of the Utrecht Center for Entrepreneurship (www.utrechtce.nl/seminars). Participation in the seminar series can be rewarded with 3 EC, when students participate in at least 8 out of 10 seminars, and deliver a report on each seminar. Attendance will be registered.

Course coordinators

Prof Erik Stam, Utrecht Center for Entrepreneurship, Utrecht University School of Economics; Email: e.stam@uu.nl; Tel.: +(31) 30 2537894;

Dr. Paul Gründeman, UMC Utrecht, Exp. Cardiothoracic and Vascular Surgery, Division Heart and Lungs; Email: P.F.Grundeman@umcutrecht.nl; Tel. + (31) 88 7556179.

2. CARDIOVASCULAR ANIMAL MODELS (3 EC)

Goal

Translational research requires adequate models to bridge the gap between *in vitro* experiments and clinical reality. Animal models basically serve 3 aims: 1) to gain mechanistic insights into (patho) physiological processes; 2) to mimic human disease; and 3) to test experimental therapeutic approaches, either separately or combined. The aim of this course is to make PhD candidates familiar with cardiovascular animal models used in the different experimental laboratories. This enables the student to better judge the implications of experimental animal studies, to get a broader view of models with their advantages and disadvantages, and to use these insights to optimize own models.

Content

In this course a total of at least 6 animal models with different experimental setups will be covered. The models include myocardial infarction and I/R injury, valve transplantation, experimental surgery concerning heart failure, hind limb ischemia, stem cell transplantation, stenting, hypertension. Techniques applied cover P/V loops, MRI, perfusion measurements, etc.

Format

The course will be given in English and in such a way that both the PhD candidates and the lecturers are able to incorporate this course in their daily work. Every week (10 times), the course will start with a 2 hours introduction given by the lecturer. Besides theoretical background of cardiovascular experimental models, the PhD students will participate in at least 6 different animal experiments. After 10 weeks of lectures, the students will be given assignments by the different laboratories providing them with a research question and the task to develop an experimental model to address this question. The course will be finished within a time frame of 6 months maximal. This allows for the right planning and visits of animal experiments. To qualify for the certificate and 3 EC, participants must attend all lectures and complete all assignments satisfactorily. Attendance will be registered.

Number of participants

Maximum 30 per course. All PhD students can register, however if more than 30 persons register, the organization reserves the right to make a selection.

Costs

No charge for registered PhD students.

Course coordinator

Imo Hoefler, MD, PhD, UMC Utrecht, Experimental Cardiology, Division Heart and Lungs;
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3. SOPHISTICATED LABORATORY TECHNIQUES IN CARDIOVASCULAR RESEARCH (3 EC)

Goal

With the development, improvement and increased availability of laboratory techniques, more and more techniques become accessible for every researcher. A lot of these techniques are generally applicable in a wide range of research fields, e.g. RT-PCR, use of siRNAs to silence gene expression, etc. Others are more specific, e.g. using the Langendorff set up to study heart function, or flow measurements in arteries. The aim of this course is to make PhD students familiar with sophisticated laboratory techniques. The focus will be on techniques that are used in cardiovascular research, but the course is not limited to this field. During the course a number of relatively new techniques will be discussed, and techniques that have been used for quite some time, but are still developing by improvement in quality and availability.

Content

Ten different techniques will be discussed in the course. Topics that will be addressed in this course are the luminex-multiplex technique, applicability of LAMA antibodies, gene expression regulation by miRNAs, bioluminescence, *in vivo* life imaging, proteomics, sequencing, flow cytometry and cell sorting, electron microscopy, Langendorff hearts for electrocardiography measurements, etc.

Format

The course will be given in English. During this course, experts in their fields will give lectures in which they will 1) focus on the technical aspects and theoretical background of a certain laboratory technique; and 2) discuss how this technique has been, or might be applied in cardiovascular research. The course consists of 10 weekly lectures and participation in this course will not (or minimally) interfere with the regular activities of students, lectures and teachers. To qualify for the certificate and 3 EC, participants must attend all lectures and complete all assignments satisfactorily. Attendance will be registered.

Number of participants

Maximum 20 per course. All PhD students can register, however if more than 20 persons register, the organization reserves the right to make a selection.

Costs

No charge for registered PhD students.

Course coordinators

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Saskia de Jager, PhD, UMC Utrecht, Experimental Cardiology, Division Heart and Lungs;
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4. INNOVATIONS IN CLINICAL CARDIOVASCULAR MEDICINE (3 EC)

Goal and content

From bench to bedside sounds like the ideal research that brings an idea based on any need in the clinic, via experiments at the bench in the lab, into the clinic. A new research line often starts in the clinic, after a discussion about possible improvements and necessary developments in tools or techniques. In recent years some of these 'wild' ideas really made it into the everyday clinic routine of cardiology.

The aim of this course is to show PhD candidates that daily measurements and routines in the clinical cardiology department nowadays, once started with an idea of possible improvement and /or experiments at the bench. It is often in the clinic, right next to the patient that research questions rise. This course will bring the researcher in contact with the clinical needs and most recent improvements in the clinical cardiology and technology.

Format

The course will be given in English. The course will exist of 10 theoretical lectures and in addition there will be three visits to the 1) cath-lab; 2) operation room; 3) outpatient clinic or radiology department or echocardiography laboratory. The participants will prepare for the lectures by reading a landmark paper covering the topics. And they will write a small report about their clinical visits. To qualify for the certificate and 3 EC, participants must attend all lectures and complete all assignments satisfactorily. Attendance will be registered.

Number of participants

Maximum 16 per course. All PhD students can register, however if more than 16 persons register, the organization reserves the right to make a selection.

Costs

No charge for registered PhD students.

Course coordinator

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APPENDIX 2: EXTERNAL COURSES BY THE DUTCH HEART FOUNDATION

1. *CARDIAC FUNCTION & ADAPTATION (1.5 EC)*

The course on **Cardiac Function & Adaptation** aims at understanding the normal (physiologic) functioning of the heart and pathologic changes in cardiac properties during heart disease. Each day of the course has a specific theme.

2. *ATHEROSCLEROSIS & THROMBOSIS (1.5 EC)*

The **Atherosclerosis & Thrombosis** course will start with an introduction into the (patho)physiology of the blood coagulation system and its significance in health and disease. Attention will be paid to both arterial and venous thrombosis. The interactions of the atherosclerotic vessel wall and blood coagulation leading to cardiovascular events will be addressed. Specific severe prothrombotic conditions (including cancer, inflammatory diseases) will complement the course.

3. *VASCULAR BIOLOGY (1.5 EC)*

The **Vascular Biology** course provides an introduction into structure and function of the vascular system, with emphasis on vascular development, vasoregulation, vascular function and activation and vascular diseases. Normal vascular function may be compromised by mechanical or biochemical influences as occur during hypertension and diabetes. This will be addressed during the course. Moreover, remodeling of the vascular wall and the vascular tree (angiogenesis, arteriogenesis) will be discussed in relation to vascular diseases.

Please visit <https://www.hartstichting.nl/wetenschappers/phd-training-courses> for more information on the format, registration, costs and the precise dates of the courses.

APPENDIX 3: COURSES TO REPAIR DEFICIENCIES

- **Biomolecular and Cellular Cardiology** (BMS master Biology of Disease): 3 EC
Molecular and cellular approaches applied in the study of the healthy and diseased heart. Subjects: alterations in miRNA expression, Ca²⁺ regulation, gap junctional communication and adrenergic signaling in cardiac disease. Moreover, the molecular basis of arrhythmias and the role of single nucleotide polymorphisms (SNPs) will be featured as well.
Application: M.F.A.Bierhuizen@umcutrecht.nl.
- **Cardiovascular immunology** (BMS master Biology of Disease): 3 EC
In this course the role of the innate and adaptive immune system in vascular disease and the consequences of vascular disease are studied. The potential future role of immune modulation to prevent primary and secondary manifestations of vascular occlusive disease is discussed.
Application: utrecht.cardioresearch@umcutrecht.nl.
- Etc.

The EC obtained by these courses come at the account of the electives.