

# Assessment of Research Quality 2010 - 2012



**UMC Utrecht**



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# Preface

Since 2010 research in UMC Utrecht is organized around six strategic programs with each a limited number of disease related targets. Patient care and education are integrated in these multidisciplinary programs. The programs are part of a matrix which also contains eleven disciplinary divisions.

This approach should provide maximal guarantee that patients benefit from the latest available expertise and innovative technological solutions. The idea behind these programs is to drive our research whenever possible, beyond publishing research articles in the literature, into clinical practice, via clinical trials and for example biomarker evaluation. Eventually we aim at implementation and evaluation in the daily practice of care. As part of the quality control of UMC Utrecht research, we performed a thorough evaluation of our research activities. This evaluation was directed by the Research Office and included an extensive self-assessment of our strategic programs followed by a site visit of six expert panels in the first quarter of 2014. The panels were exposed to selected senior investigators and poster sessions presented by young research talent. The evaluation was based on reading and discussing the reports that had been provided with the researchers involved in the programs.

Additionally the six panel chairs were invited to participate in a main panel to review the UMC Utrecht research organization in total. The panel members were all distinguished and active scientists with a high level of experience in biomedical, clinical and health care research.

To evaluate the societal impact of our research, representatives from relevant societal stakeholders were invited for an interview with the expert panel to extend the expertise on assessing the societal impact of the research. In this unique format, stakeholder representatives were advisory to the expert panel in developing an opinion on societal and clinical impact of our research. The organization and educational programs of the UMC Utrecht PhD programs, which are part of the Graduate School of Life Sciences, were also subjects of the evaluation.

This report summarizes the evaluation outcome. We are very proud that all panels were impressed by the quality of the research. The panels were supportive about our strategy to implement multidisciplinary research programs each focusing on a few selected topics and abandoning other clinical targets all together. We are pleased with the positive evaluation of our PhD education and training programs and the suggestion to take more advantage from these in the opinion of the panels unique graduate programs while attracting excellent talent in the future.

All the panels generated important, sometimes quite critical and very useful recommendations for further improvement of our research ambitions. The panels stressed that now is the moment to take the multidisciplinary programs one big step further by defining clear responsibilities as to who is directing the research and to give more steering and management power to the program chairs. We also recognize the remark by the panels that the UMC Utrecht research system is in transition and that for the assessment of the impact of our research on patient care we need to develop a set of useful and adequate criteria together with the stakeholders. Moreover, a set of novel and different criteria from the classical bibliometrics should be used for evaluation of CV's with regard to career advancement in the translational research area.

The Executive Board of UMC Utrecht recognizes and accepts these recommendations and will use this evaluation report as invaluable input for the development of the new strategy for the period 2015-2020 which will be established in the second half of this year.

We acknowledge and are very grateful for the massive amount of work that has been performed by our program chairs and researchers involved to produce this extensive overview and evaluation of the UMC Utrecht research endeavor. In addition, we thank the panel members for their very constructive and honest judgment of our research performance and clear recommendations towards our research governance. Also a special thanks to the stakeholder representatives for their valuable enthusiastic contribution.

In conclusion, we are very proud on the outcome of this research evaluation and see this as an encouragement to continue with our multidisciplinary research programs despite the inherent tensions that are typical for a matrix organization. We believe that in order to promote the translation of our research findings into innovative practice this programmatic approach is critical.

*On behalf of the Executive Board,*

*Frank Miedema*

*Dean and vice chair of the Executive Board of the UMC Utrecht*

# UMC Utrecht





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# 1 Introduction

## 1.1 The Netherlands System of Quality Assessment of Research

This quality assessment of research is part of the assessment system for all public Dutch university research, as organised by the Universities and University Medical Centers (UMCs) in the Netherlands.

The aims of the assessment system are:

- Improvement of research quality based on an external peer review, including scientific and societal relevance of research, research policy and research management.
- Accountability to the board of the research organisation, and towards funding agencies, government and society at large.

Universities and UMCs in the Netherlands have agreed to carry out a self-evaluation every three years and an external review every six years. This process is guided by the Standard Evaluation Protocol (SEP). For this evaluation the SEP 2009-2015 is used.

The present external research evaluation has the following objectives:

- To assess the quality of the research and graduate PhD programs carried out at the UMC Utrecht during the period under review (2007-2012) compared to an international benchmark (not a comparison within UMC Utrecht);
- To identify research areas that have the potential to stimulate innovation and have societal impact;
- To identify excellent research groups and young researchers with high research potential;
- To identify research areas that are currently of the highest international standard, how these may be strengthened and suggest conditions for their continued development.
- To identify research areas that have the potential to develop towards the highest level of international research and to determine what is necessary to ensure such development.
- To identify research areas that are not internationally or nationally competitive and lack evident development potential.
- To identify research areas that are missing and that could be considered to be essential for the UMC Utrecht.
- To identify the need for infrastructural support that would facilitate development towards greater excellence.

## 1.2 Organisation of the review of the University Medical Center Utrecht

The Board of the UMC Utrecht invited six expert panels to assess the research conducted at the UMC Utrecht in the newly established six strategic programs (Brain, Infection & Immunity, Circulatory Health, Personalized Cancer Care, Regenerative Medicine & Stem Cells, and Child Health). The six specific expert panels received a self-evaluation report and key publications and visited the UMC Utrecht to assess the specific strategic research programs. These program reviews took place between February 6<sup>th</sup> and April 11<sup>th</sup> 2014. All panels produced a draft assessment report. Additionally the six panel chairs were invited to participate in a main panel to review the UMC Utrecht research institute. For this institutional review a separate site visit was organised and a separate assessment report is conducted.

### **1.3 The Review Panel**

The Main Panel was appointed 22 November 2013 and consisted of the chairs of the respective program assessment panels:

- Bert van der Heijden: Child Health
- Anthony Hollander: Regenerative Medicine and Stem Cells
- Florian Holsboer: Brain
- Rene van Lier: Infection and Immunity and chair of the main panel
- Rob Reneman: Circulatory Health
- Josep Taberner: Personalized Cancer Care

Barbara van Balen was the secretary to the Review Panel.

For the curriculum vitae of the panel members see the Appendices in the respective program assessment reports.

### **1.4 Scope of the Assessment**

In 2010 a midterm self-evaluation was prepared by the UMC Utrecht of its activities for the years 2007, 2008 and 2009. The results of this midterm review were the basis for the development of a new research strategy for the UMC Utrecht: Strategy UMC Utrecht 3.0. The implementation of this strategy started in 2010.

This external review covers the period 2010-2012. The panel was asked to evaluate the success of the strategy, to identify aspects that can be improved and to provide the Board of the UMC Utrecht with comments and recommendations. The panel realises that the strategy has been launched relatively recently and that the results and the impact of the strategy in terms of scientific productivity and societal relevance can not be fully measured yet. The assessment is therefore for a large part based on discussions with the UMC Utrecht staff on strategic and organizational aspects and less on standard scientific output measures.

### **1.5 Data provided to the Committee**

The Review Panel has received a self-evaluation report provided by the UMC Utrecht. The panel also received the report on the Mid Term Review 2007-2009 and additional information about the PhD training programs.

### **1.6 Procedures followed by the review panel**

The assessment was based on the documentation provided by the UMC Utrecht and the interviews during the site visit. The interviews took place on 24 and 25 April 2014. The program of the site visit is included in Appendix 1.

The panel members had all read the Self Evaluation Report and the six preliminary program assessment reports.

The site visit started with an internal panel meeting, which was used to exchange the experiences with the program assessments and to prepare the interviews for this site visit. The panel interviewed a variety of groups: research managers of the divisions, representatives of the Graduate School of Life Sciences, PhD candidates, representatives of the Utrecht Life Sciences and the Hubrecht Institute collaboration, and Valorization and Quality ambassadors.

On the second day of the site visit, the panel discussed the assessment of and the recommendations for the institute. Finally, a meeting with the representatives of the UMC Utrecht was arranged, in which the main impressions of the panel were reported.

## 1.7 Aspects and Assessment Scale

The Protocol requires the Evaluation Committee to assess the research on the four main criteria of the *Standard Evaluation Protocol*:

- Quality, including:
  - Leadership
  - Academic reputation
  - Organisation
  - Resources
  - Research facilities
  - PhD training and supervision
- Productivity
- Societal relevance
- Vitality and feasibility (flexibility, management and leadership)

The ratings used are: Excellent (5); Very good (4); Good (3); Satisfactory (2); Unsatisfactory (1). This five-point scale used in the assessment is described in the *Standard Evaluation Protocol* as follows:

Excellent (5)	Research is world leading. Researchers are working at the forefront of their field internationally and their research had an important and substantial impact in the field.
Very Good (4)	Research is internationally competitive and makes a significant contribution to the field. Research is considered nationally leading.
Good (3)	Work is competitive at the national level and will probably make a valuable contribution in the international field. Research is considered internationally visible.
Satisfactory (2)	Work adds to our understanding and is solid, but not exciting. Research is nationally visible.
Unsatisfactory (1)	Work that is neither solid nor exciting, flawed in the scientific and or technical approach, repetitions of other work, etc.

# 2 Assessment of the UMC Utrecht

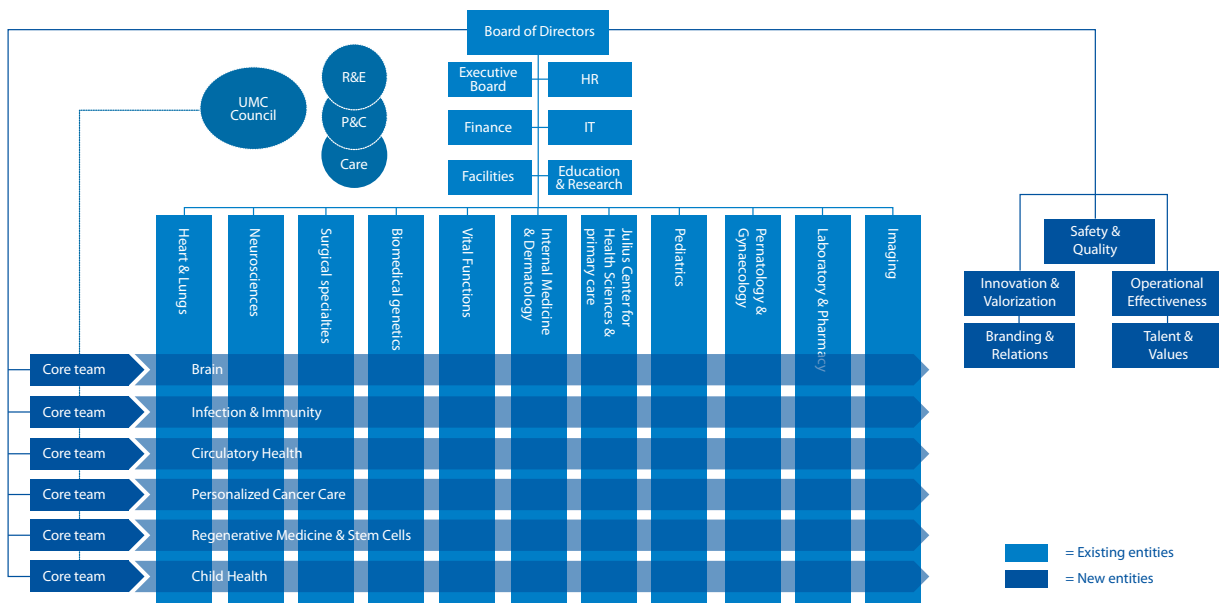
Research staff in 2012: 925 fte ( # 2401)  
 Executive board of the UMC Utrecht: Prof.J.L.L. Kimpen president  
 Prof. F. Miedema, vice president and dean  
 Mrs. M.H. van Velthuisen-Lormans, member  
 Mr. A. Bek, member

The UMC Utrecht is organized in eleven decentralized units, known as divisions, led by a management team. These divisions have their own budgets and policies. All divisions operate in the areas of direct patient care, education and research. The research managers of the divisions advise the Board on issues concerning research and PhD training programs. The Board and the division research managers meet on a monthly basis.

The strategic research programs are managed by a core team and headed by a chair. The chairs of the strategic programs meet with the Board to discuss relevant topics.

The six strategic research programs and the divisions form a semi-matrix structure. See figure 1.

Figure 1 Research matrix UMC Utrecht



## 2.1 Mission, goals and strategy of the UMC Utrecht

The mission statement as provided in the self-evaluation report: The University Medical Center Utrecht is a leading international academic medical center where knowledge of health, illness and care is generated, evaluated, shared and applied for the benefit of patients and society.

Core activities are:

- to provide state-of-the-art healthcare that requires special knowledge and expertise.
- to carry out cutting edge scientific research.
- to offer excellent healthcare programs and training to students, doctors, researchers and other healthcare providers.

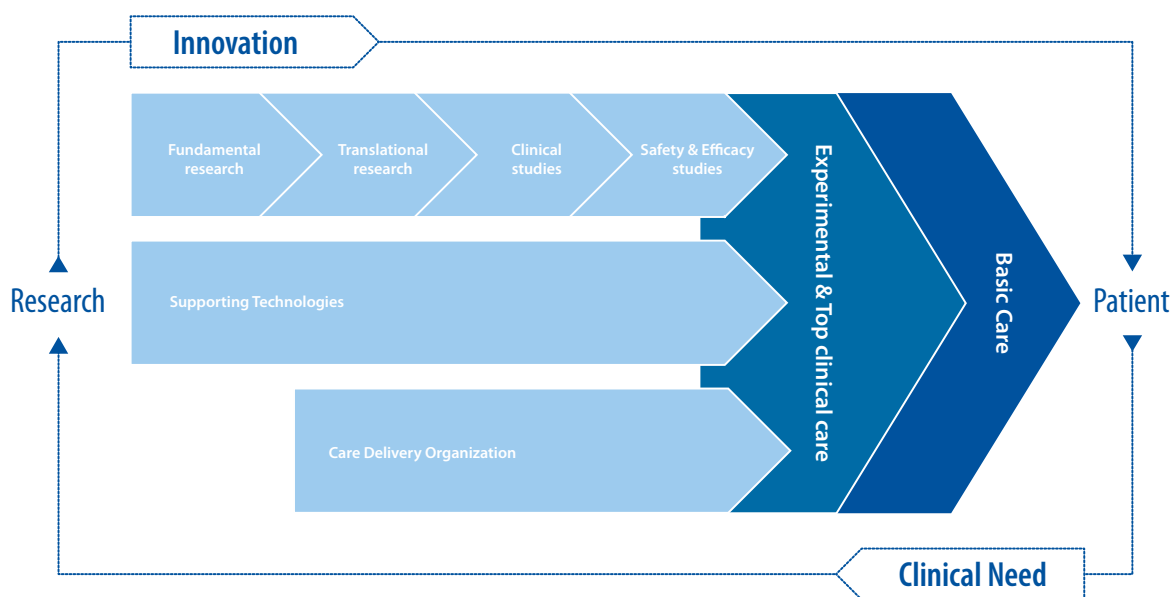
Research is concentrated in six strategic programs with a limited number of target diseases each. Patient care and education are integrated in these programs. A multidisciplinary approach should guarantee patients to benefit from state of the art medical expertise and innovative technological solutions. Interactions with patients and other stakeholders from society creates an ‘innovation loop’ where medical and societal issues help to direct scientific research and to ensure that scientific results quickly move between bench to bedside.

Information about the six strategic research programs can be found in the respective assessment reports. Complementary to the strategic programs broad “Strategic Themes” have been identified:

- Quality and Patient Safety
- Innovation & Valorization
- Branding & Relations
- Talent & Values
- Operational Effectiveness.

The UMC Utrecht strategy can be illustrated by the ‘Clinical need innovation loop’ (see figure 2). Identified clinical needs form the starting point for the research that will be performed for the clinical syndromes defined within the strategic programs. Research and innovation are induced by connecting basic research, preclinical developments, clinical trials and finally applied research. New clinical care will be developed and can eventually be implemented into standard care.

Figure 2



## 2.2 Assessment of the institute

### General remarks

The Board of the UMC Utrecht made a wise decision to implement the Strategy UMC Utrecht 3.0. The main panel applauds the strategy for defining multidisciplinary research programs, determining a portfolio and in particular for making selections: ‘not doing everything’. Most researchers believe in the new mission, support this strategy and seem very happy and enthusiastic. Not surprisingly the strategy is not yet fully implemented. The panel saw a system in transition and a number of managerial decisions still have to be made. The panel noticed that the strategic research programs can be found in different stages of development. E.g. the Circulatory Health program only started in 2012 and still has to find a way to manage the 63 cross lines of patient groups and research themes. The panel advises to tune this program down to a limited number of research lines to be able to make this program a success. The Brain program on the other hand was organised as an institute right from the beginning, has a clear focus and internationally and nationally visible research topics.

Given the recent start of the strategic research programs the panel had limited possibilities to assess the academic and societal impact. The panel, however, could identify clear and obvious benefits from the new strategy. The decision to specialise on particular areas creates focus which potentially gives power to the research in that field. That, for instance, all Dutch ALS patients are seen in the UMC Utrecht is very stimulating for the quality of the research in this area, which in the end will also give a boost to the quality of the ALS patient care.

The panel finds it very positive that the matrix system enforces the staff to cooperate across division borders. It observed a successful combination of top down and bottom up strategy in the implementation of the Strategy 3.0. Nevertheless the panel would advise to give the research program directors more steering possibilities. They should become directors instead of coordinators.

The UMC Utrecht board made the decision to provide the review panels with self-evaluation reports and a limited number of key publications for each of the strategic research programs; no full publication lists and no citation analyses were provided. This decision is understandable in the light of the UMC Utrecht strategy to focus on the translational part of the research and not on the numbers of publications. All review panels, however, faced the problem that they needed more information about the past performance of the researchers to be able to assess the programs according to the criteria of the SEP. Furthermore it was even harder to assess the impact of the research on patient care, since there are no criteria developed to measure this impact. Therefore, for the next review, the panel recommends to provide the external evaluation panel with more information about the research quality and to search for criteria to measure the translational part of the research.

#### **Quality 4**

The main panel appreciates the courage of the UMC Utrecht Board to make strategic choices. The Strategy 3.0. is widely supported by staff and students who showed a high commitment during the site visit.

The environment of the UMC Utrecht is very stimulating and supportive to reach high standards of research. The UMC Utrecht Board strategically invested in the cooperation with the Hubrecht Institute, an internationally recognized top institute. The panel concluded that this cooperation is very productive and attracts excellent researchers to the UMC Utrecht. The stimulating rich environment of the Utrecht Science park and the Utrecht Life Sciences Network should also be mentioned.

The panel was impressed by the quality of the PhD programs in the Utrecht Life Sciences Graduate School. The benefits of the cooperation with the (Life) Sciences faculties of Utrecht University are visible in these PhD programs. The panel was impressed by the way PhD students are monitored and guided. The teaching in the PhD program is excellent. The panel in particular appreciates the fact that the PhD students have substantial influence on the teaching program.

The panel was impressed by the way changes in research management are led in a complex organization. Furthermore the board shows good leadership in using opportunities to stimulate the research. The investment in the Hubrecht Institute should be mentioned in this regard, as well as the cooperation with the Prinses Maxima Centrum and the NKI (Netherlands Cancer Institute).

#### **Productivity 4.5**

For all research programs the panels could establish that the output in terms of publications is increasing and that a considerable number of PhD theses have been completed in the assessed period. The earning capacity in general is very good, several remarkable large personal and project grants have been acquired. For some programs a stronger focus on high prestigious programs (ERC and VICI) is recommended.

The relationship between input and output judged in relation to the mission and resources is excellent.

### **Societal Relevance 4.5**

Meetings with the patient groups and (industrial) stakeholders showed that these were very supportive on the mission of the UMC Utrecht. Research done is highly relevant (as was also confirmed by discussion with the patient groups). At the present state of development, however, the panel could not evaluate the impact of the new strategy on the quality of the patient care. The panel advises to develop criteria for measuring the translational part of the research and the impact on patient care. The successes of this aspect should also form part of the job evaluation procedures to guarantee a balance between the demands put on junior researchers to contribute to translational research and the criteria for promotion and tenure. The panel also recommends to substantially invest in basic research to guarantee a good balance between exploration and application.

### **Vitality and Feasibility 3.5**

The implementation of the Strategy UMC Utrecht 3.0 is not yet fully completed. As mentioned the panel applauds the strategy for defining multidisciplinary research programs, determining a portfolio and in particular for 'not doing everything'. The panel is also convinced that most researchers believe in the new mission and subscribe the strategy. However whether the strategy will be manageable in all aspects in all research areas and themes could not as yet be assessed by the main panel. The system is in transition, a number of managerial decisions still have to be made.



# 3 Conclusions and recommendations

The UMC Utrecht is a research organisation in transition. Important decisions have been made by the Board to restructure the research organisation. The main panel is of the opinion that now it is the moment to take this one step further, make the choice who is running the research and give more steering power to the research directors.

The main panel felt a mismatch between the exiting new structure aimed at translational research on the one hand and the criteria used for career steps on the other hand. Translational science should be part of the promotion criteria.

It would be wise to not have two scientific boards (research managers and program directors). The Board of the UMC Utrecht should consider establishing one scientific board that reflects the new structure. Next to the internal scientific board the panel recommends to establish an external scientific board to provide bi-annual feed-back on the content of research.

Overlap in the programs should be mapped and reconsidered, some overlap can be beneficiary, but decisions regarding the accommodation of research subjects are necessary to avoid scattered energy leading to a low performance in certain research areas.

Continue the PhD program as it is, the quality is very good.

If the UMC Utrecht Board wants to have valuable feedback from an elaborate site visit procedure, extensive information about the past performance of the research lines is mandatory.

# Appendix

## Site visit program main panel

### 24 April 2014

- 10.00-13.00 Preliminary discussion main panel
- 13.00-14.00 Meeting with UMC Utrecht Executive Board
- 14.00-15.00 Meeting with research management Divisions  
Prof. Carla Bruijnzeel (Internal Medicine and Dermatology)  
Prof. Carl Moons (Julius Centre)  
Prof. Marc Vos (Heart and Lung)
- 15.00-15.30 Break
- 15.30-16.30 Meeting with Graduate School of Life Sciences representatives  
Prof. Jos van Strijp (PhD program director I & I, vice chair Board of Studies)  
Prof. Marian Joels (PhD program director Clinical & Experimental Neurosciences)  
Prof. Susanne Lens (PhD program director Translational Oncology)  
Dr. Saskia Ebeling (secretary to the Board of Studies GS-LS)
- 16.30-18.00 Meeting with PhD candidates  
Ewoud Compeer, Genoveva Keustermans, Sjoerd van Gorp, Branko van Hulst, Diana Papazova
- 19.00-22.00 Diner

### 25 April 2014

- 09.00-10.00 Utrecht Life Sciences and Hubrecht Institute collaboration  
Prof. Alexander van Oudenaarden (scientific director HI)  
Dr. Freek van Muiswinkel (managing director ULS)
- 10.00-11.00 UMC Utrecht Valorisation and Quality ambassadors  
Drs. Jan Vos van Marken and Dr. Lucas Beekman  
Dr. Esther van Tienhoven
- 11.00-12.00 Internal discussion
- 12.00-13.00 Lunch
- 13.00-14.00 Preparation of advice Research Evaluation
- 14.00-15.00 Preliminary report and reception

# Brain



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# 1 Introduction

## 1.1 The Netherlands System of Quality Assessment of Research

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- To identify excellent research groups and young researchers with high research potential;
- To identify research areas that are currently of the highest international standard, how these may be strengthened and suggest conditions for their continued development.
- To identify research areas that have the potential to develop towards the highest level of international research and to determine what is necessary to ensure such development.
- To identify research areas that are not internationally or nationally competitive and lack evident development potential.
- To identify research areas that are missing that could be considered to be essential for the UMC Utrecht.
- To identify the need for infrastructural support that would facilitate development towards greater excellence.

## 1.2 Research organisation UMC Utrecht.

The UMC Utrecht is organized in eleven divisions. All divisions operate in the areas of direct patient care, education and research. Divisions have their own budgets and policies, which are based on their specific categories of patients. The divisions are: Biomedical Genetics, Heart and Lung, Imaging, Internal Medicine and Dermatology, The Julius Center for Health Sciences and Primary Care, Laboratories and Pharmacy, Neurosciences, Paediatrics, Surgical Specialties, Vital Functions, Woman and Baby.

In 2010 a new strategy for the years 2010–2015 was launched, Strategy 3.0. In this Strategy 3.0 the UMC Utrecht puts more emphasis on the connection between research and patient care aiming at innovation in patient care driven by identified clinical needs. Based on external developments and the strategic self-evaluation performed in 2009, it was decided to focus the UMC Utrecht core activities (patient care, research and education) on the following six strategic programs and their clinical syndromes (between parentheses):

- Brain (stroke, epilepsy, neuromuscular disorders, psychotic disorders, neurodevelopmental disorders);
- Infection & Immunity (opportunistic infections, immune deficiencies, chronic inflammation);
- Circulatory Health (atherosclerosis, heart failure, stroke);
- Personalized Cancer Care (breast cancer, gastro-intestinal cancer);
- Regenerative Medicine & Stem Cells (stem cell based therapies, cardiovascular and musculoskeletal tissues);
- Child Health (chronic inflammation, respiratory infections, orphan diseases/genetics RM, fertility interventions).

### **1.3 The Review Panel Brain**

The review panel for the Brain program was appointed 22 November 2013 and consisted of:

- Professor Florian Holsboer, chair, Max Planck Institute for Psychiatry, Munich, Germany;
- Professor Christian E. Elger, University of Bonn, Germany;
- Professor Raquel Gur, University of Pennsylvania Perelman School of Medicine, Philadelphia, USA;
- Professor Didier Leys, Lille University Hospital, University Lille, North of France, France.

Dr. Barbara van Balen, (staff member of) QANU, was appointed secretary to the review panel.

A short curriculum vitae of each member is included in Appendix 1.

### **Independence**

All members of the Review panel signed a statement of independence to ensure that

- they would judge without bias, personal preference or personal interest, and
- their judgment is made without undue influence from the institute, the program or other stakeholders.

### **1.4 Data provided to the Review Panel**

The review panel has received a self-evaluation report provided by the UMC Utrecht. The panel also received the report on the Mid Term Review 2007-2009, the assessment report 2002-2006, five key publications, an overview with biosketches of the Brain program PIs and additional quantitative information specified per research theme.

### **1.5 Procedures followed by the Panel**

The assessment was based on the documentation provided by the UMC Utrecht and the interviews during the site visit. The interviews took place on 27 and 28 March 2014. The program of the site visit is included in Appendix 2.

The panel members all read the Self Evaluation Report and the additional information. The reviewers prepared questions for the interviews, which were exchanged prior to the meeting.

During the internal panel meeting on the evening of 26 March 2014, preceding the site visit, the questions and comments were discussed and decided upon. On the second day of the site visit, the panel discussed the results of the assessment thus far and the outline of the advice in the report. Afterwards a meeting with the representatives of the UMC Utrecht, the program leaders and interested researchers was arranged, in which the main impressions of the panel were reported.

A draft version of the report was written by the secretary and the chair and sent to the review panel members for comments. Their remarks and recommendations for improvement were incorporated in the next version.

### **1.6 Assessment Criteria**

The Protocol requires the Evaluation Review panel to assess the research on the four main criteria of the *Standard Evaluation Protocol*:

- Quality (the level of the research conducted)
- Productivity (relationship between input and output)
- Societal relevance (social, economic and cultural relevance of the research)
- Vitality and feasibility (flexibility, management and leadership)

# 2 Assessment of the Brain Program

Program Leaders: Professor René S. Kahn, MD, PhD (chair)  
Professor Marian Joëls, PhD (Co-chair)  
Academic staff in 2012: 163 fte (457)

## 2.1 Mission, goals and research activities of the program

The Brain program performs research on:

- stroke, in collaboration with the strategic program Circulatory Health;
- epilepsy, especially refractory in children;
- neuromuscular disorders, with an emphasis on ALS;
- psychotic disorders, in particular schizophrenia and bipolar disorder;
- neurodevelopmental disorders, particularly autism and ADHD.

The research is aimed at the improvement of diagnostic tools and treatment strategies for the patient. Characteristic for each of these fields is that research is intertwined with patient care. By enriching the patient population sizeable patient cohorts are facilitated, to form a basis for patient-related research. Each of the research fields consists of a multidisciplinary team of experts. The fields share common approaches and expertise. To structure interactions and discourse the Brain researchers also interact along 'horizontal lines': genetic background, environment, structure & connections, translational approaches and from research to care.

The goals of the research areas are described as follows:

1. Stroke
  - resolve which genetic factors in interaction with environmental risks determine the extent to which an individual is vulnerable to stroke;
  - identify early diagnostic markers, better predictors of treatment success and long-term outcome, and the relation between stroke and cognition;
  - improve the array of treatments, including the latest developments in neurosurgery, acute interventions and neurorehabilitation.
2. Refractory epilepsy, especially in children
  - to understand disease causes, by investigating genetic risk factors and critical steps in epileptogenesis;
  - to monitor consequences of epilepsy for connections and structure of the brain and for cognitive performance;
  - to develop new strategies in treatment, with special interest in the localization of foci and functional processes, to improve surgical interventions.
3. Neuromuscular disorders
  - develop biomarkers for diagnostics and disease progression;
  - improve the understanding of the genetic and environmental causes of neuromuscular disorders;
  - improve new treatment possibilities for motor neuron diseases such as amyotrophic lateral sclerosis in adulthood, spinal muscular atrophy in children and a number of specific polyneuropathies.
4. Psychotic disorders
  - to determine genetic and environmental influences contributing to (pathological) brain development across the first decades of the lifespan;
  - to delineate brain development in individuals at risk to develop schizophrenia or bipolar disorder, prior to and during the course of these illnesses.



## 5. Neurodevelopmental disorders

- to chart brain development in typically developing children, and in children with a developmental disorder;
- to determine the overlap and distinction between developmental disorders, in terms of brain development, connectivity and function;
- to map the etiological cascades from risk factors to brain changes and ultimately behavioral changes.

The research fields share common approaches and expertise. To structure interactions and discourse the program also defined 'horizontal lines'. For each of the lines, a small group consisting of representatives of the various divisions is responsible for the content.

### **General remarks**

The "Brain-Program" of the UMC Utrecht is based on a considerable modification of the classic structure of a Neurology and Psychiatry department in a university hospital. It concentrated the scientific programs on either historically strong subfields or on diseases such as epilepsy, which were thought to be of particular importance. By doing this it is aiming high. It embarks on an ambitious roadmap where key is the departure from the classic "from bench to bed"-mantra to a patient-oriented strategy and where the demands for research are derived from the patient's needs in a certain disease in a "top down manner". This reorganisation is done successfully, as emphasized by the stakeholders as well as evidenced by successful publications and substantial acquisition of grants.

The bold step taken by the UMC Utrecht in Strategy 3.0 will not be embraced by all basic scientists. But this step reflects that patients had been too patient with basic science in the past. The new strategy avoids the risk that findings of great potential get lost on their way to patient care.

The perpendicular matrix that intertwines diseases with research methods is challenging. Nevertheless, it became obvious that it works well and is driven by enthusiasm. The review panel tried to squeeze out some criticism from the principal investigators, but failed. Only in specific cases there is room for better integration that will be enhanced with growing demand.

The most important thing to achieve, the high ranking goal of the UMC Utrecht, is the quality of the science.

The review panel could catch only a glimpse of the science conducted in the Brain program but by looking at the publication record, talking with principal investigators and PhD-students we came to the conclusion that the scientific quality is excellent. PhD-students are happy with the opportunities, the supervision and other support they receive. The PhD program attracts very enthusiastic people who are fond of participating in science. Career planning for students seems optimal.

The facilities in Utrecht to conduct any kind of research in the diseased human brain was found to be unique. It could be an ideal example in order to generate a basis for optimal research in university hospitals.

The UMC is productive at the highest level at both ends, the research in basic and clinical science as well as in patient care.

The latter was impressively demonstrated by societal stakeholders representing patient organisation and foundations for brain disorders.

## 2.2 Program Assessment

The panel will first give its assessment for the five research areas and the horizontal lines defined by the programme and, weighing its assessment of the research areas and lines will come to a general rating of the entire Brain program.

### A Research Areas

#### *Stroke*

The research on stroke in the UMC Utrecht merges, in a unique fashion, neurology and neurosurgery. That makes the group leading in clinical research on an international scale for subarachnoid haemorrhage and vascular malformation. Of particular importance is the research on paediatric stroke. The research field "stroke" is accompanied by a very strong epidemiology that is dealing with secondary prevention and emphasis on pharmaco-epidemiology.

In fact, major trials for secondary prevention are a particular strength as evidenced by the Dutch TIA trial, the ESPRIT trial, and the SPIRIT trial where the UMC is one of the five leading centers for secondary prevention in Europe.

The panel members gave some thought to the missing link with basic science. In as much as we believe that valuable discoveries in basic science may get lost on their way to the patient, we also believe that effort is needed to avoid that valuable information from the bedside gets lost on its way to basic science laboratories.

Successful research in prevention in ischemic stroke, as reflected in a number of highly influential publications, is another strength of this group that is clearly among the top-three centres in Europe and also in the top league worldwide.

The research area also started research in ICH. One of the strengths of the groups is that they have a full time epidemiologist and that there is an association with neurosurgery. Its research is published in top European journals.

#### *Neuromuscular disorders*

This group is doing excellent research on Amyotrophic Lateral Sclerosis (ALS) and exploits the unique situation that almost all ALS patients in the Netherlands are seen here at the UMC in Utrecht. Basic and clinical sciences are well integrated and receiving prestigious grants. The group not only investigates genetic underpinnings of ALS but also environmental impact and gene environment interactions. What they do is done in a very systematic way. It can be seen from the work on genes and ALS, where the research on certain susceptibility genes was systematically done with a negative outcome. This work is unique and necessary for the science community and all the board can say is that they may take the risk to tackle also bold questions, of course without reducing the systematic work.

#### *Epilepsy*

This group has an excellent reputation. It is well organized and perfectly armed to conduct the various clinical studies addressing very important clinical questions, including childhood epilepsy surgery and ESES (Electrical Status Epilepticus of Sleep). We noticed that experience in clinical studies helped here to be a leading figure in these programs.

The aims regarding implementation of basic research are ambitious and require careful consideration regarding the main hypothesis to be tested. Here especially, epilepsy surgery opens unique possibilities to conduct patient related basic research.

Epileptogenesis is a very complex and probably a very variable phenomenon in epilepsy. It needs to be focused on close collaboration with genetics, genomics, imaging and pharmacology and with the special opportunities of the UMC Utrecht, such as epidemiology. An approach toward stratification of patient samples according to biosignatures derived from neurophysiology, genetics, genomics and systems biology should be given careful consideration. The future potential of this excellent group is great and we encourage them to reach out for the big points.

### *Psychosis*

This is an internationally well-known group with main focus in schizophrenia. The patients get well characterized with state of the art tools. The program interrogates early discovery of brain changes as they are observed with imaging tools. There is a large EU-funded consortium led by the UMC Utrecht.

The “Voice Clinic” supports better understanding of clinical signs and symptoms of schizophrenia and patients suffering from hallucinations and other schizophrenia symptoms are involved in the treatment and self-support activities.

Here again we were impressed by the phrase of one of the stakeholders saying that the concept of UMC Utrecht where stroke, epilepsy and schizophrenia are assembled under the same tag “brain” gives them a big relief and reduces stigmatizing of their own mental disorder.

The youth cohort where gene-environment interaction are interrogated in a longitudinal epidemiological study will help to find neurodevelopmental trajectories, which will be useful for early detection of the disease and consequently the opportunity of early intervention. In fact, we know from many other diseases that the causal mechanism is on its way long before clinical signs and symptoms become visible. Therefore, such studies will ultimately lay the foundation on which primary prevention can be built. This study will take very long but is worth every effort although perhaps later generations of scientists and patients will be the ones who will benefit from this treasure.

Another important area is biobanking that will help to classify schizophrenia as a neurodevelopmental disorder under morphological and cell-biological aspects.

We also got detailed information on treatment studies that are addressing many unmet needs in schizophrenia. We can only applaud the great effort that is taken to recruit the perhaps most difficult-to-treat patients in medicine.

As a future concept we believe careful consideration should be given to therapeutic proof-of-concept studies administering more experimental drugs than those that are currently used in the treatment studies at the UMC Utrecht.

### *Developmental disorders*

The developmental disorders programme focuses primarily on ADHD and autism. The multidisciplinary research integrates neurobehavioral, neuroimaging and genetics. The program capitalizes on the neurogenetic 22q11.2 deletion syndrome. The programme is internationally well known and productive. Harmonizing phenotypic measures across neurodevelopmental disorders including psychosis can put the program in a leadership position as large samples will be available for genomic and neuroimaging studies. The youth cohort has a huge potential to make a significant contribution to the field. It will benefit from collaboration with genetic, genomics and pharmacology. Its current performance and future perspective are excellent.

## **B Horizontal Lines**

### *Genetics*

The group seems to be technically well equipped with state of the art devices. The expertise in statistical genetics is according to the presented publications appropriate. In light of the ambitious goals set for the future, where different levels of genetics, genomics and other ‘omics’ are to be integrated with complex clinical phenotypes and environmental information, the panel advises to strengthen the ‘horizontal team’ with bioinformatic expertise. The need to handle the expected data avalanche with bioinformatic expertise cannot be overemphasized.

### *Environment risk factors*

The in-house expertise in epidemiology is top notch in the field of stroke, in particular in secondary prevention. Given that the future of medicine will turn into preventive medicine, UMC Utrecht needs to establish its own epidemiology or collaborations with the neighbouring institutes in Utrecht to import expertise for the youth cohort and other longitudinal epidemiological projects aiming for primary prevention.

### *Structure & Connections*

The imaging core is very impressive, its devices range from the open low field scanner to the 7 Tesla machine on one side and the imaging tools on the cellular level on the other. In particular, the 2-photon microscopy devices that allow one to watch the brain in action, observing the cells while they are active in a living animal are state-of-the-art and have great future potential. Notably, the group collaborates with the Max Planck Institute for Neurobiology (Munich), which discovered 2-photon microscopy. Such collaborations are essential to keep pace with a rapid evolution of that kind of imaging.

It is a pure treasure that this group also produces mouse models on demand and provides tools for inducible pluripotent stem cells. This is an excellent support provider for all the projects to which we were exposed.

### *Translational approaches and from research to care*

Translational neuroscience is a very broad field, aiming at pathways, using and producing all kind of animals and has a strong translational approach. The key research questions are sent from the bed side. The research always starts with the clinical observation. What the panel finds worth to be reconsidered is that the UMC Utrecht and the Rudolf Magnus Brain Center seem to gradually depart from pharmacology.

The panel believes that pharmacology is the most translational science within biomedicine. Therefore, it strongly advises to give the reengineering of pharmacology at the UMC Utrecht or more specifically at the Rudolf Magnus Brain Center very careful consideration.

## **Quality 5**

The panel has seen examples of excellent science and excellent translational work. The program contains great examples of research from clinical/translational and fundamental scientists. The quality of research was also reflected in the poster session with PhD students and postdocs. The presentation of their research was excellent and the commitment and quality of the graduate students and post docs was obvious.

## **Productivity 5**

The panel has seen that the output in terms of publications is increasing and a considerable number of PhD theses have been completed in the assessed period. The earning capacity of the program is very good, several remarkable large personal grants have been acquired and the winning of NWO 'Gravitation' grant is excellent. The relationship between input and output judged in relation to the mission and resources are excellent.

## **Relevance 5**

The assessment panel got a very positive impression from the cooperation with the societal stakeholders. The patient organisations feel well connected, supported and indicate that the researchers listen to their needs. The societal reputation of the program is excellent. The panel sensed that there is a good commitment of the researchers from basic research to the clinic. Everyone is dedicated to translational work and integration of patients in the research. Social, economic and cultural relevance and in particular interaction with stakeholders and activities aimed at making research available and suitable for application, are excellent. But there is room for improvement for a drug-discovery aimed pharmacology.

## **Vitality & Feasibility 5**

The reengineering of the organisation from "bench to bed" into a patient-orientated structure is a solid proof that the brain program is able to react to important changes from outside. The assessment panel is of the opinion that this research program needs all support. It has a bright future, innovative research and a good talent programme. The ambition of the Brain program to belong to the top 3 European Research centers in the field is in the view of the panel realistic and for few of the themes (like ALS) already achieved. The program has an open eye for talents and supports young researchers in developing their career.

# 3 Recommendations

- As a future concept the panel believes consideration should be given to therapeutic proof-of-concept studies with more experimental drugs than those that are currently used in treatment studies.
- Harmonizing phenotypic measures across neurodevelopmental disorders including psychosis can put the program in a leadership position as large samples will be available for genomic and neuroimaging studies. The youth cohort provides a unique opportunity for such a comprehensive longitudinal approach. UMC Utrecht can make a significant contribution to the field and establish a unique paradigm and sample.
- The panel believes that pharmacology is the most translational science within biomedicine. Therefore, it strongly advises to give the reengineering of pharmacology at the UMC Utrecht or more specifically at the Rudolf Magnus Brain Center very careful consideration.

# Appendix 1

## Curricula vitae of the Evaluation Review panel members

### **Professor Florian Holsboer**

Studied chemistry and medicine at the University of Munich. Residency at the Department of Psychiatry, University of Munich and at the Department of Psychiatry, University of Mainz.

1984 postdoctoral lecturing qualification in psychiatry. 1987-1989 Professor of Psychiatry at the University of Freiburg. Since 1989 Director of the Max Planck Institute of Psychiatry, Munich. Honorary Professor at the Medical Faculty of the Ludwig Maximilians University of Munich since 1990.

Research: Neurobiology of stress, depression, anxiety and sleep disorders. Neuroendocrinology, biomarkers, animal models, genetics and genomics, psychopharmacology

Publication stats: 1144 pubs, 43186 citations, Hi =104

Selected publications:

Klengel, T., et al. (2013) Allele-specific FKBP5 DNA demethylation mediates gene-childhood trauma interactions. *Nat Neurosci.* 16(1):33-41.

Mehta, D., et al., (2011) Using polymorphisms in FKBP5 to define biologically distinct subtypes of posttraumatic stress disorder: evidence from endocrine and gene expression studies. *Archives of General Psychiatry* 68: 901-910

Refojo, D., et al., (2011) Glutamatergic and dopaminergic neurons mediate anxiogenic and anxiolytic effects of CRHR1. *Science* 333:1903-1907

Kohli, M., et al., (2011) The neuronal transporter gene SLC6A15 confers risk to major depression. *Neuron* 70: 252-265

Holsboer F (2008) How can we realize the promise of personalized antidepressant medicines? *Nat Rev Neurosci.* 2008 Aug;9(8):638-46

Honorary Positions: Drs. honoris causa, University of Leiden and University of Zürich

### **Prof. Christian E. Elger**

Head of the Department of Epileptology, to which the Laboratory of Experimental Epileptology is affiliated. Christian Elger has been the driving force in establishing the Department of Epileptology as one of the most renowned clinical and scientific institutes focusing on epilepsy care and epilepsy research. Major research interests include the mechanisms of cognition in humans, neuroeconomics, basic mechanisms of epilepsy and pharmacoresistance.

Research Interests: Clinical Epileptology, Epilepsy Research, Cognitive Neuroscience

Awards and Honors

2005 International Zülch-Prize for Brain Research (Max-Planck-Gesellschaft, Gertrud-Reemtsma-Stiftung), with Prof. S. Berkovic

2010 Hans-Berger Prize of the Deutschen Gesellschaft für Klinische Neurophysiologie und funktionelle Bildgebung

2011 "The Victor and Clara Soriano Award Lecturer" of the World Federation of Neurology (XX World Congress of Neurology, Marrakesh)

2012 "European Epileptology Award" of the International League against Epilepsy (ILAE)

Publication stats: 922 pubs, 23455 citations, Hi =80

### Selected Publications

- Brelie CV, et al. (2014) Surgical resection can be successful in a large fraction of patients with drug-resistant epilepsy associated with multiple cerebral cavernous malformations. *Neurosurgery*. 2014 Feb;74(2):147-53
- Elger CE, Mormann F. (2013) Seizure prediction and documentation--two important problems. *Lancet Neurol*. 12(6):531-2.
- Aru J, et al. (2012) Local category-specific gamma band responses in the visual cortex do not reflect conscious perception. *J Neurosci*. 32(43):14909-14.
- Hoppe C, Elger CE. (2011) Depression in epilepsy: a critical review from a clinical perspective. *Nat Rev Neurol*. 7(8):462-72.
- Rosburg T, et al., (2005) Subdural recordings of the mismatch negativity (MMN) in patients with focal epilepsy. *Brain* 128: 819-28.

### **Prof. Raquel Gur**

Dr. Gur is Professor of Psychiatry, Neurology and Radiology at the University of Pennsylvania Perelman School of Medicine where she directs the Neuropsychiatry Section and the Schizophrenia Research Center and is Vice Chair of Research Development in the Department of Psychiatry. Her combined training in Psychology, Neurology and Psychiatry has provided the tools to pursue an academic career working with basic and clinical neuroscientists to advance the understanding of schizophrenia. In directing these research endeavors, she has interacted with scientists of diverse backgrounds, conducted collaborative interdisciplinary research, mentored junior faculty and trainees, and has come to know many patients and their families. She has served in organizations including the Institute of Medicine of the National Academy of Sciences, the NIMH Council and the American Psychiatric Association task forces including the DSM-5 Psychosis work group. She is Past President of the Society of Biological Psychiatry and President Elect of the American College of Neuropsychopharmacology.

### Honors:

- American College of Psychiatrists Stanley Dean Award in Schizophrenia (2007)
- IRG Member, Special Reviews Committee, National Institute of Mental Health (NIMH)
- President, Society of Biological Psychiatry (2007)
- NARSAD - Lieber Prize for Outstanding Research in Schizophrenia (2009)
- American College of Physicians – William C. Menninger Memorial Award (2011)
- National Alliance on Mental Illness (Pennsylvania Montgomery County) Brain Scientific Research Award (2012)
- President-Elect, American College of Neuropsychopharmacology (2013)

Publication stats: 600 pubs, 21858 citations, Hi =83

### Selected Publications:

- Gur RE et al. (2014) Neurocognitive development in 22q11.2 deletion syndrome: comparison with youth having developmental delay and medical comorbidities. *Mol Psychiatry*. In press.
- Gur RC et al. (2014) Neurocognitive Growth Charting in Psychosis Spectrum Youths. *JAMA Psychiatry* in press.
- Ingalhalikar M et al. (2014) Sex differences in the structural connectome of the human brain. *Proc Natl Acad Sci U S A*. 111(2):823-8.
- Satterthwaite TD et al (2013) Functional maturation of the executive system during adolescence. *J Neurosci*. 33(41):16249-61.
- Wolf DH, et al., (2013) Oral alprazolam acutely increases nucleus accumbens perfusion. *Mol Psychiatry*. 18(9):960-1

## **Prof. Didier Leys**

The 3 main domains of research of Didier Leys are the links between stroke and cognition, acute stroke care organisation, and cervical-artery dissections.

Didier Leys was appointed as Professor of Neurology and Head of the Neurological Department at the Lille University Hospital in 1990. He was chairman of the French Stroke Society from 1998–2000. He was member of the Executive Committee of several national and international societies, including the International Stroke Society and the European Stroke Initiative. He was president of the European Stroke Organisation from 2010 to 2012. He is member of the Belgian Society of Neurology and honorary member of the Belgian Stroke Council. Professor Leys has authored or co-authored more than 466 scientific papers (H score = 57), book chapters, and books on stroke, and on the relationship between vascular factors and dementia. His main topic of interest over the last 10 years was on acute stroke, determinants of post stroke dementia, and genetic predisposition to cervical artery dissections. He is member of the editorial board of several scientific journals including *Stroke* and *Cerebrovascular Diseases*, and has been one of the editors of the *Journal of Neurology, Neurosurgery and Psychiatry* until 2010.

Publication stats: 466 pubs, 14376, citations, Hi =57

Selected publications :

Nardi K et al. (2012) Lipid Profile in Thrombolysis Study Group. Lipid profiles and outcome in patients treated by intravenous thrombolysis for cerebral ischemia. *Neurology* 79(11):1101-8.

De Herdt V et al. (2011) Early seizures in intracerebral hemorrhage: incidence, associated factors, and outcome. *Neurology* 77(20):1794-800.

Cordonnier C, Leys D, Dumont F, et al. (2010) What are the causes of pre-existing dementia in patients with intracerebral haemorrhages? *Brain* 133:3281-3289.

Debette S, Leys D (2009) Cervical-artery dissections: predisposing factors, diagnosis, and outcome. *Lancet Neurol* 8:668-678.

Leys D, Cordonnier C (2008) Profiling of patients and risk after carotid stenting. *Lancet Neurol* 7:193-194.



# Appendix 2

## Program of the site visit

### Wednesday 26 March 2014

- 17.00 Internal meeting of the committee, preparation of the interviews
- 19.00 Dinner

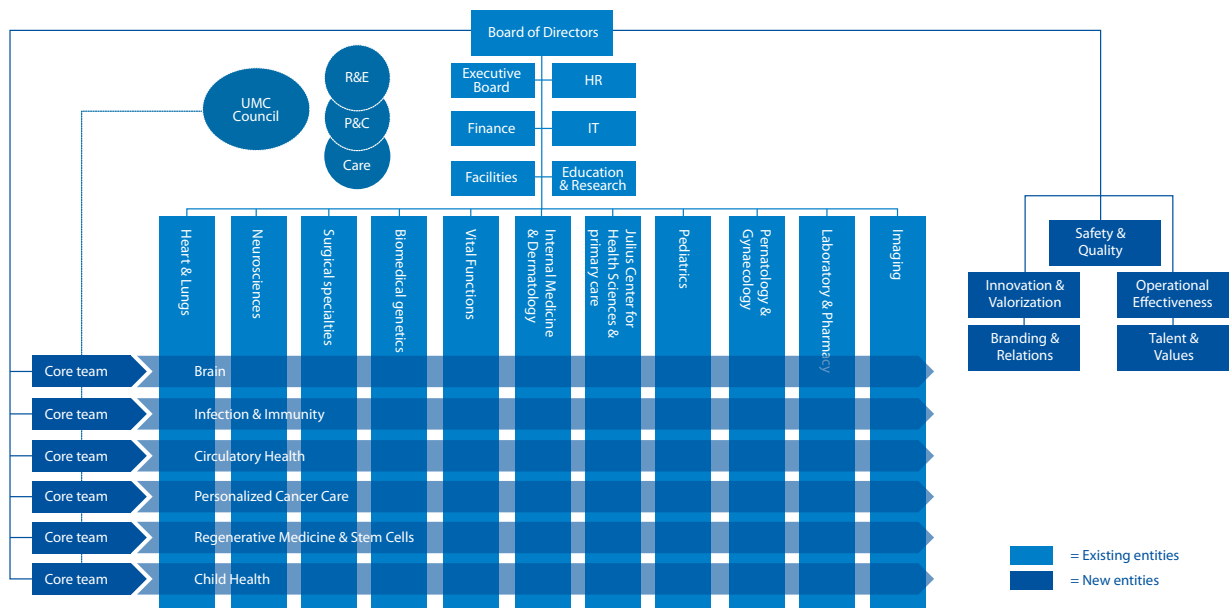
### Thursday 27 March 2014

- 09.00 Meeting with the UMC Utrecht Executive Board:  
prof.J.L.L. Kimpfen, dr. S.W.H. van Weelden
- 10.00 Meeting with program chair and management of the Brain program  
Prof. René S. Kahn, Prof. Marian Joëls, Dr. Mariken de Krom.
- 11.00 Break
- 11.30 Meeting with PIs:  
prof. Gabriël J.E. Rinkel  
prof. Kees P.J.Braun  
prof. Leonard H. van den Berg  
prof. Iris E.C. Sommer  
prof. Sarah Durston
- 12.30 Lunch
- 13.30 Meeting with PIs:  
dr. Jan H. Veldink  
prof. Chantal Kemner  
prof. Hilleke E. Hulshoff Poll  
prof. Peter R. Luijten  
prof. J. Peter H. Burbach  
prof. Casper C. Hoogenraad  
prof. Anne M.A. Visser-Meily
- 15.30 Break
- 16.00 Poster session with postdocs and PhD students
- 17.00 Internal discussion in the committee
- 19.00 Dinner

### Friday 28 March 2014

- 09.00 Meeting with Societal Stakeholders  
Esther Hosli ( Dutch Brain Foundation)  
Martin Boer (director National Epilepsy Foundation)  
Bert Stavenuiter (director Ypsilon Foundation)  
Christine Blanke and Steven Scholtus (Anoiksis)
- 10.30 Break
- 11.00 Preparation of advice
- 12.00 Lunch
- 13.00 Consulting Hour
- 14.00 Preparation of advice
- 15.00 Preliminary report

# Appendix 3



# Infection & Immunity



# Content

# Infection & Immunity

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# 1 Introduction

## 1.1 The Netherlands System of Quality Assessment of Research

This quality assessment of research is part of the assessment system for all public Dutch university research, as organised by the Universities and University Medical Centers (UMCs) in the Netherlands.

The aims of the assessment system are:

- Improvement of research quality based on an external peer review, including scientific and societal relevance of research, research policy and research management.
- Accountability to the board of the research organisation, and towards funding agencies, government and society at large.

Universities and UMCs in the Netherlands have agreed to carry out a self-evaluation every three years and an external review every six years. This process is guided by the Standard Evaluation Protocol (SEP). For this evaluation the SEP 2009-2015 is used.

The present external research evaluation has the following objectives:

- To assess the quality of the research and graduate PhD programs carried out at the UMC Utrecht during the period under review (2007-2012) compared to an international benchmark (not a comparison within UMC Utrecht);
- To identify research areas that have the potential to stimulate innovation and have societal impact;
- To identify excellent research groups and young researchers with high research potential;
- To identify research areas that are currently of the highest international standard, how these may be strengthened and suggest conditions for their continued development.
- To identify research areas that have the potential to develop towards the highest level of international research and to determine what is necessary to ensure such development.
- To identify research areas that are not internationally or nationally competitive and lack evident development potential.
- To identify research areas that are missing and that could be considered to be essential for the UMC Utrecht.
- To identify the need for infrastructural support that would facilitate development towards greater excellence.

## 1.2 Research organisation UMC Utrecht.

The UMC Utrecht is organized in eleven divisions. All divisions operate in the areas of direct patient care, education and research. Divisions have their own budgets and policies, which are based on their specific categories of patients. The divisions are: Biomedical Genetics, Heart and Lung, Imaging, Internal Medicine and Dermatology, The Julius Center for Health Sciences and Primary Care, Laboratories and Pharmacy, Neurosciences, Paediatrics, Surgical Specialties, Vital Functions, Woman and Baby.

In 2010 a new strategy for the years 2010-2015 was launched, Strategy 3.0. In this Strategy 3.0 the UMC Utrecht put more emphasis on the connection between research and patient care aiming at innovation in patient care driven by identified clinical needs. Based on external developments and the strategic self-evaluation performed in 2009, it was decided to focus the UMC Utrecht core activities (patient care, research and education) on the following six strategic programs and their clinical syndromes (between parentheses):

- Brain (stroke, epilepsy, neuromuscular disorders, psychotic disorders, neurodevelopmental disorders);
- Infection & Immunity (opportunistic infections, immune deficiencies, chronic inflammation);
- Circulatory Health (atherosclerosis, heart failure, stroke);
- Personalized Cancer Care (breast cancer, gastro-intestinal cancer);
- Regenerative Medicine & Stem Cells (stem cell based therapies, cardiovascular and musculoskeletal tissues);
- Child Health (chronic inflammation, respiratory infections, orphan diseases/genetics RM, fertility interventions).

### **1.3 The Review Panel Infection & Immunity**

The review panel for the Infection & Immunity Program was appointed 22 November 2013 and consisted of:

- Professor René van Lier (Chair), Sanquin, University of Amsterdam
- Professor David Hafler, Yale School of Medicine
- Professor Stefan H.E. Kaufmann, Max Planck Institute for Infection Biology Berlin
- Professor Sir Roy Anderson, Imperial College London

Dr. Barbara van Balen, (staff member of) QANU, was appointed secretary to the review panel.

A short curriculum vitae of each member is included in Appendix 1.

All members of the Review panel signed a statement of independence to ensure that

- they would judge without bias, personal preference or personal interest, and
- their judgment is made without undue influence from the institute, the program or other stakeholders.

### **1.4 Scope of the Assessment**

This assessment concerns the strategic program Infection & Immunity. The Board of the UMC Utrecht made fundamental decisions about the strategy, which the panel appreciates. The emphasis on translational research is, according to the panel, very valuable. It was however difficult to assess, in this stage of implementation, the impact of the strategy on the quality of the research and its societal impact. The information the panel received about the strategy was more on organisational aspects than on the research results. The panel acknowledges that it is more difficult to assess quality in translational research, than in basic science. To be able to give an accurate judgment, it needs, next to more information about the results, also parameters for assessing the impact of the research on patient care and cure and the societal impact in general.

### **1.5 Data provided to the Review Panel**

The review panel has received a self-evaluation report provided by the UMC Utrecht. The panel also received the report on the Mid Term Review 2007-2009, the assessment report 2002-2006, five key publications and five reviews of the Infection and Immunity theme.

Upon its request the panel received an overview of the top 5 publications 2010-2012 of each PI organized per research theme.

### **1.6 Procedures followed by the Panel**

The assessment was based on the documentation provided by the UMC Utrecht and the interviews during the site visit. The interviews took place on the 10th and 11th of April 2014. The program of the site visit is included in Appendix 2.

The panel members all read the Self Evaluation Report. The reviewers prepared questions for the interviews. During the internal panel meeting on the evening of 9 April 2014, preceding the site visit, a series of comments and questions regarding the program were decided upon. On the first day of the site visit, the panel met the UMC Utrecht Board to acquire general information, the Management team of Infection & Immunity, interviewed a selection of Principle Investigators (PIs) and had a meeting with stakeholders. The second day of the site visit the panel attended a poster presentation by PhD students and visited the labs. Furthermore it discussed the results of the assessment thus far and the outline of the advice in the report. Afterwards a meeting with representatives of the UMC Utrecht, the program leaders and interested researchers was arranged, in which the main impressions of the panel were reported.

A draft version of the report was written by the secretary and the chair and sent to the review panel members for comments. Their remarks and recommendations for improvement were incorporated in the next version.

## **1.7 Assessment Criteria**

The Protocol requires the Evaluation Review panel to assess the research on the four main criteria of the *Standard Evaluation Protocol*:

- Quality (the level of the research conducted)
- Productivity (relationship between input and output)
- Societal relevance (social, economic and cultural relevance of the research)
- Vitality and feasibility (flexibility, management and leadership)



# 2 Assessment of the Infection and Immunity Program

Program Leader: Professor Erik Hack (chair)  
Professor Marc Bonten (co-chair)  
Academic staff in 2012: 139 fte

## 2.1 Mission, goals and research activities of the program

The I&I program aims to become a tertiary referral centre for patients with I&I diseases that are difficult to treat. Optimal treatment of patients resulting from failing immunity and/ or infection requires, according to the self-evaluation report, a shift from typically 'organ-driven' to personalised 'immune activation pattern-driven'

The overall objectives of the I&I program are:

- to assess the molecular epidemiology of infections and antimicrobial resistance;
- to unravel the pathophysiology of infections and of failing or overreacting host responses;
- to establish common pathways in (chronic) inflammatory diseases;
- and to develop innovative strategies to diagnose, treat and prevent I&I diseases.

The research is focused on six themes:

### 1. Antimicrobial resistance

The aims of this theme are:

- to characterize the evolution of antibiotic-resistant bacteria;
- to characterize the role of the human microbiota as a reservoir of antibiotic resistance;
- to quantify the effects of antibiotic-resistance on patient outcome;
- to determine the best treatment strategies for infections by antibiotic-resistant bacteria.

### 2. Infections dynamics and prevention

The aims of this theme are:

- to understand bacterial pathogenesis, virulence factors and immune-evasion strategies;
- to characterize anti-inflammatory bacterial molecules and to explore their application for vaccine development and anti-inflammatory therapy;
- to understand the dynamics of infectious disease transmission;
- to determine optimal strategies for infection prevention in health-care and community.

### 3. Pathogen host interactions

The aims of this theme are:

- to unravel the mechanisms of HIV immunity and to develop effective strategies to control/cure HIV infection;
- to develop new strategies for anti-viral treatment against hepatitis C virus;
- to identify the mechanisms of herpes virus immune evasion.

### 4. Inflammation

The aims of this theme are:

- to assess aberrant immune regulation in immune mediated (chronic) inflammatory diseases (IMID);
- to assess the effect(s) of (epi)genetic and/or functional dysregulation of immune cells subsets function in IMIDs using high-throughput analysis;
- to identify biomarkers to assess inflammatory 'signatures' in patients that can be used as prognostic and/ or diagnostic markers for personalized medicine.

## 5. Immune deficiency

The aims of this theme are:

- to identify genetic causes of primary immune deficiencies;
- to identify molecular causes of B cell activation defects in primary antibody deficiencies;
- to unravel the relation between chronic gastro-intestinal infections and inflammatory enteropathies in primary immune deficiencies.

## 6. Tumor immunology

The aims of this theme are:

- to boost endogenous immunity against tumors by therapeutic dendritic cell vaccines;
- to evaluate the use of  $\gamma\delta$ T-cells for anti-tumor adoptive (engineered) immunotherapy;
- to develop next generation monoclonal antibody therapies;
- to identify and target key factors produced by the microenvironment that contribute to immune evasion of tumors.

## 2.2 General remarks

The panel applauds the efforts that have been made by the Board of the UMC Utrecht, as well as by the program management and PIs to move towards real translational medicine. The panel did, however, not get a complete overview of all research in the I&I program. Only a selection of PIs presented their research projects during the site visit, the panel therefore could not get the complete picture of the quality of the research of all PIs active within this program during the visit. The additional information that was provided about the top 5 publications of the involved PIs filled part of the information gap. The panel, nevertheless, found it hard to come to a argued rating of the program.

The program contains besides the mentioned six themes also two laboratories and, as is explained in the self-evaluation report, can also be divided into four sections from preclinical, to clinical, applied and diagnostics. The panel got the impression that it is a rather heterogeneous group and that the quality of the whole program would benefit from more focus.

The organization structure seems to be fairly complicated with a number of committees for which the goals and mandates could be defined in a more transparent and simple manner. The panel is furthermore of the opinion that the research program leader(s) should have more steering power and seed funding to reach the stated goals. The panel learned that next to the research management in the '*speerpunten*' there is parallel management of research within the divisions. The panel recommends to organize frequent meetings between the '*speerpunt*' managers and the research managers in the divisions to establish better tuning of priorities and a more fluent translation from preclinical to clinical research and needs and vice versa.

## 2.3 Program Assessment

### Quality 4

It was clear to the panel that certain research programs are outstanding and that the multidisciplinary cooperation stimulated by the 3.0 strategy of UMC Utrecht is stimulating excellence.

The I&I program is very broad, there are many departments are involved. The panel could establish that the PIs are dedicated to make the translational part a success. It is a bit concerned that the program is focusing too much on cohort studies and that less emphasis can be given to basic science.

Based on the information received on paper and during the site visit, the panel has seen that there are excellent groups within the program, which are internationally at the forefront and that there are also groups that could be ranked as good. The panel assessed the top 5 papers of PIs as at least good, most are very good and a few are excellent. These considerations lead to the following overall assessment for the research groups within the I&I program:

*Infection prevention: excellent*

An important achievement of this research group is the European Trial Network. Another highlight in this group is the cooperation with RIVM and the Pneumococcus Vaccination program. The group won a NWO Top Subsidy. Its work is internationally very well known.

*Anti-microbial resistance: very good*

This group is performing very well, the quality of its research is internationally competitive and relevant, although the sub group working on HIV control and cure is according to the review panel rather small. The panel would advise to seek more cooperation with larger research groups to generate more effect.

*Host-pathogen interactions: very good*

Some projects within this research group are very interesting and challenging with a high potential. The group acquired substantial money NWO and several funds. The excellent expertise within this group on computational biology should be cherished.

*Immune deficiencies: good/very good*

This group is doing relevant work. One of the strong points of this group is that four disciplines contribute. The funding of the group should be improved.

*Tumor Immunology: good*

Its work is not yet performing on the international forefront. The future cooperation with the Maxima Hospital, which is aiming to do research on this very important and relevant issue, could provide new opportunities for this group

*Inflammation: very good*

This research group combines an interesting variety of expertises. Strong points of this group are the involvement in the FP7 integration training network and the participation in international projects like: SHARE, Pharmachild, and FP7 pharmacovigilance.

For the whole program the panel balanced the rating therefore as very good. From the presentations and discussions during the site visit the panel has seen that the LTI and LLM labs are very active groups and establish a stimulating environment for performing excellent science. The presentations of the PhD students also made a very good impression and the quality of the PhD training in the program appears to be good. The students were very enthusiastic and of good quality. The panel found it in particular very positive that they on average have open access to their supervisor. To make a more substantiated evaluation however, more data are needed in terms of impact analyses.

#### **Productivity 4**

The productivity of the researchers involved in this program appears to be in terms of publications good to excellent. The earning capacity of the group is good but can still be improved, especially where it concerns top personal grants (e.g. VICI and ERC grants). The program has according to the panel possibilities to become a top center for basic research by aiming at EU funds and by building relationships with the Pharmacological Industry.

#### **Relevance 4**

The panel met with stakeholders: patient representatives and representatives of funding organizations who emphasized the relevance of basic research in this field for the development of medicines and treatment of infection and immune diseases. The patient representatives were very positive but still it was not easy for the panel to interpret the information they gave in relation to the research carried out at UMC Utrecht. It is obvious that the research performed in the I&I program has a high societal relevance, that research questions are developed on the basis of patients needs, and the UMC Utrecht puts efforts in outreach and communication with patients, but the actual impact of the research on patient care can not easily be proved.

### **Viability & Feasibility 3.5**

The panel faced a problem in assessing this criterion while strategic objectives are not very explicit. The program did not explain as to what topics it wants to be good at on the international stage. Given that no institution can be great at everything – difficult choices need to be made. The panel needs more information to be able to judge the viability & feasibility of the program. It did not get insight in the long-term strategic goals. As stated before the panel would advise to focus on the strong research areas in the program. It also sees a lot of possibilities in cooperation with other science departments on the UU campus. The program could benefit from bioinformatic experts who can bridge between the departments of applied mathematics and computer science and the UMC Utrecht.

# 3 Conclusions and Recommendations

- Measures for translational impact need to be agreed and used in part to measure success. The UMC Utrecht should clearly define a matrix to measure the success of translational science. While the committee understood the potential limited usefulness of bibliometrics such as citation indices, careful evaluation should also include review of the scientific impact of each group's publications by expert panels of senior scientists.
- Mandates of the directors should be increased to give more power to direct research. The directors should be able to direct rather than co-ordinate!
- The I&I program appears to be broad and contains many research groups, themes, laboratories and sections. The quality of the whole program would benefit from more focus, the panel advises to concentrate on the strong research areas and develop them into interdisciplinary centers to promote the visibility. It advises to contemplate centers of excellence in fields where the UMC Utrecht feels it is excellent on an international scale.
- A good infrastructure for basic science is essential for the I&I research and also for the translational activity. The panel advises to work towards a real clustering of the laboratories into general facilities for the whole UMC Utrecht.
- The technological services are good but need to be more than a service – innovation in services too. Professional scientists whose successes are not measured by publications are needed to advance technology platforms.
- The UMC Utrecht could develop into a top center for basic research in Infection & Immunity. The campus environment offers many possibilities for strategic cooperations. The panel advises to invest in bioinformatic experts who can bridge with the relevant science departments of the UU and build a bioinformatic/ computational biology platform by using the strength of science on the campus.
- The program has opportunities to develop large EU research projects. The research subjects are very relevant for the EU strategy. The panel advises to aim at these niches.
- The top pharmacological industry has no basic research any more, but is looking for strategic partnerships. There are a lot of opportunities for the I&I program in that respect.
- The researchers should be able to access other cohorts like diabetes (consider national collaboration).
- Keep on investing in talent.

# Appendix 1

## Curricula vitae of the Evaluation Review panel members

**Sir Roy Anderson** FRS, FMedSci was Rector of Imperial College London from 1 July 2008 to 31 December 2009, following a 40-year association with the College. He continues to be Professor of Infectious Disease Epidemiology in the Division of Epidemiology, Public Health and Primary Care.

Sir Roy attended Duncombe School and Hertford Grammar School in Hertfordshire. He gained a first in zoology in 1968 and a PhD in parasitology, both at Imperial College London. After completing his PhD in 1971 he became an IBM biomathematics research fellow at the University of Oxford, before moving to King's College London to become a lecturer in parasitology in 1973. He returned to Imperial in 1977 as a lecturer and was made professor in 1982 and Head of the Department of Biology in 1984, a position he held until 1993 when he became Head of the Department of Zoology and Linacre Chair of Zoology at the University of Oxford.

In 2000 he returned to Imperial, bringing with him a research team of around 40 people, to set up and lead the Department of Infectious Disease Epidemiology, focused on the epidemiology, population biology, evolution and control of infectious diseases such as AIDS and HIV, SARS, bird flu and pandemic influenza, BSE and vCJD and the epidemic viral infections of livestock including foot and mouth. Sir Roy has also served as Director of the Wellcome Centre for Parasite Infections from 1989 to 1993 (at Imperial) and as Director of the Wellcome Centre for the Epidemiology of Infectious Disease from 1993 to 2000 (at Oxford). He is the author of over 450 scientific articles and has sat on numerous government and international agency committees advising on public health and disease control including the World Health Organisation and UNAIDS. From 1991-2000 he was a Governor of the Wellcome Trust.

He currently chairs the science advisory board of WHO's Neglected Tropical Diseases programme, is a member of the Bill and Melinda Gates Grand Challenges advisory board, and chairs the Schistosomiasis Control Initiative advisory board (SCI) funded by the Gates Foundation. He is a non-executive director of GlaxoSmithKline. Sir Roy was elected Fellow of the Royal Society in 1986, a Founding Fellow of the Academy of Medical Sciences in 1998, a Foreign Associate Member of the Institute of Medicine at the US National Academy of Sciences in 1999 and he was knighted in the 2006 Queen's Birthday Honours.

**Prof. David Hafler** is the Gilbert H. Glaser Professor and Chairman Department of Neurology, Yale School of Medicine and is the Neurologist-in-Chief of the Yale-New Haven Hospital. He graduated magna cum laude in 1974 from Emory University with combined B.S. and M.Sc. degrees in biochemistry, and the University of Miami School of Medicine in 1978. He then completed his internship in internal medicine at Johns Hopkins followed by a neurology residency at Cornell Medical Center-New York Hospital in New York. Dr. Hafler received training in immunology at the Rockefeller University and then at Harvard where he joined the faculty in 1984 where he was the incumbent of the Breakstone Professorship of Neurology at Harvard and was a founding Associated Member of the Broad Institute at MIT. In 2009 he move to Yale as the Chair of the Department of Neurology.

Dr. Hafler is a clinical scientist with a research interest in understanding the mechanism of multiple sclerosis with over 300 publications in the field of MS, autoimmunity and immunology. He is a founder of the International MS Genetic Consortium, a group formed to define the genetic causes of MS; his paper in the New England Journal of Medicine was the first to identify the genes causing MS. Dr. Hafler has been elected to membership in the American Society of Clinical Investigation, the Alpha Omega Society, and was a Weaver Scholar of the NMSS. He is a member of the editorial boards for *Journal of Clinical Investigation* and the *Journal of Experimental Medicine*, and is co-founder of the Federation of Clinical Immunology Societies. Hafler leads the NIH Autoimmunity Prevention Center Grant at Yale, and is a Jacob Javits Merit Award Recipient from the NIH. He has won many awards including 2010 Dystel Prize for MS research from the AAN.

**Prof. Stefan H. E. Kaufmann** is founding director and managing director of the Max Planck Institute for Infection Biology in Berlin where he heads the Department of Immunology. Professor for microbiology and immunology, Charité University Clinics Berlin. Honorary Professor of the Universidad Peruana Cayetano Heredia, Lima, Peru and Guest Professor at the Tongji University, School of Medicine, Shanghai, China. He holds a Doctor Honoris Causa from Université de la Méditerranée, Aix-Marseille II. Past President and honorary member of the German Society for Immunology. Past President of the European Federation of Immunological Societies (EFIS) and Past President of the International Union of Immunological Societies (IUIS). Studied biology at the Johannes Gutenberg University of Mainz, 1977 PhD (highest degree, summa cum laude). From 1987 to 1991 professor for medical microbiology and immunology, and from 1991 to 1998 full professor for immunology at the University of Ulm. Scientific interests: immunity to bacterial pathogens with emphasis on tuberculosis and rational vaccine and biomarker design. Co-Developer of a recombinant BCG-vaccine candidate which is in a phase II-clinical trial.

He is Alternate Board Member of the Global Alliance for Vaccines and Immunisation (GAVI Alliance) and member of the Strategic Advisory Committee of the European and Developing Countries Clinical Trials Partnership (EDCTP). Initiated the global Day of Immunology to raise public awareness in immunology. Numerous scientific awards. He is coordinator of several international and interdisciplinary projects. More than 700 publications mostly in high-ranking journals. Highly cited immunologist (ISI Thomson) with an h-Index (according to J. E. Hirsch) of 86. Editor or member of editorial boards of more than 20 international scientific journals. Member of numerous professional societies and academies including American Academy of Microbiology, Berlin-Brandenburg Academy of Sciences and Humanities, German National Academy of Sciences Leopoldina, World Innovation Foundation and European Molecular Biology Organization.

**Prof. René van Lier** studied medicine at the University of Amsterdam (1976-1983), and obtained his PhD in 1988 at the same university on research aimed to characterize properties of cell surface receptors expressed on human T cells. He continued working in the field of immunology at CLB first as a post-doc later as a group leader (now Sanquin). In 2000, he was appointed as Professor of Experimental Immunology and Head of the Department of Experimental Immunology at Academic Medical Center (AMC) in Amsterdam. In 2010 he became director of research and member of the executive board at Sanquin Blood Supply Foundation.

The unifying theme of his research program is the regulation of effector/memory T cell formation in human and mice. The goal is to identify functionally distinct T-cell subsets, study their regulation at the molecular level and define their roles in normal and pathophysiological immune reactions, e.g. persistent virus infections, allo-reactivity and immunodeficiency. René van Lier has published more than 300 papers in international journals.

René van Lier is president-elect of EFIS and member of the scientific advisory boards of the Dutch MS Foundation, Dutch Lung Foundation and the Landsteiner Foundation for Bloodtransfusion Research.

# Appendix 2

## Program of the site visit

### Wednesday 9 April 2014

- 18.00 Internal meeting of the committee, preparation of the interviews
- 19.00 Dinner

### Thursday 10 April 2014

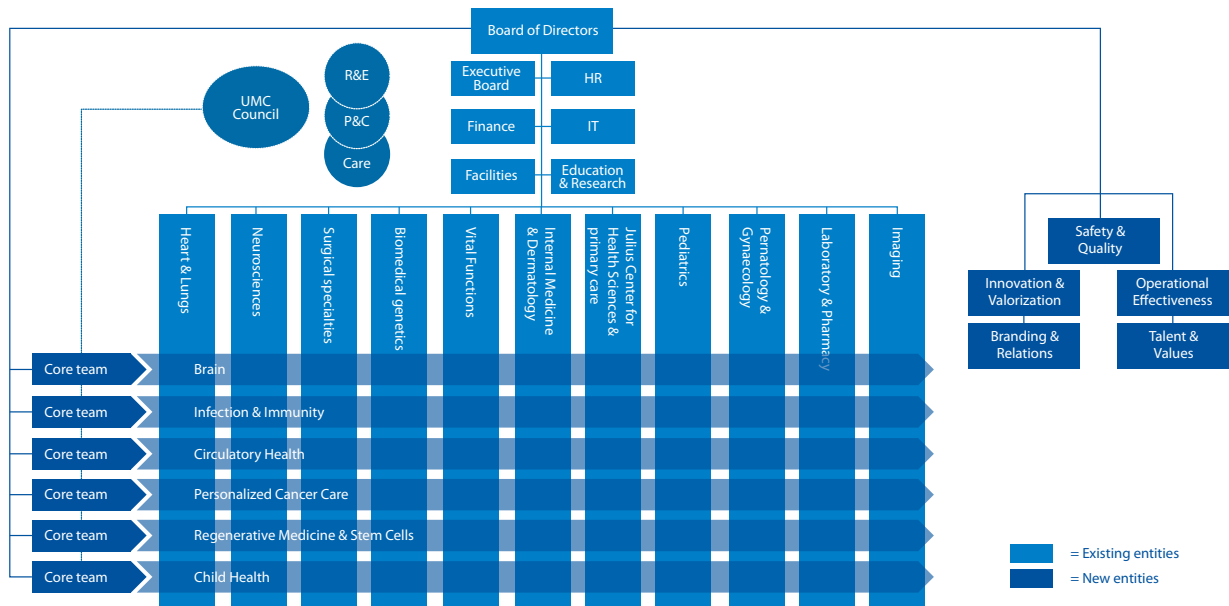
- 09.00 Meeting with the UMC Utrecht Executive Board:  
prof.J. van Kimpen, prof. F. Miedema, dr. S. van Weelden
- 10.00 Meeting with program chair and management  
prof.M. Bonten, prof. E. Hack, prof. J. van Strijp, prof. C. Bruijnzeel- Koomen, prof. J.W. Lammers,  
prof. B. Prakken, dr. M. Jansen, dr. E. van Wilsem
- 11.00 Break
- 11.30 Meeting with PIs:  
Theme: Infection Prevention  
Prof. M. Bonten and prof. L. Sanders  
Theme: Antimicrobial resistance  
Dr. R. Willems and Dr. M. Nijhuis
- 13.00 Lunch
- 13.30 Meeting with PIs:  
Theme: Host Pathogen interaction  
prof. E. Wiertz, prof. J. van Strijp, dr. J. Borghans  
Theme: Immunodeficiencies & tumor immunology  
dr. J.J. Boelens, dr. J. Montfrans  
Theme: Inflammation  
prof. L. Meyaard, prof. T. Radstake, prof. N. Wulffraat
- 15.30 Break
- 16.00 Meeting with societal stakeholders  
R. Foppen (HIV Society The Netherlands)  
B. Arents (VMCE)  
I. Lether (Arthritis Foundation)
- 17.00 Internal discussion in the committee
- 19.00 Dinner

### Friday 11 April 2014

- 09.00 Poster session with postdocs and PhD candidates
- 10.00 Lab visit
- 11.00 Preparation of advice
- 12.00 Lunch
- 13.00 Consulting hour
- 14.00 Preparation of advice
- 15.00 Preliminary report



# Appendix 3





# Circulatory Health



# Content Circulatory Health

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# 1 Introduction

## 1.1 The Netherlands System of Quality Assessment of Research

This quality assessment of research is part of the assessment system for all public Dutch university research, as organised by the Universities and University Medical Centers (UMCs) in the Netherlands.

The aims of the assessment system are:

- Improvement of research quality based on an external peer review, including scientific and societal relevance of research, research policy and research management.
- Accountability to the board of the research organisation, and towards funding agencies, government and society at large.

Universities and UMCs in the Netherlands have agreed to carry out a self-evaluation every three years and an external review every six years. This process is guided by the Standard Evaluation Protocol (SEP). For this evaluation the SEP 2009-2015 is used.

The present external research evaluation has the following objectives:

- To assess the quality of the research and graduate PhD programs carried out at the UMC Utrecht during the period under review (2007-2012) compared to an international benchmark (not a comparison within UMC Utrecht);
- To identify research areas that have the potential to stimulate innovation and have societal impact;
- To identify excellent research groups and young researchers with high research potential;
- To identify research areas that are currently of the highest international standard, how these may be strengthened and suggest conditions for their continued development.
- To identify research areas that have the potential to develop towards the highest level of international research and to determine what is necessary to ensure such development.
- To identify research areas that are not internationally or nationally competitive and lack evident development potential.
- To identify research areas that are missing and that could be considered to be essential for the UMC Utrecht.
- To identify the need for infrastructural support that would facilitate development towards greater excellence.

## 1.2 Research organisation UMC Utrecht.

The UMC Utrecht is organized in eleven divisions. All divisions operate in the areas of direct patient care, education and research. Divisions have their own budgets and policies, which are based on their specific categories of patients. The divisions are: Biomedical Genetics, Heart and Lung, Imaging, Internal Medicine and Dermatology, The Julius Center for Health Sciences and Primary Care, Laboratories and Pharmacy, Neurosciences, Paediatrics, Surgical Specialties, Vital Functions, Woman and Baby.

In 2010 a new strategy for the years 2010-2015 was launched, Strategy 3.0. In this Strategy 3.0 the UMC Utrecht put more emphasis on the connection between research and patient care aiming at innovation in patient care driven by identified clinical needs. Based on external developments and the strategic self-evaluation performed in 2009, it was decided to focus the UMC Utrecht core activities (patient care, research and education) on the following six strategic programs and their clinical syndromes (between parentheses):

- Brain (stroke, epilepsy, neuromuscular disorders, psychotic disorders, neurodevelopmental disorders);
- Infection & Immunity (opportunistic infections, immune deficiencies, chronic inflammation);
- Circulatory Health (atherosclerosis, heart failure, stroke);
- Personalized Cancer Care (breast cancer, gastro-intestinal cancer);
- Regenerative Medicine & Stem Cells (stem cell based therapies, cardiovascular and musculoskeletal tissues);
- Child Health (chronic inflammation, respiratory infections, orphan diseases/genetics RM, fertility interventions).

### **1.3 The Review Panel Circulatory Health**

The review panel for the Circulatory Health Program was appointed 22 November 2013 and consisted of:

- Professor Rob Reneman (Chair), Maastricht University
- Professor Rodolphe Fischmeister (Vice Chair), INSERM
- Professor Ulrich Keil, University of Münster
- Professor Dudley Pennell, Imperial College London
- Professor Frank Vermassen, University of Ghent
- Dr. Andy Molyneux, Nuffield Department of Surgery, University of Oxford

Dr. Barbara van Balen,(staff member of) QANU, was appointed secretary to the review panel.

A short curriculum vitae of each member is included in Appendix 1.

### **Independence**

All members of the Review panel signed a statement of independence to ensure that

- they would judge without bias, personal preference or personal interest, and
- their judgment is made without undue influence from the institute, the program or other stakeholders.

### **1.4 Scope of the Assessment**

This assessment concerns the strategic program Circulatory Health. This program was launched in January 2012. The program builds upon the existing portfolio of cardiovascular research in the UMC Utrecht and on the existing infrastructure of the research departments involved. Evaluation of the program performance therefore necessarily addresses the period before the program was initiated. The review panel tried to use the performances of the researchers now cooperating in the program in its quality assessment regarding the contributing research areas and in this way to identify the weaker and stronger areas in the program. The review panel will use the evaluation criteria of the protocol to substantiate its assessment and recommendations, but is of the opinion that at this moment in the development of the program it cannot, as yet, be graded according to SEP.

### **1.5 Data provided to the Review Panel**

The review panel has received a self-evaluation report provided by the UMC Utrecht. The panel also received the report on the Mid Term Review 2007-2009, the assessment report 2002-2006. Prior to the site visit, additional information on achievements and future plans for three clusters of research areas and patient groups were supplied, including 15 key references (letter to the chair, dd. January 31st). Additionally, the review panel received upon its request the following information after the site visit: the Thomson Reuters business Evidence report, the bibliometrical analysis of Circulatory Health research 2007-2011 per research area and the publication list of all researchers involved.

### **1.6 Procedures followed by the Panel**

The assessment was based on the documentation provided by the UMC Utrecht and the interviews during the site visit. The interviews took place on the 6th and 7th of February 2014. The program of the site visit is included in Appendix 2.

The panel members all read the Self Evaluation Report. The reviewers prepared questions for the interviews, which were partially exchanged prior to the meeting.

During the internal panel meeting on the evening of 5 February 2014, preceding the site visit, a series of comments and questions regarding the program were decided upon. On the days of the site visit, the panel met the UMC Utrecht Board to acquire general information, the Management team of Circulatory Health, interviewed Principle Investigators (PI's), attended a poster presentation by PhD students, had a meeting with the stakeholders and discussed the results of the assessment thus far and the outline of the advice in the report. Afterwards a meeting with representatives of the UMC Utrecht, the program leaders and interested researchers was arranged, in which the main impressions of the panel were reported.

A draft version of the report was written by the secretary and the chair and sent to the review panel members for comments. Their remarks and recommendations for improvement were incorporated in the next version.

### **1.7 Assessment Criteria**

The Protocol requires the Evaluation Review panel to assess the research on the four main criteria of the *Standard Evaluation Protocol*:

- Quality (the level of the research conducted)
- Productivity (relationship between input and output)
- Societal relevance (social, economic and cultural relevance of the research)
- Vitality and feasibility (flexibility, management and leadership)

As mentioned before, the review panel decided not to use any ratings in this phase of the development of the program Circulatory Health. Quality is expressed only in wording.



# 2 Assessment of the Circulatory Health Program

Program Leader: Professor Diederick Grobbee  
Academic staff in 2012: 191

## 2.1 Mission, goals and research activities of the program

It is the ambition of the Circulatory Health Program to create a state-of-the-art, internationally competitive, integrated research and patient care program that stimulates translational, multi-disciplinary research, innovative patient care and excellent education and training with the aim to improve prediction, prognosis and prevention of vascular disease that benefits patients and society. The research program concerns seven patient groups (hemorrhagic stroke, ischemic stroke, peripheral artery disease, coronary heart disease, heart failure, renal failure/hypertension and high risk groups) and nine research themes (proteomic & biomarkers, genetics, molecular & cellular biology, metabolism, imaging, clinical interventions and therapeutic innovations, clinical research methods, prevention & public health and regenerative medicine). The program is currently in the phase of developing a strategy for the future.

The Circulatory Health program has set the following objectives:

- Establishment of a common research focus on prediction, prognosis and prevention across disciplines and departments.  
The added value of Circulatory Health lies in the cross-links that will be created between scientists from the different participating research groups, as well as linkage of research infrastructures (patient cohorts, databases, laboratories), all with a common research focus.
- Integration of research and patient care.  
Circulatory Health aims at an integrated program for research and patient care with basic and translational research that will be applied in patients. The patients to be addressed range from the 'complex patient' needing top clinical care to the 'high-risk' patient in primary and secondary care and in the general population.
- Provisions of optimal clinical care for the cardiovascular patient referred to the UMC Utrecht and expert advice to specialists consulting the UMC Utrecht expertise.
- Creation of an optimal research infrastructure, in collaboration with top research groups abroad, multinational imaging centres, and the pharmaceutical industry.
- Creation of an environment that stimulates and attracts top talent in clinical care and (pre-) clinical research.
- Placement of global cardiovascular health on the UMC Utrecht/UU research agenda.

The program contacted Thomson Reuters to make a bibliometrical analysis from publications and their citations of involved researchers. This analysis was, upon request, also made available to the review panel per patient group and research line. This allowed the panel to get an impression about the quality of the patient groups and research lines, contributing to the total program.

## 2.2 General remarks

The new program actually is a collection of running activities rather than the start of a new program based upon a chosen strategy and the expertise required for realization. The review panel fully realizes that the program leaders did not have an alternative for the start of a program on circulatory health, but expresses concern regarding the approach chosen. Seven patients groups and nine research areas in a matrix implies 63 clusters of activities; an endeavor impossible to be handled in practice. Choices have to be made for the potentially most successful and competitive clusters. To be able to make such choices, the program leaders need delegated competence as far as reallocation of personnel and money is concerned.

For a better structuring of the program and for setting priorities, the lack of a substantial amount of free money is a serious handicap for the program leaders. Seeding money will be very helpful. This was already recognized in the 2006 evaluation. In the 2006 evaluation report it was recommended to direct money towards the directors of the programs.

Another aspect of concern is the organizational structure chosen. A total of 16 theme leaders and 106 principal investigators have been identified based upon preset criteria. To the opinion of the review panel, this is far too many for an effective operation! Also in this respect selections have to be made and the organization has to be simplified.

The output of the program as a whole is nicely presented, so is the impact of the publications. A substantial percentage of the papers is published in top journals in the last two years: 21% in the top 10-25% journals. When only 1st, 2nd and last authorships were considered this number was higher (31%) in 2011 and similar in 2012. The impact of the scientific contributions of the various research lines was evaluated by using a Thomas Reuter analysis. In the relative analysis the research areas showed a slightly to a substantial better performance. The same holds for the patient groups. For technical reasons the research areas Clinical Research Methods, Prevention and Epidemiology and Clinical Interventions were grouped together, hampering evaluation of the separate areas.

The panel members were not familiar with the Thomson Reuters analysis and wondered about the high ratios (up to 3) as compared to, for example, the Van Rahn analysis showing a maximum of nearly 2 for cardiovascular programs in the Netherlands. In the midterm review reports, making use of the van Rahn analysis, the more familiar ratios of on the average between less than 1.0 and 2.0 were found. Besides, discrepancies were observed between the data. For example, a ranking 86 internationally in table 3.1 was associated with a relative ratio of more than 2 in figure 4.3. The management was asked to provide the panel with a more detailed analysis per research area and per patient group to be able to better evaluate the quality of the various contributing components. This information was provided by the end of the meeting. For the same purpose the committee also asked for a detailed list of publications per research area and per patient group. This information was provided some time after the meeting.

The SWOT analysis was realistic as far as identification of weaknesses, strengths and threats are concerned. It was clearly recognized that further integration was recognized as an important necessity without indicating how this should be realized.

### **2.3 Program Assessment**

#### **Quality**

The program as a whole can be considered potentially very good. The grants collected at the national level are very good to excellent, but the success in acquiring grants at the European level, is limited. The quality will certainly improve when the necessary selections in the program are made (see Vitality & Feasibility). The Julius Center can already be considered as excellent. The center is internationally very active in networks and in collaborations with industry and with publications in top journals.

The focus is on translational research: a logical consequence of the strong position in clinical and epidemiological research but this will only flourish, if sufficiently supported by basic research groups. It is the impression of the review panel that the amount of basic research is relatively limited. In the view of the review panel the applied sciences have to be fed by basic research. It is acknowledged that basic research is the main focus of the teams of the Hubrecht Institute, which is affiliated with the UMC Utrecht. Stronger links between Circulatory Health and the Hubrecht Institute are to be encouraged, particularly in the field of regenerative medicine.

#### **Productivity**

For the program as a whole the number of SCI publications has been increasing substantially over the years, especially those with 1st, 2nd and last authorships. The output can be considered to be very good to excellent (more than 5 papers per fte in SCI journals in 2012).

## **Relevance**

A very strong aspect of the program is its focus on clinical and epidemiological research. The scientists do have a variety of important clinical and epidemiological cohorts at their disposal. They have the ability to create an excellent platform on translational medicine. The importance of these developments was reassured by the representatives from the Dutch Heart Foundation and the Patient Platform on Cardiovascular Diseases during the meeting with the stakeholders.

The impact of the research on society is excellent. Important problems in cardiovascular disease are addressed and the outcome of the clinical studies and drug trials will without doubt contribute to better patient care and treatment. Also, the program contributes substantially to technical developments in the field of imaging, predominantly in collaboration with Philips. The latter company, as indicated by the representative of Philips during the stakeholders meeting, is not only interested in imaging developments, but wishes to broaden the interaction also in the research activities in circulating cells and biosensors as well as in the health care aspects investigated in the epidemiological studies.

The management of the program certainly has a focus on valorization. This especially holds for Julius Clinical and the creation of an elaborate technology platform for imaging, using a variety of imaging modalities. It is indicated that the management considers the establishment of an industrial platform where university scientists and scientists from industry meet and may plan the creation of startups. These are interesting and logic initiatives. When creating such a platform, the independence of the scientists has to be guaranteed as in Julius Clinical. However, the success of startups should not be overestimated. Seven patents were filed, but no indication is given about their success in commercial terms, also not during the interviews.

## **Vitality & Feasibility**

The program as presented is certainly feasible. The vitality as a whole, however, strongly depends on the further developments regarding focusing of the research activities in relation to relevance and the quality of the contributors. To realize this, the management of the program should have the possibility to influence reallocation of money and personnel.

## **2.4 Assessment at the research area and patient group levels.**

### **General**

To be able to evaluate the scientific activities at these levels properly the review panel decided to ask for additional information. The management of Circulatory Health provided the panel with the Thomson Reuters bibliometrical analysis per patient group and per research line as well as with a detailed list of publications. This information also would give the panel the opportunity to support the program management in focusing on the potentially most successful activities in the program. However, the panel faced several problems in this exercise:

- In a variety of listed papers it was impossible to relate the publication to Circulatory Health based upon the titles provided. Therefore, the panel has the impression that in the survey, papers are listed from the programs in general. For example, there is a strong program on Molecular and Cellular Biology within the UMC Utrecht. Scientists active in this program are participating in Circulatory Health, but to what extent? Are they bringing in their non-Circulatory Health related publications? The same question can be asked regarding the university program on Regenerative Medicine and Stem Cells.
- Second, the number of papers presented in the survey is substantially larger than the number of papers presented in the Self Evaluation Report over the years 2010-2012 (3283 vs 2616), which is in support of the remarks under bullet 1.
- Things do get even more complicated when reading that the Thomas Reuter analysis per research area and patient group was performed on the basis of only 2171 publications over the period 2007- 2011. The reduction in numbers is likely due to the distinction between real research publications and remaining ones in the analysis.
- Finally, adequate evaluation was hampered by the inadequate description of the achievements and future plans within most of the research areas and patient groups, with one exception: the Julius Center. Their activities and plans were laid out very well. The evaluation panel got the impression that the Julius Centre is strongly present in several of the research lines.

Therefore, assessment of the quality at the levels of the research areas and the patient groups based upon the Thomas Reuter analysis can only be used in a relative way with the necessary precautions. In this assessment, use was made of the percentage of the papers published in the top 10% of the journals in their field and especially of the journal normalized citation impact, the field-normalized citation impact, specific aspects as leading by output and impact at both the program and the personal level, and whether they published in the real top journals as Science, Nature, The New England Journal of Medicine and The Lancet. An additional problem was the fact that the evaluation panel did not have information about the number of fte's per research area and patient group. Therefore, normalization is impossible, hampering appropriate comparative analysis. In the quality assessment, we also have tried to make use of the information provided during the discussions with the program leaders.

## **Research areas**

### *1. Proteomics and Biomarkers*

Good productivity of good quality. 34.0% of the publications in the top 10 % journals in their field. Internationally visible (NCIf is 1.43, but NCIj is only 1.02). No papers in the real top journals as Nature, The Lancet, etc.

Conclusion: good

### *2. Genetics*

Good productivity with 37.7 % of the publications in the top 10 % journals in their field. NCIf is 1.81. Nine publications in Nature Genetics! Internationally clearly visible and nationally very competitive.

Conclusion: very good to excellent

### *3. Molecular and Cellular Biology*

Very good productivity with 31.2 % of their publications in top 10 % journals. Despite this publication record, the group is barely visible internationally (NCIj is 0.99 and NCIf is 1.27). Certainly competitive at the national level. No papers in the real top journals as Nature, The Lancet, etc.

Conclusion: Good

Remark: in the field of Molecular and Cellular Biology, UMC Utrecht as a whole was ranked in the top ten global institutions by output. So, as a whole it has a very strong position internationally.

### *4. Metabolism*

Very productive with 42.8 % of their publications in the top 10 % journals in their field. Very high relative impact ratios. Clearly visible internationally (NCIj is 1.80 and NCIf is 2.89). Leading nationally. No papers in the real top journals as Nature, The Lancet, etc.

Conclusion: Very good

### *5. Imaging*

Good productivity with 36.0 % of the publications in the top 10 % journals in the field. No papers in the real top journals as Nature, The Lancet, etc. Visible internationally (NCIf is 1.76, but NCIj is only 1.05) and nationally competitive. Substantial increase in productivity in the past years. The group established a unique platform on imaging techniques, incorporating various imaging modalities.

Conclusion: very good

Remark: in the field of imaging, UMC Utrecht as a whole was ranked in the top ten global institutions by output. So, as a whole it has a very strong international position.

### *6. Clinical Interventions and Therapeutics, Clinical Research Methods and Prevention and Epidemiology*

In the Thomas Reuter analysis the three areas were grouped. As a whole these areas are very productive with 39.3 % of the publications in the top 10 % journals in their field. They published 16 research papers in the Lancet. The cluster is internationally very competitive and leading nationally and internationally (NClj is 1.39 and NClf is 2.55). It is unclear, however, whether this is the achievement of the group as a whole or of a specific research area in the cluster. It may quite well be that, considering the excellent performance of the Julius Center and Julius Clinical, Epidemiology contributes substantially to this very good performance.

Conclusion: very good to excellent

### *7. Regenerative Medicine*

No Thomas Reuter analysis available. The description of ongoing activities and plans for the future were rather confusing. Not clear where the group is heading to. No specific publication in relation to Circulatory Health was provided. The information presented upon request during the interview was average.

Conclusion: unsatisfactory

## **Patients groups**

### *1. Hemorrhagic Stroke*

This patient group is ranked in the top ten global institutions by output and citation impact, despite the fact that NClj is only 0.78 (not really visible internationally). Their NClf is 1.49. No papers in the real top journals as Nature, The Lancet, etc. We are facing a discrepancy here! Nearly half of their papers are published in the top 10 % journals in their field.

Conclusion: good to very good

### *2. Ischemic Stroke*

Ranked in the top ten global institutions by output and citation impact, despite the fact that NClj is only 0.98 (not really visible internationally). Their NClf is 1.90 (clearly visible internationally). Eight papers in The Lancet. Two of their leaders are identified as global opinion leaders. Again discrepancies! Nearly half of their papers are published in the top 10 % journals in their field.

Conclusion: very good to excellent

### *3. Peripheral Vascular Disease, including carotid artery disease*

Ranked in the top ten global institutions by output and citation impact. Their NClj and NClf, is 1.29 and 2.09, respectively. Two of their leaders are identified as global opinion leaders. 35.1 % of their papers are published in the top 10 % journals in their field. No papers in the real top journals as Nature, The Lancet, etc.

Conclusion very good

### *4. Coronary Heart Disease*

37 % of their papers published in the top 10 % journals in their field. No papers in the real top journals as Nature, The Lancet, etc. Clearly visible internationally. (NClj is 1.38 and NClf is 2.87).

Conclusion: very good to excellent

### *5. Heart Failure and Arrhythmias*

24.6 % of their papers published in the top 10 % journals in their field. Clearly visible internationally (NClj is 1.75 and NClf is 2.55). Seven papers in Circulation, but no papers in the real top journals as Nature, The Lancet, etc. One of the leading groups in the Netherlands in arrhythmias and related heart failure. Not in heart failure as such.

Conclusion: very good

*6. Renal Failure Hypertension and the Elderly*

31.3 % of their papers published in the top 10 % journals in their field. Their NCij is 1.00 (average impact) and their NCif is 1.47 (clearly visible internationally). No publications in top journals as Nature, The Lancet, etc.

Conclusion: good

*7. High Risk Groups, including Diabetes Type 2, Ovarian Failure and HIV*

49% of the papers in this group are published in the top 10 % journals in the field. Five papers in The Lancet and 5 papers in The New England Journal of Medicine. Ranked globally fourth by output and ninth by citation impact. . Two of the leaders are identified as global opinion leaders. Internationally, very visible (NCij is 1.69 and NCif is 2.93).

Conclusion: excellent

# 3 Conclusions and Recommendations

The newly started program (early 2012) actually is a collection of running activities rather than the start of a new program based upon a chosen strategy and the expertise required for realization. The review panel fully realizes that this pragmatic approach was chosen to realize this program on Circulatory Health, but expresses concern regarding the structure and the organization of the program chosen. Realization of the matrix implies 63 clusters of activities; an endeavor impossible to be handled in practice. Also an organization with 16 program coordinators and 106 principal investigators (PI's) will be impossible to manage. During the interviews it became clear that the management of the program on Circulatory Health fully realizes that the number of clusters has to be scaled down substantially and that selections have to be made. This was also clearly expressed in the SWOT analysis. Selections based upon strategy and quality, however, require delegated competence as far as reallocation of personnel and money is concerned as well as a substantial amount of free money. Seeding money is essential in reorganizing the program. This was already recognized in the 2006 evaluation report. Restructuring the program also requires a substantial reduction of the number of program coordinators and PI's. The evaluation panel strongly recommends to give priority to restructuring and reorganizing the program and to provide the management with the handles necessary to realize this. The panel wants to emphasize that when restructuring the program, considering the fast developing world of medical research, focus should not be at the cost of flexibility.

At present, the program as a whole can be considered potentially very good. A substantial percentage of the papers is published in the top journals for the respective fields. The number of grants collected at the national level is very good to excellent, but in acquiring grants at the European level it is less successful with a success rate of 16 % at the program and project level. Two starting grants were obtained from the ERC for one and the same person. No consolidated and advanced grants were acquired. The quality will certainly improve when the necessary selections in the program are made. Julius Clinical can already be considered as excellent. The center is internationally very active in networks and in collaborations with industry, with publications in the top journals.

The focus on translational research is a logic consequence of the strong position in clinical and epidemiological research. Circulatory Health has at its disposal a substantial number of important clinical and epidemiological cohorts. It has the ability to create an excellent platform for translational medicine. It is the impression of the evaluation panel that the amount of basic research is relatively limited. It is strongly recommended to pay sufficient attention to basic studies to be able to unravel causal mechanisms underlying the relations observed in the clinical and epidemiological studies. A unique technology platform, using a variety of imaging modalities, has been successfully established in close collaboration with Philips.

The program as described has an excellent impact on society. The problems in cardiovascular disease addressed are relevant and the outcome of the clinical and drug studies (RCTs) will contribute to better patient care and treatment. A conclusion confirmed by the stakeholders.

There is a clearly recognizable emphasis on valorization of knowledge. This is most noticeable in the activities of Julius Clinical. The knowledge of this center is effectively shared with industry, while keeping its own identity and freedom. Several activities are foreseen to commercialize its knowledge to generate extra funding. This is understandable, but the evaluation panel recommends being careful in such exercises. They should not be at the cost of generating new knowledge.

Seven patents were filed, but the evaluation panel was not informed about the execution of these patents. Were innovative ideas indeed transferred into innovations? Neither was the evaluation panel informed of the research line or patient group these patents originated from.

The evaluation panel was facing a problem assessing the quality and relevance of the contributing building blocks. In the Self Evaluation Report, with the exception of Julius Clinical, no detailed information about the state of the art of the developments and the future plans within the research lines and the patient groups was provided adequately. Only very short descriptions of the activities and only one key publication per research line were presented. Prior to the site visit bibliometrical analysis was only performed for the program as a whole. Therefore, the evaluation panel was unable to assess the activities at the sub-program level adequately. Upon request of the evaluation panel a bibliometrical analysis of the research lines and patients groups as well as a detailed list of publications were provided after the site visit. The list of publications presented was difficult to handle by the evaluation panel for the reasons outlined in the report. Therefore, assessment of the quality at the level of the research lines and the patient groups could only be made based upon the Thomas Reuter analysis, using the criteria as described in the report. This analysis, however, is relative and should be interpreted with the necessary precautions. An appropriate comparative analysis could not be made, because information about the number of fte's per research line and patient group was not available. The evaluation panel also made use of the information provided during the interviews with the PIs. In this light the evaluation panel decided not to rate the activities, but to express the quality in wording.

Quality analysis based upon the bibliometrical analysis, making use of the criteria as described in the report, revealed a quality varying between good and excellent with one exception: Regenerative medicine. No bibliometrical analysis was available on Regenerative Medicine, while the evaluation panel was not impressed by the answers given during the interview. This research line was considered to be unsatisfactory.

The evaluation panel was impressed by the enthusiasm of the PIs during the interviews. They believed in their mission and the members of the evaluation panel sincerely do hope that they will not be frustrated in their endeavor. We recommend the Board of the UMC Utrecht to give them the handles to realize their plans.



# Appendix 1

## Curricula vitae of the Evaluation Review panel members

**Prof. Robert S. Reneman** Professor Emeritus, Maastricht University, Maastricht, the Netherlands

### *Training*

University of Amsterdam	M.D.	1961
Academic Hospital Utrecht	Registered Anaesthesiologist	1966
University of Utrecht	PhD Clinical Physiology	1968

### *Previous positions*

1966-1970	Anaesthesiologist, Department of Cardiovascular Surgery, Academic Hospital Utrecht
1970-1971	Post-doc Virginia Mason Research Centre and University of Washington, Seattle
1972-1975	Head Department Life Sciences, Janssen Research Foundation, Beerse, Belgium
1974-1990	Professor/Chairman Dept. Physiology, Maastricht University, Maastricht, the Netherlands
1985-1999	Professor of Physiology, Technical University Eindhoven, Eindhoven, the Netherlands
1988-1999	Scientific Director Cardiovasc. Res. Inst. Maastricht
1990-2000	Professor of Cardiovascular Research, Maastricht University, Maastricht, the Netherlands
2000-present	Professor Emeritus of Cardiovascular Research, Maastricht University, Maastricht, the Netherlands

### *Research*

Interest: Cardiovascular (Patho)Physiology; Non-invasive Vascular Ultrasound. (Co)author 454 publications in international refereed journals; 165 books and book chapters, supervisor 65 PhD theses.

Served as chairman and member of a variety of Dutch and European scientific evaluation committees. Was consultant to medical electronic and pharmaceutical companies.

### *Grants/ honors/ honorary positions*

Served as principal investigator on many project and program grants funded by the Netherlands Foundation of Scientific Research (NWO), the Netherlands Heart Foundation and the European Union.

Many honours and awards were received. Among the most important honours are Member Academia Europaea, since 1989; Member Royal Netherlands Academy of Arts and Sciences, since 1990; Member European Academy of Arts and Sciences, since 1991, Affiliate Professor of Bioengineering, University of Washington, Seattle, since 1990; Knight in the Order of the Netherlands Lion, 1998; Foreign Correspondence Member Royal Academy for Medicine of Belgium, since 1999; Malpighi Award of the European Society of Microcirculation, 2000; Commandeur l'Ordre de la Légion d'Honneur, 2000. Fellow International Academy for Medical and Biological Engineering, since 2003.

Many honorary positions were held, among which, President of the Benelux Society for Microcirculation, President of the European Society for Microcirculation, President of the Federation of European Physiological Societies, Vice President and President of the Royal Netherlands Academy of Arts and Sciences and Member of the Board of Trustees of Leiden University.

Editorial Boards (selection): Circ. Res., 1993-1999; J. Vasc. Invest. (Chief Editor), 1994-1999; Int. J. Microcirc., 1980-1998; Microvasc. Res, 1988-1993; News in Physiological Sciences, 1987-1994; Eur. J. Physiology (Pflügers Archiv), (Field Editor 1987-1996, Executive Editor 1996-2003), Cardiovasc. Res. 1983-1992; Ultrasound Med. Biol. since 1978.

**Prof. Andrew Molyneux** Nuffield Department of Surgical Sciences, University of Oxford.

*Training*

University of Cambridge MD

University of Cambridge PhD

*Previous positions*

He was a Consultant Neuroradiologist at the Radcliffe Infirmary, Oxford for 25 years and at Frenchay Hospital Bristol for 4 years. He was until recently a Senior Clinical Research Fellow, at the Nuffield Department of Surgery, University of Oxford. He led the MRC funded International Subarachnoid Aneurysm Trial (ISAT).

*Research*

He has been working in the field Stroke and Interventional treatment of brain vascular lesions for more than 25 years and pioneered the treatment of intracranial aneurysms by endovascular techniques with detachable for more than 20 years.

He has published widely in many aspects of Stroke, interventional treatment of brain lesions and intracranial aneurysm treatment in particular, with a personal experience of well over 1000 cases over the last 14 years.

He is first author on 2 major publications in the Lancet in 2002 and 2005 reporting the results of the ISAT study, which has transformed the management of patients with ruptured brain aneurysm in many countries of the developed world.

He was on the Royal College of Physicians, Stroke Guidelines Group published in 2003 and on the National Institute for Clinical Excellence (NICE), Guidelines development group which issued national guidelines for Acute Stroke care published in 2008.

He has been providing expert witness evidence for Medico-legal cases for over 15 years in the field of Neuroradiology, both diagnostic (reading scans) and in cases of Interventional procedures and stroke and spinal disease.

**Prof. Ulrich Keil** Dr. med., MPH, PhD, FAHA, FESC, FRCP, Professor Emeritus, Department of Epidemiology and Social Medicine, University of Münster. Adjunct Professor, Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill. Director of the WHO Collaborating Centre for Epidemiology and Prevention of Cardiovascular and other Chronic Diseases at the University of Münster

*Training*

Heidelberg University Medical School	Medical State Examination and Dr. med. Dissertation	1968/69
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UNC Chapel Hill, School of Public Health	PhD in Epidemiology	1980
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*Previous positions*

1979-1987 Director, Department of Epidemiology, Institute for Medical Informatics and Health Services Research (MEDIS), Gesellschaft für Umwelt und Gesundheit (GSF), Munich

1987-1993 Professor and Chair, Department of Social Medicine and Epidemiology, Ruhr-University Bochum

1989 – Adjunct Professor, University of North Carolina at Chapel Hill, School of Public Health, Department of Epidemiology

1993 –2009 Chair, Department of Epidemiology and Social Medicine, University of Münster

1994 – Director, WHO Collaborating Centre for Epidemiology and Prevention of Cardiovascular and other Chronic Diseases, University of Münster

*Research*

Epidemiology and prevention of cardiovascular diseases; member and chair (1986-89) of the steering committee of the WHO MONICA Project 1979-2002. Chair of the steering committee of EUROASPIRE III.

Epidemiology of asthma and allergies in childhood; Co-initiator and member of the steering committee of ISAAC

Occupational epidemiology.

About 350 publications in journals with peer review. Close to 100 contributions to books.

Co-author of three books. More than 16 000 citations in the web of science (Thomson Reuters)

*Grants/ honorary positions/ prizes*

Many honorary positions and prizes, among which

- 1985 Curt Adam Preis. Award for the best contribution to "primary and secondary prevention of cardiovascular diseases", awarded by Kongressgesellschaft für Ärztliche Fortbildung, Berlin.
- 1989 Hufeland Prize, Stiftung Hufeland Preis, Cologne, , together with H.W. Hense
- 1997 Franz Gross-Science Prize 1997. awarded by German Society of Hypertension
- 2006 Research Prize "Smoke Free Life". Awarded by Association of Physicians for Smoking or Health, Heidelberg.
- 2007 Frederick H. Epstein Memorial Lecture Award by American Heart Association , Orlando), USA
- 2010 Honorary Award Lecture on Prevention, Deutsche Gesellschaft für Kardiologie, Mannheim
- 2012 Jan J. Kellermann Memorial Award from International Academy of Cardiology, Toronto

Editorial Boards (selection):American Journal of Epidemiology(Associate Editor 1991-1997)

Journal of the Royal Society of Medicine (1993-2001), European Journal of Public Health( 1991-1996). European Journal of Preventive Cardiology (Associate Editor 1999-2012), Annals of Epidemiology (1997-2013), Preventive Medicine (1990-2013).

**Prof. Rodolphe P. Fischmeister** Director of Research INSERM, Head of Laboratory

*Training*

University of Paris-Sud XI, Orsay,	B.Sc. (Maths & Physics),	1975
Ecole Supérieure d'Électricité, Gif-sur-Yvette,	Engineer Degree,	1978
University of Paris-Sud XI, Orsay:	Doctorat-Ingénieur (Ph.D.), Physiology & Biophysics	1980
University of Paris-Sud XI, Orsay	Doctorat d'Etat ès Sciences Naturelles	1987
		France

*Previous positions*

- 2006-2010: Head of Institute IFR141 - Innovation Thérapeutique: du Fondamental au Médicament, University of Paris-Sud, Faculty of Pharmacy, Châtenay-Malabry, France
- 2006-: Director of Research INSERM, Head of Laboratory INSERM U769, University of Paris-Sud, Faculty of Pharmacy, Châtenay-Malabry, France
- 1996-2005: Director of Research INSERM, Head of Laboratory INSERM U446, University of Paris-Sud, Faculty of Pharmacy, Châtenay-Malabry, France
- 2003-2004: Visiting Professor, Department of Cell Biology, Emory University, Atlanta, Georgia, USA
- 1992-2001: Director or Research and later Head of Institute IFR75 – Signalisation et Innovation Thérapeutique, University of Paris-Sud, Faculty of Pharmacy, Châtenay-Malabry, France
- 1983-1992: Research Associate and later director of Research INSERM, University of Paris-Sud, Orsay, France
- 1982-1983: Research Associate in Anatomy, Dept of Anatomy, Emory University, Atlanta, Georgia, USA
- 1981-1982: Post-doctoral Research Fellow, Department of Physiology & Biophysics, Dalhousie University, Halifax, Nova Scotia, Canada

*Grants/ honorary positions/ prizes :*

- 1982-1983: NIH Post-doctoral Research Fellowship
- 1981-1982: Nova Scotia Heart Foundation Post-doctoral Research Fellowship
- 1978-1980: Délégation Générale à la Recherche Scientifique et Technique, Pre-doctoral Research Fellowship

**Prof. Dudley Pennell** is Professor of Cardiology at the National Heart and Lung Institute, Imperial College, London; He is Director of the Cardiovascular Magnetic Resonance (CMR) Unit, and Director of Non-Invasive Cardiology at Royal Brompton and Harefield NHS Foundation Trust. He is also Director of the NIHR Cardiovascular Biomedical Research Unit and an NIHR Senior Investigator.

*Research:*

His research interests are in CMR, specifically in the measurement of myocardial iron and the assessment of chelation treatment, the assessment and differentiation of cardiomyopathies, the detection and assessment of early atherosclerosis, and myocardial perfusion imaging.

**Prof. Frank Vermassen**, MD, PhD

Professor and Head of the department of Vascular and Thoracic Surgery at Ghent University Hospital, Belgium  
Chair of the division of Metabolic and Cardiovascular Diseases

*Training:*

Ghent University MD	1984
Registration as specialist in Surgery	1990
Ghent University PhD in Biomedical Sciences	1991

*Previous positions:*

Fellow in Cardiothoracic Surgery St-Antonius Ziekenhuis Nieuwegein  
Fellow at Barnes Hospital St-Louis, USA

*Research:*

Areas of interest:

- Evaluation of new materials, devices and techniques in peripheral open surgical and endovascular interventions
- Treatment of end-stage vascular disease (endovascular interventions, homologous veins, free flaps, angiogenesis)
- Organization of training and evaluation in vascular surgery
- Use of virtual reality techniques in training programs and for procedure rehearsal
- Computational analysis of medical devices and their performance
- Neuro-psychological evaluation of patients with peripheral arterial disease and carotid disease in particular

(Co-)author of more than 150 publications in peer-reviewed international journals and 15 book chapters.

- Scientific communications (>400) at all major international vascular congresses and symposia, mostly as invited speaker.
- Participation in more than 60 clinical studies, both sponsored and investigator-driven in all fields of endovascular and vascular surgery mainly to evaluate the safety and performance of new devices and techniques.

*Grants/ honorary positions/ prizes*

Principal investigator for several projects and grants by the National Fund for Scientific Research Belgium and the Special University Research Fund

Principal investigator in many industry supported and investigator driven clinical studies

Member of the Board of the European Society for Vascular Surgery – Chair of the Education and Training Coimmittee

President of the Endovascular Working Group of the Belgian Society for Vascular Surgery

# Appendix 2

## Program of the site visit

### Wednesday 5 February 2014

- 17.00 Internal meeting of the committee, preparation of the interviews
- 19.00 Dinner

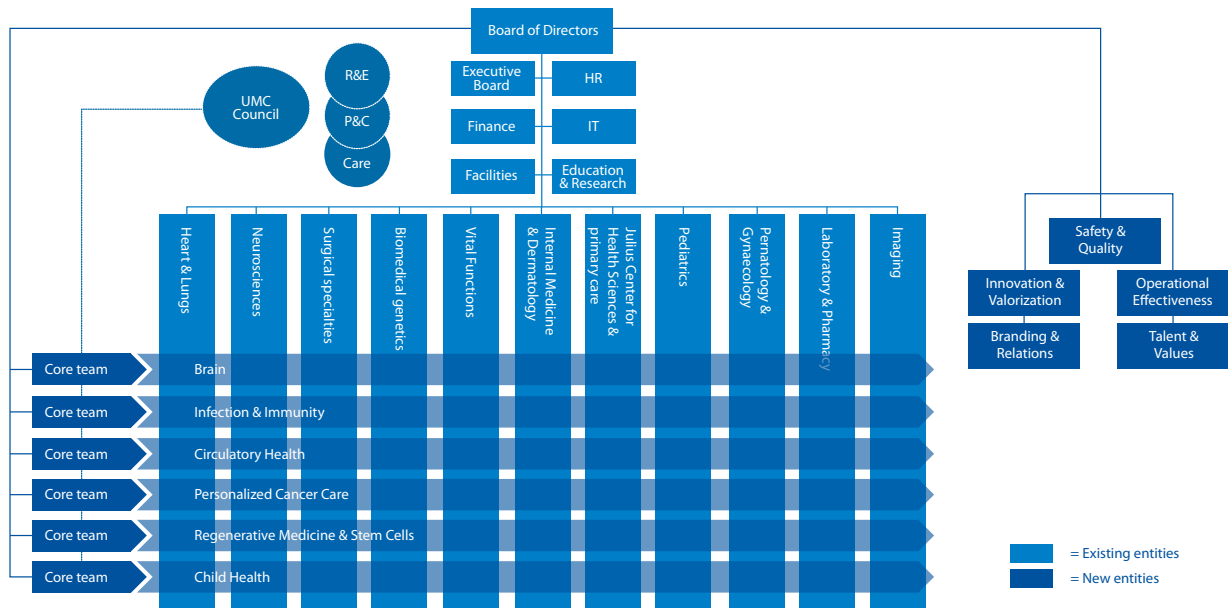
### Thursday 6 February 2014

- 09.00 Meeting with the UMC Utrecht Executive Board:  
prof.J. van Kimpen, prof. F. Miedema, dr. S. van Weelden
- 10.00 Meeting with program chair and management  
prof.D.E. Grobbee, prof. W.P.T. Mali, Prof. G. Pasterkamp, Prof. G.J.E. Rinkel, Prof. Y.T. van der Schouw,  
Prof. F.L.J. Visseren, prof. M.A. Vos, drs. A.J. Boendermaker
- 11.00 Break
- 11.30 Meeting with PIs: Prof. L.J.Kappelle, Prof. G.J. de Borst, Prof. G. Pasterkamp, prof. P.I.W.de Bakker,  
Prof. W.P.T. Mali
- 12.30 Lunch
- 13.30 Meeting with PIs: prof. F.L.J.Visseren, dr.H.M.Nathoe, dr.W. Spiering, prof. D.E. Grobbee,  
prof. K.G.M. Moons, dr. E. Kalkhoven, prof. H.A. Smit
- 15.30 Break
- 16.00 Poster session with postdocs and PhD students
- 17.00 Internal discussion in the committee
- 19.00 Dinner

### Friday 7 February 2014

- 09.00 Meeting with Societal Stakeholders  
drs.M. Senten Dutch heart foundation, drs. H. van Laarhoven Dutch association of patient platforms,  
dr. H. Hofstraat Philips research strategic partner ships
- 10.30 Break
- 11.00 Consulting hour with program management
- 12.00 Lunch
- 13.00 Preparation advice
- 15.00 Preliminary report

# Appendix 3



# Personalized Cancer Care





# Content Personalized Cancer Care

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# 1 Introduction

## 1.1 The Netherlands System of Quality Assessment of Research

This quality assessment of research is part of the assessment system for all public Dutch university research, as organised by the Universities and University Medical Centers (UMCs) in the Netherlands.

The aims of the assessment system are:

- Improvement of research quality based on an external peer review, including scientific and societal relevance of research, research policy and research management.
- Accountability to the board of the research organisation, and towards funding agencies, government and society at large.

Universities and UMCs in the Netherlands have agreed to carry out a self-evaluation every three years and an external review every six years. This process is guided by the Standard Evaluation Protocol (SEP). For this evaluation the SEP 2009-2015 is used.

The present external research evaluation has the following objectives:

- To assess the quality of the research and graduate PhD programs carried out at the UMC Utrecht during the period under review (2007-2012) compared to an international benchmark (not a comparison within UMC Utrecht);
- To identify research areas that have the potential to stimulate innovation and have societal impact;
- To identify excellent research groups and young researchers with high research potential;
- To identify research areas that are currently of the highest international standard, how these may be strengthened and suggest conditions for their continued development.
- To identify research areas that have the potential to develop towards the highest level of international research and to determine what is necessary to ensure such development.
- To identify research areas that are not internationally or nationally competitive and lack evident development potential.
- To identify research areas that are missing and that could be considered to be essential for the UMC Utrecht.
- To identify the need for infrastructural support that would facilitate development towards greater excellence.

## 1.2 Research organisation UMC Utrecht.

The UMC Utrecht is organized in eleven divisions. All divisions operate in the areas of direct patient care, education and research. Divisions have their own budgets and policies, which are based on their specific categories of patients. The divisions are: Biomedical Genetics, Heart and Lung, Imaging, Internal Medicine and Dermatology, The Julius Center for Health Sciences and Primary Care, Laboratories and Pharmacy, Neurosciences, Paediatrics, Surgical Specialties, Vital Functions, Woman and Baby.

In 2010 a new strategy for the years 2010-2015 was launched, Strategy 3.0. In this Strategy 3.0 the UMC Utrecht put more emphasis on the connection between research and patient care aiming at innovation in patient care driven by identified clinical needs. Based on external developments and the strategic self-evaluation performed in 2009, it was decided to focus the UMC Utrecht core activities (patient care, research and education) on the following six strategic programs and their clinical syndromes (between parentheses):

- Brain (stroke, epilepsy, neuromuscular disorders, psychotic disorders, neurodevelopmental disorders);
- Infection & Immunity (opportunistic infections, immune deficiencies, chronic inflammation);
- Circulatory Health (atherosclerosis, heart failure, stroke);
- Personalized Cancer Care (breast cancer, gastro-intestinal cancer);
- Regenerative Medicine & Stem Cells (stem cell based therapies, cardiovascular and musculoskeletal tissues);
- Child Health (chronic inflammation, respiratory infections, orphan diseases/genetics RM, fertility interventions).

### **1.3 The Review Panel Personalized Cancer Care**

The review panel for the Personalized Cancer Care Program was appointed 22 November 2013 and consisted of:

- Professor Joseb Tabernero (Chair), Vall d'Hebron University Hospital, Institute of Oncology, Barcelona, Spain;
- Professor Bob Löwenberg, Erasmus MC Cancer Institute, Rotterdam;
- Professor Peter Hoskin, Professor of Clinical Oncology, University College London, UK.
- Professor Nancy Hynes, Senior Scientist, Friedrich Miescher Institute for Biomedical Research, Basel Switzerland

Dr. Meg Van Bogaert, (staff member of) QANU, was secretary to the review panel.

A short curriculum vitae of each member is included in Appendix 1.

### **Independence**

All members of the Review panel signed a statement of independence to ensure that

- they would judge without bias, personal preference or personal interest, and
- their judgment is made without undue influence from the institute, the program or other stakeholders.

### **1.4 Data provided to the Review Panel**

The review panel has received a self-evaluation report provided by the UMC Utrecht. The panel also received the report on the Mid Term Review 2007-2009, the assessment report 2002-2006 and five key publications.

### **1.5 Procedures followed by the Panel**

The assessment was based on the documentation provided by the UMC Utrecht and the interviews during the site visit. The interviews took place on the 20<sup>th</sup> and 21<sup>st</sup> of February 2014. The program of the site visit is included in Appendix 2.

The panel members all read the Self Evaluation Report. The reviewers prepared questions for the interviews, which were partially exchanged prior to the meeting.

During the internal panel meeting on the evening of 19<sup>th</sup> February 2014, preceding the site visit, a series of comments and questions regarding the program were decided upon. On the second day of the site visit, the panel met the UMC Utrecht Board to acquire general information, the Management team of Personalized Cancer Care, interviewed Principle Investigators (PI's), attended a poster presentation by PhD students, had a discussion with stakeholders and discussed the results of the assessment thus far and the outline of the advice in the report. Afterwards a meeting with representatives of the UMC Utrecht, the program leaders and interested researchers was arranged, in which the main impressions of the panel were reported.

A draft version of the report was written by the secretary and the chair and sent to the review panel members for comments. Their remarks and recommendations for improvement were incorporated in the next version.

### **1.6 Assessment Criteria**

The Protocol requires the Evaluation Review panel to assess the research on the four main criteria of the *Standard Evaluation Protocol*:

- Quality (the level of the research conducted)
- Productivity (relationship between input and output)
- Societal relevance (social, economic and cultural relevance of the research)
- Vitality and feasibility (flexibility, management and leadership)

# 2 Assessment of the Personalized Cancer Care Program

Program Leaders: Professor E. van der Wall

Professor J.L.Bos

Academic staff in 2012: 191

## 2.1 Mission, goals and research activities of the program

The program emphasizes the systematic use of information about an individual patient and/or tumour (including genetic information), and novel (imaging) technologies to select or optimize the individual patient's preventive and therapeutic care.

The UMC Utrecht Cancer Centre aims to develop and apply innovative approaches on focused tumour types, in the areas of diagnostics, treatment and care. The goal is to merge all aspects of UMC Utrecht care with the Antoni van Leeuwenhoek Hospital (AvL) Amsterdam to form a new entity.

The program focuses on two main tumour types, breast cancer and upper GI cancer, as most of the translational and clinical research was focussed in these areas in the past. The other three tumour types that the program focuses on, for which the UMC Utrecht currently has top clinical care, namely head and neck cancer, neuro-oncology and the multiple endocrine neoplasia, have been identified as having the potential to become areas of high quality research in the future.

There is a fundamental cancer biology program and a translational and clinical research program. Themes for the fundamental program are developmental biology, cancer genomics and systems biology, molecular cancer cell biology, models of tumour invasiveness and mouse models. Themes for the translational and clinical research are prevention, early detection and diagnosis, and innovative treatment. The connective lines between fundamental, and translational and clinical research are centred on three main focus areas, all directed towards the further development of 'personalized cancer care': the organoid technology, the centre for personalized cancer treatment (CPCT) and the centre for image-guided oncologic intervention (CBOI).

## 2.2 Program Assessment

### Quality 4

Overall the quality of research in the PCC program is assessed to be very good. Parts of the research are excellent, while other parts require attention. Moreover, the coherence of the research reflects the relatively recent setup of the program.

The quality of the PCC program was evaluated with reference to the loop that was adopted from the institutional reorganisation, relating to basic research towards translational and clinical research. Thus, the committee focussed its assessment on all parts of the cycle.

Given the recently re-oriented goals of the program there is a need for strong and broadly established clinical leadership. Scientific leadership currently is clearly strong, but does need a clear succession plan. The committee noted that the above mentioned developmental process is still in progress; specifically the closure of the loop with respect to clinical research is not yet completed. The program has a strong history in fundamental research, specifically with an excellent academic reputation for a number of (senior) staff members. Parts of the fundamental work are innovative, unique and will very likely have tremendous impact in the future, for example the work on organoids. The committee also found that the work done by the PhD students is of excellent quality.

During the site visit it became clear that the focus of the UMC Utrecht had long been on fundamental scientific research; although this focus has clearly shifted at the institutional level to also include clinical research and patient care, this remains the part of the program that requires more attention. More emphasis within the program is needed on the clinical part of the loop since the activity and coherence throughout the clinical departments dealing with oncology is still limited. The committee strongly recommends that in order to promote clinical research the Institution needs to invest more, in terms of patient numbers, in critical areas. This should be done by the implementation of multidisciplinary boards in which all patients are discussed to decide on the best treatment options and the potential options for clinical trials. If integration of clinical research is in the vision of UMC Utrecht, an effort should be made to promote this concept in all the medical oncology staff. This would require allocating part of the working time within the existing FTEs to ensure that clinical research is promoted. It is likely that additional medical oncologists with a clear research or translational scientific vision and commitment will be needed in order to have the minimum critical mass to potentiate the clinical research program. The committee recognizes that the program has made an effort in the last years to include patients in clinical trials, with particular emphasis in the phase I studies. The PCC should continue to promote more clinical trials, especially those that are innovative and based on the CPCT profiling facilities.

The committee noticed that in the previous evaluation report that the radiology and radiotherapy program did exceptionally well. With the shift in focus from divisions towards programs, the imaging division no longer has an independent assessment.

The exact relationship between the imaging division and the PCC program did not become entirely clear to the committee. For the PCC program one of the priority areas is imaging, while for the imaging division, oncology is one of their focus areas. The clinical research on imaging in the field of oncology is of very good quality and, given the profile of the program, the committee recommends further integration of the imaging disciplines with the PCC program. Although there is formally a threefold leadership of the program (clinical, preclinical and imaging), in practice this does not yet seem to work.

#### **Productivity 4.5**

Overall productivity is considered to be very good to excellent. Similar to the assessment of quality of the program, the committee assessed the productivity strategy and the output with reference to the loop relating to basic research towards translational and clinical research.

Productivity with respect to publications in the fundamental research area is excellent. The number of papers and theses, and the quality of the articles are very good to excellent. Furthermore, the core facilities are excellent and open to third parties (animal facilities, genomics and imaging facilities).

In contrast to the strength in preclinical productivity, the program has a more modest track record with respect to output based on clinical trial activities. The program has the ambition to not only be productive in the preclinical work, but also in clinical activities. However, no clear publication strategy for clinical outcomes is present. Of the approximately 6000 new oncology patients presenting in the UMC Utrecht per year, only a small minority appears to enter into clinical trials (rough estimate is less than 5%). The clinical trials that are being set up and run in the UMC Utrecht are of high quality though.

## **Relevance 5**

When assessing the societal relevance over the past period, the committee was impressed by the results. Examples of excellent relevance towards society are multiple; some of them will be given.

First is the training of the next generation of researchers. Not only are bachelor's students trained to teach, but the DNA bus that goes to Dutch secondary schools is a fine example of outreach. Furthermore, there are a number of spin offs that had their point of departure in the PCC program. Also valorization and implementation of new technologies is prominently present, as is collaboration with industrial partners.

The committee was positively impressed by the active link between the PCC program and the Hubrecht laboratory and has high expectations of the future collaboration with the Amsterdam AvL.

The committee noticed a point that will require attention in the future, which is the changing position of stakeholders. When discussing with stakeholders about societal relevance measurements, it became clear to the committee that clinical outcomes of the research will be focused upon by stakeholders, specifically clinical utility. This strengthens the need for a clear translational/clinical strategy in the near future. More and more stakeholders strongly demand that results from fundamental research end up having clinical relevance. There will be a need for treatment outcome measurements.

## **Vitality & Feasibility 3.5**

The organization has a clear vision on building alliances and cooperation with other institutions that have related interests in oncology research and treatment. The institution as a whole also has imposed on the organization a clear strategy to be engaged in the complete loop from basic research to clinical application. In the PCC program the actual implementation, realization and evaluation of the clinical part are still relatively underdeveloped. This is apparent from the number of trials conducted and apparent from the engagement of various clinical departments involved with oncology. Moreover, the infrastructure for clinical trials is currently fragmented over multiple divisions.

There is a strong need for reinforcing the clinical activities with a research minded orientation across different medical specialties and for instance implementing multidisciplinary tumor board interactions as a basic foundation for future clinical trials. Also, there is a need for a trial management infrastructure that will facilitate clinical research activities.

The committee subscribes to the weakness in the SWOT analysis of the institute part of the report (part A), which states that 'clinical obligations for medical researchers complicate the establishment of strong patient-driven research lines'. With respect to the PCC program the institute needs to focus on the recruitment of patients for clinical trials, both from within the UMC Utrecht and from the adherent hospitals. This goes beyond the PCC program, since oncology is part of a large number of divisions in the hospital. Currently, the program leader has multiple responsibilities in a range of areas and – looking at it realistically – as a consequence is lacking time and impact to influence the organization to such an extent that it will go forward. Nevertheless, progress is being made in some areas, most prominently in the launch of the CPCT. The committee feels that focus areas of clinical trial research will benefit from cooperative (networking) collaborations with other institutions like AvL in Amsterdam.

The SWOT analysis of the PCC program seems not to take into consideration the clinical and translational research of the program, which is – according to the committee – the part of the program that needs most attention. The SWOT analysis does reflect a realistic view of the preclinical setting.

Heading the translational and clinical aspects of the program towards a successful future will require strong leadership, resources and an implementation plan. Chair and co-chairs of the program will have to receive allocated time to lead the program over the next years.

# 3 Conclusion and recommendations

Overall, the committee was impressed by the program and by the new mission of the institute as a whole. The change in the organization is remarkable; the change from divisions to core programs makes a lot of sense. Like all major changes, difficulties are encountered in adapting to the new reality. In addition, alliances with external partners, like the AvL, will stimulate the program, but also take additional time and resources before working optimally.

In the past there was a large investment in molecular profiling and other (fundamental) techniques. This clearly led to very high quality basic research. The change that was launched at the institute level has to be implemented in the programs; this will require a cultural change. Specifically in the clinic this is a challenge, tools are needed to achieve a cultural change among physicians with limited time. The leadership should formulate a strategy on how to achieve its goals. The committee emphasizes that if there are no multi-disciplinary tumor boards and no frequent interaction amongst all participants, there will be no seeds for initiatives that can be launched. Closing the loop from fundamental towards translational and clinical research leading to patient care is a challenge, but essential if the UMC Utrecht wants to achieve its ambition.

# Appendix 1

## Curricula vitae of the Evaluation Review panel members

### **prof. Joseb Tabernero**

MD, PhD, of Vall d'Hebron University Hospital, Barcelona. Head, Medical Oncology Department

Josep Tabernero holds MD and PhD degrees from the Universitat Autònoma de Barcelona, Spain. He is currently the Head of the Medical Oncology Department at the Vall d'Hebron University Hospital in Barcelona and the Director of the Vall d'Hebron Institute of Oncology. He is very actively involved in translational research and pharmacodynamic phase I studies with molecular targeted therapies. He is especially devoted to phase I and II studies with pharmacodynamic endpoints with novel agents directed to the membrane receptors, like the EGFR-family and IGF-1R, the PI3K and ERK signalling pathways, as well as downstream cytoplasmatic and intranucleous effectors like Mdm2/p53 and aurora kinase. Based in the idea that each tumor has an independent genetic identity, the group he is leading very actively participates in the development of molecular therapies targeting specific oncoproteins, with the purpose of developing personalized therapies (e.g. against EGFR, HER2, BRAF, MEK, PI3K, Akt, mTOR or IGF1-R among others) for those patients displaying genetic lesions or pathway dysregulation. One of the main objectives of the group is to identify new predictive markers of response to diverse treatments and to identify markers of primary resistance (de novo) and secondary treatment. At a preclinical level, the group he is leading is developing new xenograft models with explant tumors from patients ("xenopatients") in mice in order to mimic the patient's disease and study the tumor development in optimized research models. It also leads a program devoted to the study of circulating biomarkers (detection and genotyping of circulating free DNA).

In addition, Dr. Tabernero is a member of the European Society for Medical Oncology (ESMO), the American Association for Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO), and different Editorial Boards including the Journal of Clinical Oncology, Clinical Cancer Research, Cancer Discovery, Clinical Colorectal Cancer and Annals of Oncology. He has (co)authored approximately 250 peer-reviewed papers. He has also been member of the Educational and Scientific Committees of the ESMO, ECCO, ASCO, AACR, AACR/NCI/EORTC, ASCO Gastrointestinal, and WCGIC meetings.

### **prof. Peter Hoskins**

Peter Hoskin trained in clinical oncology at the Royal Marsden Hospital London and has been consultant in clinical oncology at Mount Vernon Cancer Centre, Northwood UK since 1992. He is also Professor in Clinical Oncology at University College London. Research interests have ranged from palliative radiotherapy to the use of radiosensitisers and brachytherapy. Current research programmes focus on palliative radiotherapy, hypoxic radiosensitisers, the interaction of vascular targeting agents with radiotherapy, functional imaging and the role of HDR brachytherapy in prostate cancer; over 300 original papers and reviews and 6 textbooks have been published. Other activities include: chair of the ESTRO brachytherapy group GEC ESTRO and the prostate brachytherapy group UROGEC in ESTRO, course organiser for the ESTRO prostate brachytherapy course, Chair of the FRCR examination board, Chair of the UK Radiotherapy Clinical Information Group, Editor of Clinical Oncology and Clinical Editor of Radiotherapy and Oncology, member of the Editorial Boards of the Journal of Clinical Oncology, Contemporary Brachytherapy and the Journal of Bone Oncology.



**Prof. Nancy E. Hynes**

received her BSc in Chemistry in 1970 at St. Francis College, Loretto, PA, USA and her PhD in Biochemistry in 1975, University of Pittsburgh, Pittsburgh, PA, USA. She worked as a postdoctoral fellow at the Max Planck Institute Genetics, Berlin, Germany and the Swiss Cancer Institute, Lausanne, Switzerland and as staff scientist at the Nuclear Research Center, Karlsruhe, Germany and the Ludwig Institute for Cancer Research, Bern, Switzerland. Since 1988 she works at the Friedrich Miescher Institute, Basel, Switzerland. She is since 2003 titular professor at the University of Basel.

The Hynes laboratory has been studying molecular alterations in human breast cancer for more than 25 years. One of its most important achievements was to be one of the first groups to discover ERBB2 gene amplification and receptor overexpression in primary breast tumors (Berger et al 1989). Following on this, it produced monoclonal antibodies targeting ErbB2's ectodomain and used these to generate ErbB2 specific single-chain antibodies (scFv) and scFv-toxins that were recombinantly produced and shown to inhibit in vivo growth of ErbB2-overexpressing tumors (Wels et al 1992). It also developed a novel technique to study the roles of individual ErbB receptors by using scFvs to retain ErbB2 or EGFR in the endoplasmic reticulum. Using this technology it made a number of conclusions about ErbB2's role in the ErbB receptor family and in cancer: ErbB2 is the preferred partner for the other ligand-activated receptors (Graus-Porta et al 1997) and the ErbB2/ErbB3 heterodimer functions as a unit that controls proliferation of ErbB2-overexpressing breast cancer cells (Holbro et al 2003).

Recipient of the German Cancer Prize (2009) and the Swiss Cancer Prize (2003), the Swiss Nominee for the UNESCO-L'Oreal Prize for Women in Science (2000), the recipient of the Dora Seif Prize from the Kantonsspital Basel (1995) and the Swiss Cancer League Robert-Wenner-Prize (1989). I am a member of a number of review boards and panels, the most important are: Swiss National Research Foundation (2002-2005); Science Review Panel of the "Excellence Initiative" of the German Research Society, the panel that made the final decision on all the research programs that have been funded since 2006 with federal money (2006-current); Member of Breakthrough's Scientific Advisory Committee (London) since 2006 and chair from 2007-2010; Chair for the Physiology, Pathophysiology and Endocrinology Advanced Grants Review Panel of the European Research Council (2007-2013); Scientific Advisory Board member and board of Trustees member of the Max Delbrück Center for Molecular Medicine, Berlin, Germany (2011-2015); Komen Scholar Council Member, Susan G. Komen Race for the Cure (2010-2014).

**Professor Bob Löwenberg**

is Professor of Hematology at Erasmus University in Rotterdam, the Netherlands. Professor Löwenberg's research activities are in the treatment and the pathobiology of leukemia. He has extensively published in the area of developmental diagnostics and therapeutics in leading scientific journals.

For more than 20 years he has been on the editorial board of The New England Journal of Medicine, he currently serves as the Editor-in-Chief of the Blood Journal, the major scientific journal in hematology. He is one of the founders of the Dutch-Belgian HOVON Cooperative Group and is the chair of the HOVON leukemia trial group.

Bob Löwenberg has held various leading positions. He has been the scientific director of the Rotterdam Cancer Institute, department chair of hematology and chair of the division of oncology within Erasmus University Rotterdam. He is the founder and first president of the Dutch-Belgian Cooperative Group on Hemato-Oncology in Adults (HOVON Cooperative Group) and currently is the chair of the HOVON Leukemia trial group. Professor Löwenberg was one of the founders and has served as President of the European Haematology Association (EHA). He has also served as president of the International Society of Experimental Hematology and the International Society of Hematology. He is the Chairman of Scientific Advisory Board of the European School of Hematology (Paris, F).

Bob Löwenberg is an elected member of the Royal Academy of Sciences and Arts of The Netherlands and he has received various honors and awards.

# Appendix 2

## Program of the site visit

### Wednesday 19 February 2014

- 17.00 Internal meeting of the committee, preparation of the interviews
- 19.00 Dinner

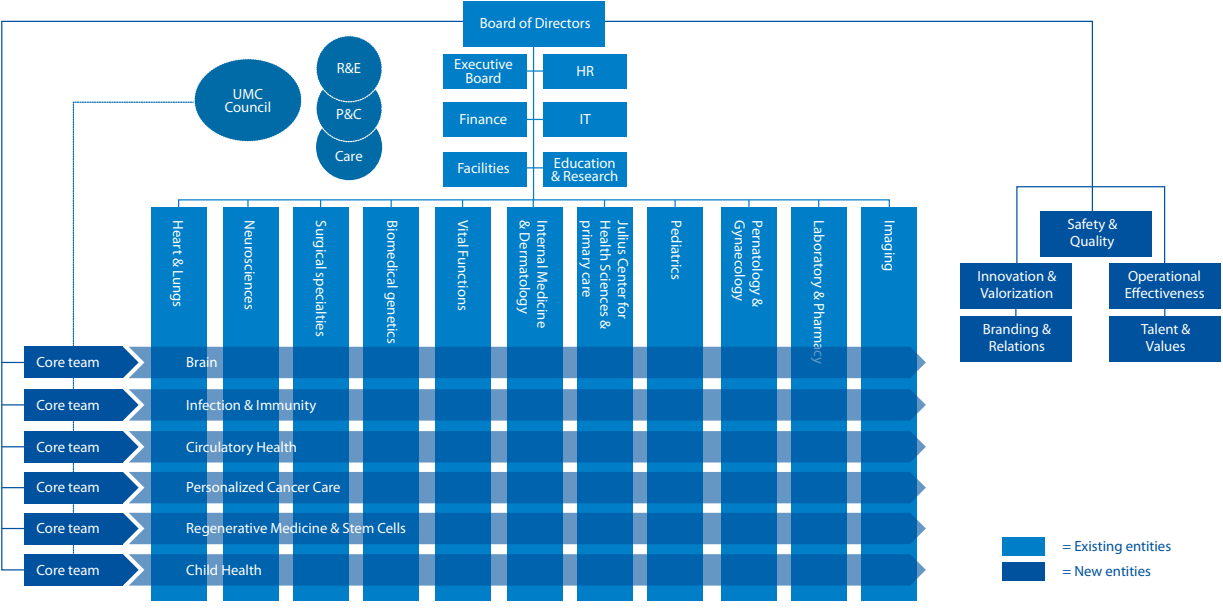
### Thursday 20 February 2014

- 09.00 Meeting with the UMC Utrecht Executive Board:  
prof. F. Miedema, M.H. van Velthuisen-Lormans, dr. S. W.H. van Weelden
- 10.00 Meeting with program chair and management Personalized Cancer Care:  
prof. I.B. Rinkes, prof. E. van de Wall, prof. H. Bos, prof. W.P.T. Mali, Prof. P. Siersema
- 11.00 Break
- 11.30 Meeting with PIs: Prof. G. Kops, prof. B. Burgering, dr. H. Snippert, dr. J. van Rhenen
- 13.00 Lunch
- 14.00 Meeting with PIs: prof. E. Cuppen, prof. P. van Diest, dr. M. Lam, dr. G. Valk
- 15.30 Break
- 16.00 Postsession with postdocs and PhD students
- 17.00 Internal discussion in the committee
- 19.00 Dinner

### Friday 21 February 2014

- 09.00 Meeting with Societal Stakeholders  
Patient-representatives: Nicole Plum, Carin Hoogstraten, Leo Kruik  
Dutch Cancer Foundation: Wia Timmerman  
Achmea: Rinke Geels  
Ipsen Farma: Bas van Hees  
AVL/NKI: Hans Schoo  
Language of the Tumor: Ragna Snef
- 10.30 Break
- 11.00 Preparation of advice
- 12.00 Lunch
- 13.00 Consulting hour
- 14.00 preparation of advice
- 15.00 Preliminary report

# Appendix 3





# Regenerative Medicine and Stem Cells



# Content Regenerative Medicine and Stem Cells

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# 1 Introduction

## 1.1 The Netherlands System of Quality Assessment of Research

This quality assessment of research is part of the assessment system for all public Dutch university research, as organised by the Universities and University Medical Centers (UMCs) in the Netherlands.

The aims of the assessment system are:

- Improvement of research quality based on an external peer review, including scientific and societal relevance of research, research policy and research management.
- Accountability to the board of the research organisation, and towards funding agencies, government and society at large.

Universities and UMCs in the Netherlands have agreed to carry out a self-evaluation every three years and an external review every six years. This process is guided by the Standard Evaluation Protocol (SEP). For this evaluation the SEP 2009-2015 is used.

The present external research evaluation has the following objectives:

- To assess the quality of the research and graduate PhD programs carried out at the UMC Utrecht during the period under review (2007-2012) compared to an international benchmark (not a comparison within UMC Utrecht);
- To identify research areas which have the potential to stimulate innovation and have societal impact;
- To identify excellent research groups and young researchers with high research potential;
- To identify research areas that are currently of the highest international standard, how these may be strengthened and suggest conditions for their continued development.
- To identify research areas that have the potential to develop towards the highest level of international research and to determine what is necessary to ensure such development.
- To identify research areas that are not internationally or nationally competitive and lack evident development potential.
- To identify research areas that are missing that could be considered to be essential for the UMC Utrecht.
- To identify the need for infrastructural support that would facilitate development towards greater excellence.

## 1.2 Research organisation UMC Utrecht.

The UMC Utrecht is organized in eleven divisions. All divisions operate in the areas of direct patient care, education and research. Divisions have their own budgets and policies, which are based on their specific categories of patients. The divisions are: Biomedical Genetics, Heart and Lung, Imaging, Internal Medicine and Dermatology, The Julius Center for Health Sciences and Primary Care, Laboratories and Pharmacy, Neurosciences, Paediatrics, Surgical Specialties, Vital Functions, Woman and Baby.

In 2010 a new strategy for the years 2010-2015 was launched, Strategy 3.0. In this Strategy 3.0 the UMC Utrecht put more emphasis on the connection between research and patient care aiming at innovation in patient care driven by identified clinical needs. Based on external developments and the strategic self-evaluation performed in 2009, it was decided to focus the UMC Utrecht core activities (patient care, research and education) on the following six strategic programs and their clinical syndromes (between parentheses):

- Brain (stroke, epilepsy, neuromuscular disorders, psychotic disorders, neurodevelopmental disorders);
- Infection & Immunity (opportunistic infections, immune deficiencies, chronic inflammation);
- Circulatory Health (atherosclerosis, heart failure, stroke);
- Personalized Cancer Care (breast cancer, gastro-intestinal cancer);
- Regenerative Medicine & Stem Cells (stem cell based therapies, cardiovascular and musculoskeletal tissues);
- Child Health (chronic inflammation, respiratory infections, orphan diseases/genetics RM, fertility interventions).



### **1.3 The Review Panel Regenerative Medicine**

The review panel for the Regenerative Medicine & Stem Cells program was appointed 22 November 2013 and consisted of:

- Professor Anthony Hollander, chair, University of Bristol;
- Professor Ruud Bank, University Medical Center Groningen;
- Professor Andrew Brack, Massachusetts General Hospital;
- Professor Stefan Janssens, Leuven University.

Dr. Barbara van Balen, (staff member of) QANU, was appointed secretary to the review panel.

A short curriculum vitae of each member is included in Appendix 1.

### **Independence**

All members of the Review panel signed a statement of independence to ensure that

- they would judge without bias, personal preference or personal interest, and
- their judgment is made without undue influence from the institute, the program or other stakeholders.

### **1.4 Data provided to the Review Panel**

The review panel has received a self-evaluation report provided by the UMC Utrecht. The panel also received the report on the Mid Term Review 2007-2009, the assessment report 2002-2006 and five key publications. Additionally, the review panel received a recently established book with an overview of the research done in the area of Regenerative Medicine in UMC Utrecht.

### **1.5 Procedures followed by the Panel**

The assessment was based on the documentation provided by the UMC Utrecht and the interviews during the site visit. The interviews took place on 6 and 7 March 2014. The program of the site visit is included in Appendix 2.

The panel members all read the Self Evaluation Report. The reviewers prepared questions for the interviews, which were exchanged prior to the meeting.

During the internal panel meeting on the evening of 5 March 2014, preceding the site visit, the questions and comments were discussed and decided upon. On the second day of the site visit, the panel discussed the results of the assessment thus far and the outline of the advice in the report. Afterwards a meeting with the representatives of the UMC Utrecht, the program leaders and interested researchers was arranged, in which the main impressions of the panel were reported.

A draft version of the report was written by the secretary and the chair and sent to the review panel members for comments. Their remarks and recommendations for improvement were incorporated in the next version.

### **1.6 Assessment Criteria**

The Protocol requires the Evaluation Review panel to assess the research on the four main criteria of the *Standard Evaluation Protocol*:

- Quality (the level of the research conducted)
- Productivity (relationship between input and output)
- Societal relevance (social, economic and cultural relevance of the research)
- Vitality and feasibility (flexibility, management and leadership)

# 2. Assessment of the Regenerative Medicine and Stem Cells Program

Program Leaders: Professor Wouter Dhert, MD, PhD (chair)

Professor Paul Coffey, PhD (Co-chair)

Academic staff in 2012: 64 fte (177 )

## 2.1 Mission, goals and research activities of the program

It is the ambition of the Regenerative Medicine and Stem Cells Program to establish a center through which:

1. novel regenerative /stem cells treatments for patients are developed;
2. high quality biomedical research is performed that attracts talented scientists;
3. future biomedical professionals receive state-of-the art education.

The program is centred around fundamental stem cell research, from which it is – supported by a broad range of enabling technologies – focused at three patient- centred themes: stem cell-based therapies, musculoskeletal tissue regeneration, and cardiovascular tissue regeneration. Several clinical problems with high societal relevance, such as heart failure, osteoarthritis or gut disease, are targeted. At the core of the program, increased understanding of the basic principles of stem cell biology is pursued in order to develop cellular therapy for a variety of human diseases. This includes strategies to recruit and utilize endogenous stem cells. In the translational steps towards the three patient-centred themes, overall research efforts will focus on the complexity and spatial organization of biological tissues and organs, as well as on the multifactorial approach of tissue re- and degeneration, which is an interplay of many catabolic and anabolic factors, growth factors, cells, biomaterials or physical stimuli.

## General remarks

The board of the UMC asked the review panel to evaluate the research strategy 2010-2015. In this strategy the UMC Utrecht puts more emphasis on the connection between research and patient care aiming for innovation in patient care driven by identified clinical needs. The strategy includes a matrix structure for the research programs (see appendix 3). Despite obvious potential difficulties, the structure appears to work well. Researchers involved were quite satisfied with the possibilities the structure of the research program offers them. For the review panel it remained unclear who is in the end responsible or making the final decisions. But the researchers themselves didn't report any difficulties. The panel sensed that all researchers are happy with the fact that there are no boundaries, and that there is an open communication with the different research communities. In their view, the integration of disciplines and diversity of expertise in one research program stimulates innovation and creativity.

## 2.2 Program Assessment

### Quality 4.5

The panel has seen examples of excellent science and excellent translational work. The program contains great examples of research from clinical/translational and fundamental scientists. The quality of research was also reflected in the poster session with PhD students and postdocs. The presentation of their research was excellent and the commitment and quality of the graduate students and post docs was obvious.

With regard to the three pillars (musculoskeletal, cardiovascular and stem cell therapies), the musculoskeletal part seems to be the most mature, both in terms of scientific topics and market pull. Cardiovascular seem to be more diverse, but certainly very good as well. The Stem cell therapies pillar seems to lack focus (a wide variety of pathologies /organ systems are addressed) – although there are excellent opportunities, especially because of the in-house cell production facilities that are operational under GMP.

The panel is very positive about the connected post graduate teaching program. This program appears to be excellent and well integrated with the research. There is also room for further expansion of this teaching activity and for further enhanced quality in an international context. We recommend an International Scientist invited speaker program to provide even greater breadth and depth to the teaching

The research program has a very clear link with the research in the Hubrecht Institute and the program benefits from this connection by the attraction of the Institute for top researchers. There seems to be good outcomes of joint appointments and for co-alignment of strategies and therefore evidence of good value for money from the €40M investment – but only time will tell.

The program also benefits from the alliance with Eindhoven (TU/e). There seem to be tangible collaborations from this – in particular the successful collaboration in the heart valve program could be used as a model to be rolled out to other domains of cardiac cell therapy/tissue engineering where this is not yet been exploited to the same extent

#### **Productivity 4.5**

The earning capacity of the research program RM seems to be impressive, as the UMC Utrecht has been able to obtain leading roles in prestigious programs such as BMM (Biomedical Materials Program), NIRM (Netherlands Institute of Regenerative Medicine) and TAS (Translational program of Adult Stem cells). Also, a good number of personal grants have been received (via the NWO scheme and via the ERC), as well as grants from private organizations. It is not clear whether the UMC Utrecht plays a leading role in several European FP7 consortia. There seems to be relatively little financial support from industry.

Although the output in terms of publications is considerably increasing, also (and especially) in the top 10% of journals, the panel was not able to get a good insight what UMC Utrecht topics are considered as world-leading or internationally as “making a difference”. Furthermore, although the number of Ph.D. theses in 2012 (30) has been doubled compared to 2011 (12), this is not reflected in the number of publications as 1st, 2nd and last author (198 in 2011; 208 in 2012), which is an interesting discrepancy.

#### **Relevance 5**

The societal reputation seems to be excellent. The panel also sensed that there is a good commitment of people along the entire pipeline from basic research to the clinic. There is a strong market pull, and many scientists consider this as positive, and not as a threat.

Despite the positive assessment of the societal relevance of the program, which is in the view of the panel beyond doubt and of world class, there remain some concerns that the panel wants to share:

Is the program pioneering enough with respect to First in Man trials? In the view of the panel innovation should not just focus on numbers, but also on new approaches – pull through from the basic science. Orthopedics is already highly innovative in this way but the other two themes need to match this. The panel advises to look for more innovative targets and cell types beyond the MSC era: LGR5 cells should particularly be exploited as a Utrecht discovery. The newly recruited expertise in MicroRNA should lead to First in Man trials with this technology.

Clinical awareness among health care professionals is well established in the Utrecht Mobility Clinic for the musculoskeletal theme. If planned well, this Clinic could serve as paradigm for similar initiative for cardiac patients. The program should focus on end-stage heart failure e.g. Such a strategy may be better than alignment with circulatory health which could potentially reduce visibility of the RM program.

First in Man does not necessarily need to involve ATMP in every application: the example of novel engineering technology in OA (hinged distraction device) is also relevant to society and patients as it may promote endogenous repair in affected joints. Similar applications in cardiac patients could also be envisioned

Early involvement of patients and companies in defining research programs is very important and could be facilitated by external agencies such as the Reumafonds and the Dutch Heart Foundation.

### **Vitality & Feasibility 3.5**

The research strategy of the UMC Utrecht board is very strong. It's objectives to focus on the translation of basic science results to the patient and to take clinical needs as a starting point for research and innovation is recognized by the researchers of the RM program. Robustness of the strategy however still can be improved. During the interviews it became clear that in practice the research done is not yet based on clinical needs. The panel did not hear many examples of research that took a clinical need as starting point. This should still develop and the researchers need incentives to be able to work that way.

The UMC Utrecht board should be transparent about the next steps from 2015 onwards. Can programs look forward to funding for collaboration and innovation? There should be a clear plan for sustainability and seed grants and collaborative grants for exciting initiatives that foster new unexplored arenas will be essential. Properly defining areas of unmet clinical need will be essential for driving this process. Retaining and promoting staff at all levels will need clear criteria for assessing translational as well as core academic activity.

There appears to be a lack of commitment to the long-term future of large animal laboratory and investments needed for its upgrade. This facility is a central part of most regenerative medicine translational programs and it is unclear how UMC Utrecht will be able effectively to get into the clinic without it. A similar remark can be made for the GMP cell production facility. During the site visit concerns were put forward over financial sustainability. Can the facility remain and does it need greater core funding from UMC Utrecht?

The removal of several basic scientists to the UMC Utrecht floors in the new Hubrecht Institute building is both an opportunity, for those who move into the new building and a threat, to clinical groups remaining in the Hospital building. The board should pay close attention to this.

# 3. Recommendations

## **Key Recommendations**

1. A plan for financial sustainability after 2015 is urgently needed and should be communicated to all staff within the RMSC spearhead
2. Establish a working group to develop much clearer criteria for promotion or for continuation of contracts at the end of a funding period. These criteria need to reflect the paradigm shift that has happened in the way science is done at UMC. Since the research program is driven by societal need, so assessment of research success should also measure impact of a PI's work on society (in the short and long term). This group could usefully involve external stakeholders such as the Dutch Heart Foundation and Reumafonds
3. Establish a working group to specifically look at the concern of clinical research groups that may be damaged by the move of staff into the new lab facility; strategic planning is vital as not all labs will be able/willing to move over
4. Upgrading and continuation of the large animal facility should be a priority, with specific attention for integrated large animal imaging facilities (MRI/SPECT/ or CT)

## **Additional recommendations**

5. Core facilities such as proteomics, genomics, and imaging should be made more easily available – it seems clear that these facilities exist but accessibility needs to be ensured even for junior staff that lacks the key contacts.
6. Expanding the successful educational program with involvement of invited guest faculty and high profile lecture series, targeted to the needs of PhD students.
7. Strengthen links with the Dutch Heart Foundation with the potential to build towards funded Chairs as is already the case with Reumafonds.
8. Strengthen links with industry partners and provide incentives for PIs to build sustainable relationships with particular companies.

# Appendix 1

## Curricula vitae of the Evaluation Review panel members

### **Professor Anthony Hollander**

BSc (First Class with Honours) in Pharmacology from The University of Bath, UK (1987);  
PhD in Pathology from The University of Bristol, UK (1990).

Professor of Rheumatology & Tissue Engineering at The University of Bristol, UK (2000 – 2014)  
Research Fellow at McGill University, Montreal, Canada (1990 – 1993);  
Research Fellow and Lecturer at The University of Sheffield, UK (1993 – 2000).

#### *Research area and main achievements:*

Over two decades of research experience in the fields of cartilage biology, osteoarthritis, stem cells and tissue engineering. In 2008, Professor Hollander and a team of scientists and surgeons successfully created and then transplanted the first tissue-engineered trachea (windpipe), using a patient's own stem cells. The bioengineered trachea immediately provided the patient with a normally functioning airway, thereby saving her life.

#### *Major Grants / Honorary Positions/ Prizes*

Elected as President of The International Cartilage Repair Society, 2012- 2013. He has been a member of grant review boards for the UK Medical Research Council, the California Institute for Regenerative Medicine and Arthritis Research UK. In 2013 he was made a Fellow of the Leadership Foundation. Received approximately £7 million of peer-reviewed funding over the past 10 years from The UK government, medical charities, the EU framework programmes and from biotechnology companies. Named inventor on several patents. Co-founder and Scientific Director of a University of Bristol spin-out company, Azellon Cell Therapeutics which is currently running a World's first clinical trial of a "Cell Bandage" for the treatment of torn knee cartilage.

### **Professor Ruud Bank (1960)**

received his Ph.D. in 1993 at the Vrije Universiteit (Amsterdam) for his work regarding the posttranslational modifications and genetics of the isozymes of human amylase and pepsinogen.

In 1993 he started as a research associate at TNO Quality of Life (Leiden), a non-profit contract research organization, where he investigated the role of the collagen network in connective tissue diseases (osteoarthritis, osteogenesis imperfecta, Bruck syndrome, osteoporosis, fibrosis).

In 2004 he became head of the Department Tissue Repair at TNO, and in 2006 he was appointed as a professor (0.2 fte) at the VU Medical Center (Amsterdam). In 2008 he became head of the Stem Cell & Tissue Engineering Research Group at the University Medical Center Groningen, and since 2009 he is a full professor in the field of Matrix Biology and Tissue Repair at the Rijksuniversiteit Groningen.

#### *Research area and main achievements*

He has focused his research on cell/matrix interactions, on collagen in connective tissues, on tissue engineering, on the foreign body reaction, and on cellular and molecular mechanisms involved in fibrosis.

#### *Major Grants / Honorary Positions/ Prizes*

In 1982 he was awarded with the first prize in the European Contest for Young Scientists and Inventors; because of that he was invited by the Royal Family of Sweden to visit the Nobel prize ceremonies of that year in Stockholm.

He co-founded in 2000 the Dutch Society for Matrix Biology, and is a board member of the Dutch Society for Tissue Engineering and Biomaterials. In 1996 he was a visiting scientist at the Technion (Haifa, Israel).

He was vice-president of the Dutch Program for Tissue Engineering (DPTE; 2004-2008), a 25 million euro national program, and is since 2009 the scientific co-director of the Netherlands Institute for Regenerative Medicine (NIRM), a 42 million euro national program. He is the first president (2012-2014) of the federation "Matrix Biology Europe".

### **Prof. Andrew Brack**

Associate Professor of Medicine, Harvard Medical School  
Harvard University Program in Biological and Biomedical Sciences

#### *Research Area*

In uninjured muscle, the rare satellite cells are in a functionally dormant, quiescent state. Upon an injury stimulus, these cells proliferate and their progeny will either differentiate to form new muscle fibers or undergo self renewal to replenish the stem cell pool.

We believe that the temporally coordinated cell fate decisions of the stem cell and its progeny are reliant on the communication between the local environment (the muscle stem cell niche) and the stem cell itself. We are using *cre/lox* gene recombination and genetic knock in technology to deconstruct the communication between the niche and the muscle stem cell to investigate the cell fate decision making process during regeneration. In the future we hope this will lead to strategies that improve stem cell based therapies targeting aging and muscle disease.

#### *Funding and awards*

2012-	NIH-NIAMS R01-AR061002
2011-	NIH-NIAMS R01-AR060868
2011-	Sanofi-Aventis
2011-	Muscular Dystrophy Association Research Award
2010-2012	Harvard Stem Cell Institute Seed Grant
2009-2012	Harvard Stem Cell Institute Junior Faculty Award
2009-2013	Ellison Medical Foundation Young Investigator Award

### **Prof. Stefan Janssens**

obtained his medical degree in 1984 from the University of Leuven, Belgium, *summa cum laude*, and finished his clinical cardiology fellowship at Gasthuisberg University Hospital, Leuven, Belgium. He subsequently obtained an international John E. Fogarty fellowship from the NIH (Bethesda, MD, USA) to continue his studies in cardiovascular medicine at Massachusetts General Hospital, Harvard University in Boston from 1989-1992.

He was appointed Professor of Medicine in 2002 at KU Leuven and Chairman of the Department of Cardiovascular Diseases in 2010.

#### *Top Publications*

Janssens S, Dubois C, Bogaert J, Theunissen K, Deroose C, Desmet W, Kalantzi M, Herbots L, Sinnaeve P, Dens J, Maertens J, Rademakers F, Dymarkowski S, Gheysens O, Van Cleemput J, Bormans G, Nuyts J, Belmans A, Mortelmans L, Boogaerts M, Van de Werf F. Autologous bone marrow-derived stem-cell transfer in patients with ST-segment elevation myocardial infarction: double-blind, randomized, controlled trial. *Lancet*. 2006 Jan 14; 367(9505):113-21.

With accompanying editorial: *Lancet*. 2006; 367: 87-88.

Liu X, Huang Y, Pokreisz P, Vermeersch P, Marsboom G, Swinnen M, Verbeken E, Santos J, Pellens M, Gillijns H, Van de Werf F, Bloch KD, and Janssens S. Nitric oxide inhalation improves microvascular flow and decreases infarction size after myocardial ischemia and reperfusion. *J Am Coll Cardiol* 2007; 50:808-17.(Imp Factor 12.5)

Vermeersch P, Buys E, Pokreisz P, Marsboom G, Ichinose F, Sips P, M Pellens M, Gillijns H, Swinnen M, Graveline A, Collen D, Dewerchin M, Brouckaert P, Bloch KD, Janssens S. Soluble Guanylate Cyclase  $\alpha 1$  Deficiency Selectively Inhibits the Pulmonary Vasodilator Response to NO and Increases the Pulmonary Vascular Remodeling Response to Chronic Hypoxia. *Circulation* 2007; 117; 936-43. (Imp Factor 14.5)

Marsboom G, Pokreisz P, Gheysens O, Vermeersch P, Gillijns H, Pellens M, Swinnen M, Liu X, Collen D, and Janssens S. Sustained Endothelial Progenitor Cell Dysfunction After Chronic Hypoxia-Induced Pulmonary Hypertension. *Stem Cells* 2008; 26:1017-26 (Imp Factor 8.3)

Dubois C, X. Liu, G. Marsboom, P. Pokreisz, H. Depelteau, W. Streb, L. Chaothawee, F. Maes, H. Gillijns, M. Pellens, T. Vandendriescche, M. Chuah, D. Collen, A. Belmans, Van de Werf F, Bogaert J, Janssens S. Differential effects of progenitor cell populations on left ventricular remodelling and myocardial neovascularization after myocardial infarction *J Am Coll Cardiol* 2010; 55:2232-2243. (IF 12.5)



# Appendix 2

## Program of the site visit

### Wednesday 5 March 2014

- 17.00 Internal meeting of the committee, preparation of the interviews
- 19.00 Dinner

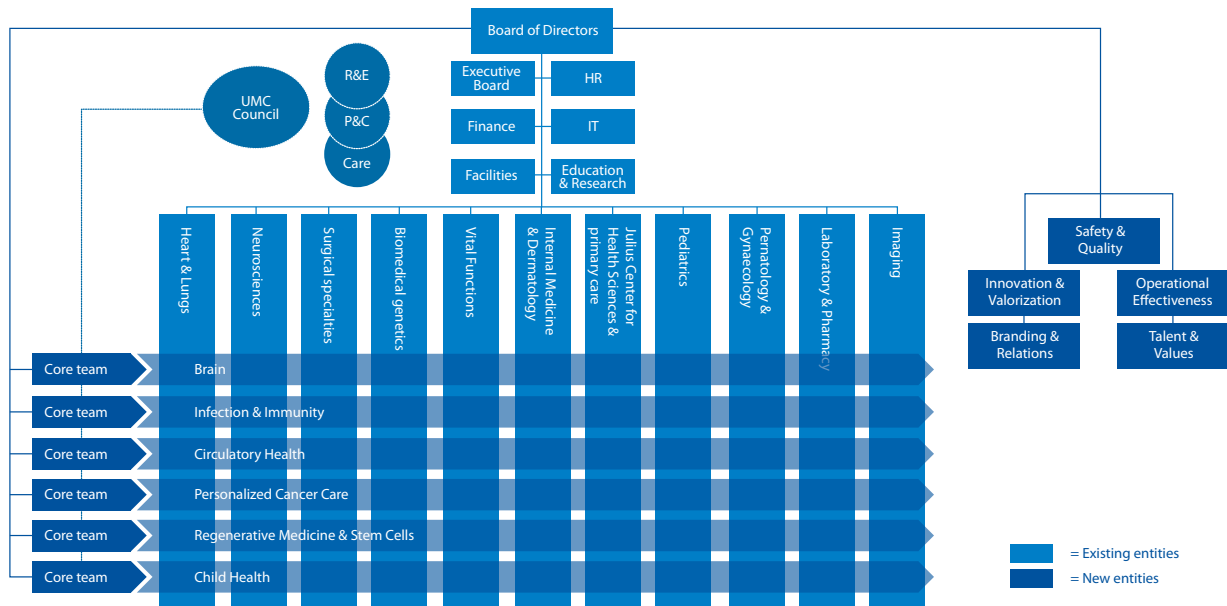
### Thursday 6 March 2014

- 09.00 Meeting with the UMC Utrecht Executive Board:  
prof.J.L.L. Kimpen, prof. F. Miedema, dr. S.W.H. van Weelden
- 10.00 Meeting with program chair and management  
prof. W. Dhert, prof. N. Geijsen, prof. M. Verhaar, S. Opitz.
- 11.00 Break
- 11.30 Meeting with PIs: dr. D. Gawlitta, dr. J.J.Boelens, dr. S.Mastbergen, dr. D. Saris, prof. H.Weinans,  
dr. I. Slaper-Cortenbach
- 12.30 Lunch
- 13.30 Meeting with PIs: dr. C.Robin, dr. C. Cheng, dr. J. Sluijter, dr. E. van Rooij, dr. K. Schepers.
- 15.30 Break
- 16.00 Poster session with postdocs and PhD students
- 17.00 Internal discussion in the committee
- 19.00 Dinner

### Friday 7 March 2014

- 09.00 Meeting with Societal Stakeholders  
drs.M.R. Abma-Schouten Dutch Heart Foundation, drs. I. Lether Dutch Rheumatology Foundation,  
dr. A. Dias DSM
- 10.30 Break
- 11.00 Consulting hour with the dean and the program director
- 12.00 Lunch
- 13.00 Preparation advice
- 15.00 Preliminary report

# Appendix 3



# Child Health



# Content Child Health

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# 1 Introduction

## 1.1 The Netherlands System of Quality Assessment of Research

This quality assessment of research is part of the assessment system for all public Dutch university research, as organised by the Universities and University Medical Centers (UMCs) in the Netherlands.

The aims of the assessment system are:

- Improvement of research quality based on an external peer review, including scientific and societal relevance of research, research policy and research management.
- Accountability to the board of the research organisation, and towards funding agencies, government and society at large.

Universities and UMCs in the Netherlands have agreed to carry out a self-evaluation every three years and an external review every six years. This process is guided by the Standard Evaluation Protocol (SEP). For this evaluation the SEP 2009-2015 is used.

The present external research evaluation has the following objectives:

- To assess the quality of the research and graduate PhD programs carried out at the UMC Utrecht during the period under review (2007-2012) compared to an international benchmark (not a comparison within UMC Utrecht);
- To identify research areas which have the potential to stimulate innovation and have societal impact;
- To identify excellent research groups and young researchers with high research potential;
- To identify research areas that are currently of the highest international standard, how these may be strengthened and suggest conditions for their continued development.
- To identify research areas that have the potential to develop towards the highest level of international research and to determine what is necessary to ensure such development.
- To identify research areas which are not internationally or nationally competitive and lack evident development potential.
- To identify research areas that are missing that could be considered to be essential for the UMC Utrecht.
- To identify the need for infrastructural support that would facilitate development towards greater excellence.

## 1.2 Research organisation UMC Utrecht

The UMC Utrecht is organized in eleven divisions. All divisions operate in the areas of direct patient care, education and research. Divisions have their own budgets and policies, which are based on their specific categories of patients. The divisions are: Biomedical Genetics, Heart and Lung, Imaging, Internal Medicine and Dermatology, The Julius Center for Health Sciences and Primary Care, Laboratories and Pharmacy, Neurosciences, Paediatrics, Surgical Specialties, Vital Functions, Woman and Baby.

In 2010 a new strategy for the years 2010-2015 was launched, Strategy 3.0. In this Strategy 3.0 the UMC Utrecht put more emphasis on the connection between research and patient care aiming at innovation in patient care driven by identified clinical needs. Based on external developments and the strategic self-evaluation performed in 2009, it was decided to focus the UMC Utrecht core activities (patient care, research and education) on the following six strategic programs and their clinical syndromes (between parentheses):

- Brain (stroke, epilepsy, neuromuscular disorders, psychotic disorders, neurodevelopmental disorders);
- Infection & Immunity (opportunistic infections, immune deficiencies, chronic inflammation);
- Circulatory Health (atherosclerosis, heart failure, stroke);
- Personalized Cancer Care (breast cancer, gastro-intestinal cancer);
- Regenerative Medicine & Stem Cells (stem cell based therapies, cardiovascular and musculoskeletal tissues);
- Child Health (chronic inflammation, respiratory infections, orphan diseases/genetics RM, fertility interventions).

### **1.3 The Review Panel Child Health**

The review panel for the Child Health program was appointed 22 November 2013 and consisted of:

- Professor Bert van der Heijden, chair, Erasmus Medical Centre, Rotterdam;
- Professor Paul Devroey, Devroeyconsulting, Aalst, Belgium;
- Professor Niels Hoiby, University of Copenhagen, Denmark;
- Professor Norman Rosenblum, University of Toronto, Canada;
- Professor Joris Vermeesch, University Hospital Leuven, Belgium.

Dr. Barbara van Balen, (staff member of) QANU, was appointed secretary to the review panel.

A short curriculum vitae of each member is included in Appendix 1.

### **Independence**

All members of the Review panel signed a statement of independence to ensure that

- they would judge without bias, personal preference or personal interest, and
- their judgment is made without undue influence from the institute, the program or other stakeholders.

### **1.4 Data provided to the Review Panel**

The review panel has received a self-evaluation report provided by the UMC Utrecht. The panel also received the report on the Mid Term Review 2007-2009, the assessment report 2002-2006 and four key publications.

### **1.5 Procedures followed by the Panel**

The assessment was based on the documentation provided by the UMC Utrecht and the interviews during the site visit. The interviews took place on 3 and 4 April 2014. The program of the site visit is included in Appendix 2.

The panel members all read the Self Evaluation Report. The reviewers prepared questions for the interviews, which were exchanged prior to the meeting.

During the internal panel meeting on the evening of 2 April 2014, preceding the site visit, the questions and comments were discussed and decided upon. On the second day of the site visit, the panel discussed the results of the assessment thus far and the outline of the advice in the report. Afterwards a meeting with the representatives of the UMC Utrecht, the program leaders and interested researchers was arranged, in which the main impressions of the panel were reported.

A draft version of the report was written by the secretary and the chair and sent to the review panel members for comments. Their remarks and recommendations for improvement were incorporated in the next version.

### **1.6 Assessment Criteria**

The Protocol requires the Evaluation Review panel to assess the research on the four main criteria of the *Standard Evaluation Protocol*:

- Quality (the level of the research conducted)
- Productivity (relationship between input and output)
- Societal relevance (social, economic and cultural relevance of the research)
- Vitality and feasibility (flexibility, management and leadership)

# 2 Assessment of the Child Health Program

Program Leaders: Professor Edward Nieuwenhuis, MD, PhD (chair)  
Professor Lieke Sanders, MD, PhD (Co-chair)  
Academic staff in 2012: 78 fte (276)

## 2.1 Mission, goals and research activities of the program

It is the ambition of the Child Health Program to link top referent care for pediatric patient groups and prevention of chronic disorders in children. The program covers the period from pre-conception, pregnancy and birth, to adulthood and focuses at specific patients groups:

- children with infrequent but severe diseases with lasting consequences (orphan diseases, chronic inflammation, Cystic Fibrosis and immunodeficiencies);
- children with highly prevalent diseases that have a high burden and high medical costs in childhood (e.g. respiratory infections like otitis media, pneumonia, RSV infections and asthma);
- children with potential risk of early development of chronic diseases in adolescence or adulthood (e.g. cardiovascular disease).

Instrumental in reaching the ambitions of the program is invested in young talented people by e.g. participating in training like Eureka and Tulips and targeted programs for stimulating female talents: the leading ladies program.

The program has four research themes:

### 1. chronic inflammation

Main goals of this research theme are to further enhance translational research by integrating basic laboratory research and clinical databases for specific targeted patient cohorts, incorporated and linked with PED & Biobank and to develop novel diagnostic and prognostic treatment algorithms based on immune biomarkers.

### 2. orphan diseases

This theme aims to identify genes causing rare diseases, to develop diagnostic and screening tests, to establish organoid culture systems for therapeutic usage and implement results in clinical care including somatic stem cell transplantation. Various inherited rare disorders like intestinal and liver failure are an important focus in this research line of regenerative medicine. The theme encompasses stem cell based organ cultures, the development of a biobank for intestinal and liver diseases, development of relevant animal models and gene mutation correction strategies.

### 3. fertility interventions

The goals of this research theme are to evaluate current and novel techniques of infertility treatment on (cost-) effectiveness and long-term safety for mothers and their offspring.

### 4. respiratory infections.

This research theme aims to unravel mechanisms that may trigger respiratory disease both in children with recurrent upper respiratory infections, as in patients with Cystic Fibrosis, and immunodeficiency with a focus on the respiratory microbiome. Current strategies are evaluated in order to optimize interventions in the first years of life for optimal cost-effectiveness and to avoid long-term adverse health effects like in respiratory syncytial virus infections in infants.

## General remarks

The board of the UMC Utrecht asked the review panel to evaluate the research strategy 2010-2015. In this strategy the UMC Utrecht puts more emphasis on the connection between research and patient care aiming for innovation in patient care driven by identified clinical needs. The strategy includes a matrix structure for the research programs (see appendix 3). The panel appreciates that the UMC Utrecht made important choices



in their research strategies. The effectiveness of the new organization still is to be evaluated. It is obvious that the Child Health program is happy that child health is chosen as a research area. Whether this program leads to more effective output in Child Health research needs to be evaluated. The panel appreciates the value attached to integration of basic research and patient care and the integration of the involved medical expertises. The panel agrees with the UMC Utrecht board and the program management that it is important that the pediatric department has a strong base in science and it can see that the new research organization facilitates this. Researchers within the Child Health program seem to appreciate the possibilities the research strategy provides. This positive evaluation is supported by the panel, but the program management needs to keep an open mind for flexibility to change priorities and to adjust easily and rapidly to the ever faster changing field. It should be clear what the process is of nurturing the development of new ideas. The panel recommends to reserve a certain amount of money to support new research lines. A risk of the UMC Utrecht strategy could be that it brings too much bureaucracy in defining research projects and finding money to finance research within the UMC Utrecht, which could easily lead to burn out.

Furthermore the infrastructure in the whole of the UMC Utrecht is important for the potential of the research programs. The panel has the impression that the infrastructure is fine, based on the information given in the interviews during the site visit. For a next assessment the panel would advise to give a more comprehensive overview of the facilities in the self-evaluation report.

The panel appreciates the talent programs. A risk could be that the talent programs are mainly recruiting from within the UMC Utrecht; this can hamper the dynamics international recruitment can bring. The effects of the talent programs still have to be evaluated. While the talent programs consist of important content and experiences and are very much appreciated by attendees, a more objective analysis of what did these programs add to the career of the participants should be undertaken. The panel understands that the leading ladies program is needed considering the actual proportion of women in the leading academic positions in the field. When more gender balance is achieved, this program should, however, be closed.

## **2.2 Program Assessment**

It is not easy for the panel to assess the program with the information and the data available. It would recommend the Board of the UMC Utrecht to consider to whom or to what they want to compare themselves. When they want to see improvement, concrete data about performance five years ago and now could be compared. And it would also be helpful when the panel could have compared the UMC Utrecht with other universities or medical centers. The panel is asked to rate the Child Health program as a whole. The panel, however, observed large differences between the four research themes and in its explanation will describe how it weighed the assessment of the themes to come to the rates for the program as a whole.

### **Quality 3**

The program leaders seem pretty happy with the structure of the programme. The program leaders indicate that it covers the most important parts of research in Child Health and that the research quality significantly improves. The program leaders suggest that they are more enabled now than before, that they are able to do more and do it better.

It was, however, difficult for the assessment panel to judge how the program is doing in the new situation in comparison to the old situation, since detailed quantitative data are missing to evaluate the progress of the different themes. Up to the present these data are still publications from the different groups, SCI indexes etc. The panel would advise the program to make an analysis of the output along the lines of the aims in the strategy, e.g. output in terms of diagnostic status, clinical trials and multidisciplinary collaborations.

As expected, the research groups that were performing strongly in the old situation remained strong. The panel supports the idea to split the group in researchers, clinicians and educators and to define the scope of the research from prenatal to adulthood.

The panel has seen examples of excellent science and excellent translational work. The program contains great examples of research from clinical/translational and fundamental scientists. The quality of research was also reflected in the poster session with PhD students and postdocs.

The quality of the research in the theme *Respiratory Infections* is very good, although it was a bit confusing that the panel did not get an overview of the whole group involved in this theme. The research in this group has a long tradition in the UMC Utrecht. The researchers are the better ones in this field. The research in the group is harnessed by the work done in the Hubrecht laboratory.

The researchers of the theme *Orphan Diseases* showed very nice work individually; as a theme it is less clear. The researchers working on the subjects gathered in this theme still have to carve their niche. The investigators individually did not seem to be leaders in the field, e.g. reverse genetics and exome sequencing in patients with unusual phenotypes is common practice nowadays.

The research done in the theme *chronic inflammation* is outstanding. The researchers are excellent, world leading and performing on an excellent level.

The theme *fertility interventions* is not yet integrated in the program. The research group has been performing in the past, had a good reputation but the panel did not see any recent research of importance. The theme is called fertility interventions, but the panel did not see any proof of interventions. There is no connection with the child health program and there is no research plan. The panel advises to either stop this theme or make major investments in attracting researchers. The connection with Child Health should become visible.

The Child Health program description in the Self-evaluation report (page 154) also mentions the pillar Public Health. During the site visit it became clear the kind of research this pillar is referring to can be described as 'follow up' research. The figure presented seems to be somewhat misleading and raises more questions than providing answers. The panel would advise to rethink the structure of the program and the position of public health within it.

#### **Productivity 4.5**

The program provided some figures concerning the output assigned to each of the four themes. In relation to the input of PIs in these themes the output is impressive. Considering the number of PIs involved the most productive group in the review period was the theme fertility interventions. Per fte input of PIs in the respective themes the average number of refereed articles in 2012 was:

chronic inflammation:	14
orphan diseases:	36
fertility interventions:	64
respiratory tract infections:	23

Even when we count the fte of non-tenured staff and PhD's as input the output in terms of refereed articles remains very high. The earning capacity of the themes is very good. In particular the chronic inflammation theme has an impressive list. The orphan diseases theme is very promising in this regard.

The number of PhD. theses, however, in 2012 (9 for the division and 16 for Child Health as a whole) is rather low considering the number of PhD students (106) according to table 2.1. The program however informed the panel that the number of PhD theses was higher in 2013 with 16 theses for the division and 27 for Child Health, which is more in line with the number of PhD's (106).

#### **Relevance 4.5**

The societal reputation of the research themes is very good to excellent. The panel also sensed that there is a good commitment of people along the entire pipeline from basic research to the clinic. Everyone is dedicated to translational work and integration of patients in the research. The relevance of the respiratory infections theme is outstanding, there are not many researchers in the world working on this theme, and the group has a really good connection with the stakeholders, patient groups and patient organizations. The orphan diseases theme is based on an obvious clinical need and clinical awareness is well established. The chronic inflammation group is outstanding on all four criteria.

The fertility theme has a tradition in reacting to societal needs, but as described it was not clear to the committee what the focus of recent research is.

### **Vitality & Feasibility 3**

The vitality of the research themes Respiratory Infections and Chronic Inflammation is excellent. Both groups are doing very well and have a bright future. The established leaders of the chronic inflammation group have to facilitate the upcoming new generation. The theme Orphan Diseases is a young theme that still has to be developed. The research theme needs to be more articulated, more visible. When the Child Health program management believes in this theme they have to empower it, with a dedicated second theme leader with a more clinical background. The theme has future, in the view of the panel, and could function as a bridge. Work needs to be done on this theme. The panel did not see the connection between the Fertility Interventions theme and the other research in the Child health program. Furthermore the group does not have a plan. Without major interventions this theme does not have a future within the Child Health program.

# 3 Recommendations

1. For future research assessments the Board of the UMC Utrecht should consider to whom or to what they want to compare themselves. When they want to see improvement, data about performance five years ago and now could be compared. And it would also be helpful when the panel could have compared the UMC Utrecht with other universities or medical centers.
2. It should be clear what the process is of nurturing the development of new ideas. The panel recommends to reserve a certain amount of money to support new research lines.
3. The effects of the talent programs still have to be evaluated. What did these programs add to the career of the participants? A more objective analysis of what did these programs add to the career of the participants should be undertaken.
4. The leading ladies program is seen as positive in the actual situation. When more gender balance is achieved, this program should, however, be closed.
5. The theme *fertility interventions* is not integrated in the program. The panel advises to either stop this theme or make major investments in attracting researchers.
6. The *Orphan Diseases* theme needs attention in order to grow into a real coherent research theme. Investments should be made. The theme needs also a dedicated clinician as prominent leader.
7. The pillar Public Health is limited to follow-up research. The panel advises to reconsider the position of public health within the program.

# Appendix 1

## Curricula vitae of the Evaluation Review panel members

**Prof. Paul Devroey** is a prominent Belgian researcher and professor specialized in human fertility. He worked more than 30 years in the university hospital of the Vrije Universiteit Brussel, where he directed the Center for Reproductive Medicine. Together with André Van Steirteghem and other colleagues from the Center he developed the Intracytoplasmic Sperm Injection (ICSI) technique, in which a single sperm is injected into an egg-cell. This technique is particularly useful in cases where infertility is caused by poor sperm production, thus solving most problems of male infertility. His center also pioneered various other techniques that increase the chances of successful in vitro fertilization, such as preimplantation genetic diagnosis. After his retirement from the VUB in September 2012 Professor Devroey joined the team of IVF centre Jan Palfijn Hospital in Ghent, where he focuses on the most challenging cases of infertility. Paul Devroey (co-)authored over 440 international peer reviewed articles, some of which have over 1000 citations, and three books. Over his career, he has received three national and four international research awards, including the IVI award 2007.

**Prof. Niels Høiby**, M.D., Dr. Med. Sci.R (Ridder af Dannebrog 1. grad) is chairman of the Department of Clinical Microbiology at Rigshospitalet (since 1981) and professor of Medical Microbiology, University of Copenhagen (since 1988).

Member of the medical advisory board of the Danish Cystic Fibrosis Association, 1979-present  
Co-founder and Chairman of the Scandinavian Society for Antimicrobial Chemotherapy, 1987-1990.  
Executive member of the medical/scientific advisory council, The International Cystic Fibrosis (Mucoviscidosis) Association, 1984-2002, Secretary 1996-2000, Vice-chairman 2000-02  
President for European Working Group (Society) for Cystic Fibrosis, 1987-1998  
Council member of the International Society of Chemotherapy, 1985-1988  
Member of the executive committee 1992-2001 & 2004-06 and Danish Council member of European Society for Clinical Microbiology & Infectious Diseases (ESCMID)  
Danish Representative, European Union of Medical Specialities (UEMS) 1991-98  
Secretary, Cystic Fibrosis Group, European Respiratory Society, 2004-07.

List of publications: 945, original papers (477), survey articles, books and proceedings concerning topics in clinical microbiology, immunology, taxonomy and cystic fibrosis. Oral presentations: 695 lectures at national and international scientific meetings, 484 of which were invited lectures in many countries. Posters: 485 presented at congresses.  
Bibliometry (Google Scholar): H-I (Hirsch Index): (2012) 66 Total citations: (2012) 15823  
i10-indeks: (2012) 280

Academic honours: Stipendium, Univ. Copenhagen 1968 for highest examination marks that year.  
The family Hede Nielsen foundation, research Award 1976.  
The Essex Award for Danish Clinical Microbiologists 1978.  
Visiting professor, University of Hannover Medical School 1989.  
Fellow of American Academy of Microbiology 1992  
The German President's wife, Mrs. Christiana Herzog's "Cystic Fibrosis Aid" research grant 1995  
Professor honoris causa, Guangxi Medical University, Nanning, China 1998  
Ridder af Dannebrogordenen 1999.  
The Richard C. Talamo Distinguished Clinical Achievement Award Cystic Fibrosis Foundation (USA) October 2005. The American Society of Microbiology International Member of the Year Award 2006 (first ward winner).  
The William Nielsen Foundation Award 2006. Visiting professor, Chinese PLA Postgraduate Medical School & Chinese PLA General Hospital, Beijing, China 2010.  
Professor honoris causa, West China School of Stomatology, Sichuan University, Chengdu, China 2011.

**Prof. Norman Rosenblum** is Professor of Paediatrics, Physiology, and Laboratory Medicine and Pathobiology at the University of Toronto, and a Paediatric Nephrologist and Senior Scientist in the Research Institute, the Hospital for Sick Children. He is the recipient of a Canada Research Chair in Developmental Nephrology. Dr. Rosenblum is a MD graduate of Dalhousie University. He completed a Pediatric residency and a fellowship in Pediatric Nephrology at the Children's Hospital, Boston followed by a postdoctoral fellowship in the laboratory of Bjorn Olsen in the Department of Anatomy and Cell Biology, Harvard Medical School. Dr. Rosenblum was recruited in 1993 as a clinician scientist to the Hospital for Sick Children and University of Toronto. Since then, the focus of his research has been to elucidate molecular mechanisms that control normal and malformed kidney and cerebellar development in genetic mouse models with a focus on signaling by bone morphogenetic, WNT and Hedgehog proteins. He has published over 90 peer-reviewed original manuscripts and book chapters and is the recipient of the 2011 Kidney Foundation of Canada Medal for Research Excellence.

Dr. Rosenblum is deeply engaged in developing and managing career development programs for clinician scientists. He founded and led the Canadian Child Health Clinician Scientist Program from 2001-2012. In his present role as Associate Dean, Physician Scientist Training in the Faculty of Medicine, University of Toronto, he is Director of both the MD/PhD and Clinician Investigator Programs. Dr. Rosenblum presently serves as President of the Canadian Society for Clinical Investigation and Chair of the Canadian Society of Nephrology Research Committee.

Dr. Rosenblum has developed strong collaborative relationships with colleagues at UMC Utrecht via the Training Upcoming Leaders in Pediatrics (TULIPS) Program, and the EUREKA Institute for Translational Medicine and in his work devoted to discovering molecular mechanisms that underlie congenital kidney-urinary tract malformation.

**Prof. Joris Vermeesch** Laboratory for cytogenetics and genome research UZ Leuven received his master in Bioengineering in 1988 University of Gent in 1988 and Ph.D. Chemistry and Biotechnology, University of Nebraska, USA (on de novo telomere biosynthesis) in 1993

1993-1999	FWO postdoctoral fellow at CME- Leuven
1999-2001	Group leader genomics in Aventis CropScience, Ghent, Belgium
2001-	Head Cytogenetics unit CME-UZ and part time full professor.

#### Research Domains

cytogenetics, genomics, genetics, single cell genomics, preimplantation, prenatal and postnatal genetic diagnosis

#### Memberships and affiliations

2008-2010 President-elect of the Belgian Society of Human Genetics  
Elected board member of International Standards on Array CGH Consortium (ISCA)  
(Founding) Member of the steering committee of the European Cytogenetics external Quality Control  
Board member of the International Society of prenatal Diagnosis  
Founder of a spin-off company Cartagenia ([www.cartagenia.com](http://www.cartagenia.com))  
Scientific board member of European Cytogenetics Association  
Scientific board member of European Society of Human Genetics 2012-2014  
Editorial board member of molecular cytogenetics

Scientific output: over 200 publications in peer reviewed journals and H-index 38.

# Appendix 2

## Program of the site visit

### Wednesday 2 April 2014

- 17.00 Internal meeting of the committee, preparation of the interviews
- 19.00 Dinner

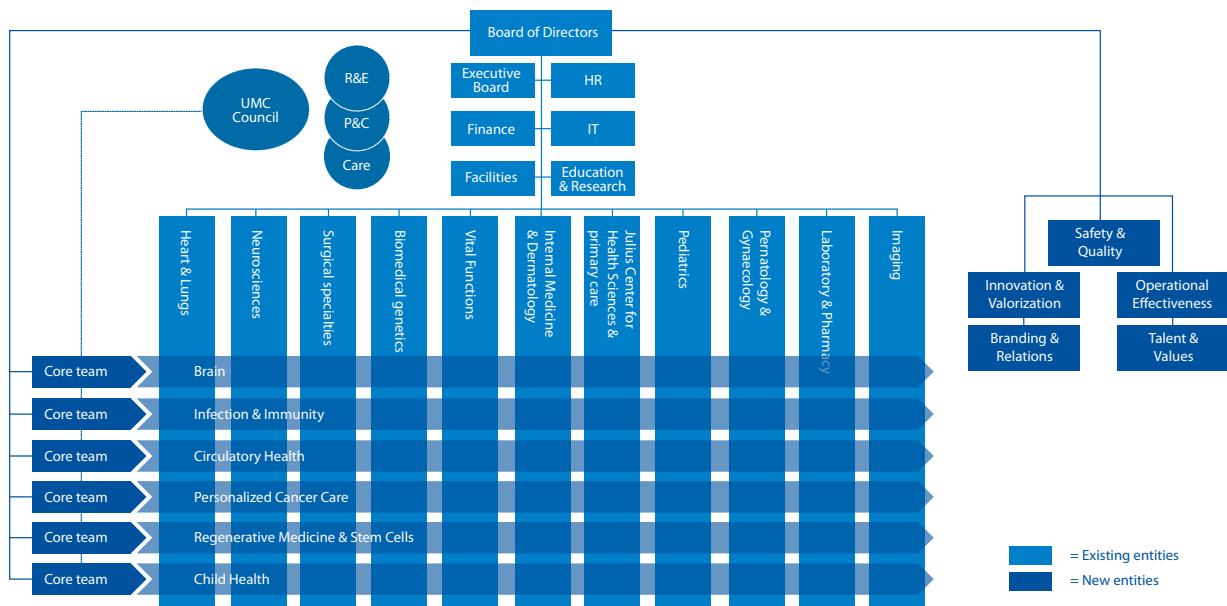
### Thursday 3 April 2014

- 09.00 Meeting with the UMC Utrecht Executive Board:  
prof.J.L.L. Kimpen, dr. S.W.H. van Weelden
- 10.00 Meeting with program chair and management Child Health program  
Prof. Edward Nieuwenhuis, Prof. Jet Smit, Prof. Edwin Cuppen, Prof. Kors van der Ent,  
Prof. Lieke Sanders, Prof. Frank Broekmans, Prof. Berent Prakken, Prof. Nico Wulfraat,  
Dr Roderick Houwen, Dr ir Petra Baarendse
- 11.00 Break
- 11.30 Meeting with PIs: Respiratory Tract Infections: Dr Jeffrey Beekman, Dr Louis Bont, Dr Debby Bogaert,  
Orphan diseases & RM: Dr Gijs van Haften, Dr Michal Mokry, Dr Peter van Hasselt,  
Prof. Edward Nieuwenhuis, Prof. Lieke Sanders
- 12.30 Lunch
- 13.30 Meeting with Principal Investigators:  
Chronic Inflammation: Dr Bas Vastert, Dr Jorg van Loosdregt  
Fertility Interventions: Prof. Frank Broekmans  
Prof. Edward Nieuwenhuis, Prof. Lieke Sanders, Dr Femke van Wijk, Sytze de Rook
- 15.00 Talent Programs Dr Sabine Fuchs (EUREKA, TULIPS, masterclass, leading ladies)
- 15.30 Break
- 16.00 Postsession with postdocs and PhD students
- 17.00 Internal discussion in the committee
- 17.30 Wilhelmina Children's Hospital walking tour
- 19.00 Dinner

### Friday 4 April 2014

- 09.00 Meeting with Societal Stakeholders  
Jacqueline Noordhoek (director CF Foundation)  
Michiel Korte (patient representative)  
Ingrid Lether (Arthritis Foundation)
- 10.30 Break
- 11.00 Consulting hour
- 12.00 Lunch
- 13.00 Preparation advice
- 15.00 Preliminary report

# Appendix 3



## Colofon

### Vormgeving

Multimedia, UMC Utrecht

### Uitgave

UMC Utrecht

juli 2014







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**Universiteit Utrecht**

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