Research Assessment 2011

Nijmegen Centre for Molecular Life Sciences
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1 Introduction

1.1 The Netherlands System of Quality Assessment of Research

This report presents the findings of the external evaluation committee that visited the Nijmegen Centre for Molecular Life Sciences in October 2011 to evaluate its research. This evaluation was commissioned by the executive board of the Radboud University Nijmegen.

This quality assessment is part of the assessment system for all publicly funded Dutch research, as organised by the Association of Universities in the Netherlands (VSNU), the Royal Netherlands Academy of Arts and Sciences (KNAW) and the Netherlands Organisation for Scientific Research (NWO).

The aims of the assessment system are:
• Improvement of research quality
• Accountability to the board of the research organisation, and towards funding agencies, government and society at large

The assessment takes place at the level of research institutes and research programmes within the institutes.

The site visit to each institute by an external committee, once every six years, is an essential part of the assessment system. A committee of peers is appointed and asked to review the research, including scientific and societal relevance of research, research policy and research management. Important elements of the site visit are the interviews which the evaluation committee conducts with the management (university board, faculty board) and the programme directors, as well as with PhD students, post docs and technicians.

Before the site visit, the research institute submits a self-evaluation report, containing a short outline of the mission of the institute, the objective of each of its research programmes, a description of the results that have been achieved in the programmes during the previous six years (including quantitative data about staff input, PhD’s, publications, financial resources), and developments anticipated in the context of the research profile of the faculty or institute.
1.2 The Evaluation Committee

The evaluation committee was appointed in April 2011 and consisted of:

- Prof. dr. H.C. Clevers (chair), Molecular Genetics, Hubrecht Institute, Utrecht, The Netherlands
- Prof. J. Chelly, Human Genetics, Institut Cochin – Hôpital Cochin, Paris, France
- Prof. dr. B.G. Davis, Chemistry, University of Oxford, United Kingdom
- Prof. dr. A.M. Göpferich, Pharmaceutical Technology, University of Regensburg, Germany
- Prof. dr. B. Nilius, emeritus, Molecular Cell Biology, KU Leuven, Belgium
- Prof. dr. R. Rizzuto, Biomedical Sciences, University of Padova and Neuroscience Institute of the National Research Council, Padova, Italy
- Prof. dr. E.J.H.J. Wiertz, Medical Microbiology/Experimental Virology, University Medical Centre Utrecht, The Netherlands

Mrs. Willy van Strien (science journalist, Leiden, The Netherlands) was appointed secretary to the evaluation committee.

A short curriculum vitae of each of the members is included in Appendix 2.

Independence

All members of the committee 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 programme or other stakeholders.

1.3 Scope of the Assessment

This assessment covers the period 2005-2010, and recent developments have been taken into account as much as possible.

The committee was asked to operate according to the Standard Evaluation Protocol 2009-2015 for Public Research Universities and all members received a hard copy of this document. The protocol specifies the information that must be provided to the committee and the criteria for the research assessment.

1.4 Data provided to the Committee

One month before the visit, the evaluation committee received the self-evaluation report 2005-2010 provided by the Nijmegen Centre for Molecular Life Sciences. It consists of a part A, concerning the institute as a whole, and a part B for documentation at the level
of the seven research programmes (themes). A cd-rom was added to the report with supplementary information and the six annual reports (2005-2010). During the visit, a few PhD theses were available, as well as the abstracts of the 17th NCMLS PhD Retreat where PhD presented posters and lectures, and abstracts from NCMLS symposia. The documentation included all the information required by the Protocol.

1.5 Procedures followed by the committee

The programme of the site visit to NCMLS, which took place on October 2-4 is included in Appendix 3.

The committee members all had read the self-evaluation report before the visit. During the internal meeting in the evening of 02-10-2011 – and after meeting with the scientific director and scientific manager of NCMLS – the committee prepared the site visit by discussing procedural matters and aspects of the assessment as prescribed by the SEP, and deciding upon a number of comments and questions to be addressed during the visit.

At the start of the visit, the committee was welcomed by the theme leaders, and there was a welcome speech by the Rector Magnificus of the Radboud University, prof. mr. S.C.J.J. Kortmann. The scientific director prof. dr. R.J.M. Bindels shortly introduced the NCMLS.

The committee assessed the seven themes of NCMLS. Presentations by theme leaders and theme members, interviews with these scientists and discussions were organised in parallel sessions. In each of these sessions, one of the committee members took the lead in the interview and the discussion. Right after each session the attending committee members discussed the findings, assessed the rates and one of them (the one leading the discussion) was responsible for writing down the preliminary scores and findings. To guarantee consistency, finally all seven theme assessments were discussed by the whole commission, and the final assessments were agreed upon.

In order to assess the whole institute, the committee interviewed the Dean of the Faculty of Science and the Dean of the Faculty of Medical Sciences; talked with a selected group of 6 PhD students; interviewed the PhD committee; and in parallel sessions interviewed 3 technicians and 6 post docs. At the request of the committee, interviews with the head of the genomics facility, the head of the central animal facility and the head of the microscope imaging platform were added to the programme.
After the interviews, the committee discussed the findings and prepared the report. At the end of the visit, the chair of the committee reported the main findings to the Rector Magnificus, both Deans, the scientific director and scientific manager of NCMLS, the theme leaders and other affiliates of NCMLS during a plenary meeting.

Within two weeks after the visit, a draft version of this report was sent to the NCMLS and to the Dean of the faculties of Science and Medicine for factual corrections. Subsequently, the report was submitted to the Executive Board of the Radboud University on November 8.

1.6 Aspects and Assessment Scale
The Protocol requires the Evaluation Committee to assess the research on 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)

The ratings used are on a five-point scale that 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 Nijmegen Centre for Molecular Life Sciences

Nijmegen Centre for Molecular Life Sciences
Director of the institute: Prof. dr. R.J.M. Bindels
Research staff in 2010: 57 chairs; 404 fte; (including support staff: 521)

2.1 Institute, mission, goals

The Nijmegen Centre for Molecular Life Sciences (NCMLS) was formerly known as the Institute of Cellular Signalling, which was established in 1994. It is part of the Faculty of Medical Sciences (RUNMC) and of the Faculty of Science (FNWI) of Radboud University Nijmegen. The previous external evaluation of NCMLS’s research was performed in 2004.

Mission:
NCMLS seeks to achieve greater insights into the complexity of living cells and organisms in order to obtain comprehensive knowledge of both normal and pathological processes. The NCMLS will pursue its goals in the interests of curiosity-driven research and education. The MCMLS aims to advance innovation in translational research, based on integrating diverse areas of scientific expertise within the molecular and medical sciences.

Goals:
• To generate basic knowledge in the molecular medical science and to translate this knowledge into clinical applications, into the development of diagnostics and into the treatment of patients through translational research programs.
• To create a challenging yet enriching learning environment where researchers of all levels are exposed to societal-relevant multidisciplinary research questions along the theme of understanding the molecular basis of disease.

Research topics are clustered in seven themes.

Within RUNMC, NCMLS was the first institute to implement a Principal Investigator (PI) model: group leaders are evaluated every three years according to internationally competitive quantitative and qualitative criteria and rewarded accordingly with extra research money. NCMLS comprises 105 group leaders, of which 51 meet PI criteria and 15 meet junior PI criteria. The Faculty of Science also applies a funding system based on performance.
More information on the institute and its activities can be found in appendix 1 of this report, and on the institute’s website: www.ncmls.eu

2.2 Quality

2.2.1 Leadership

The NCMLS building is a major asset of the institute. The governance system is complicated because the institute has no budgetary independency from the two partners, the RUNMC and the Faculty of Science. This could easily hamper its ability to define and execute its own strategies. Nevertheless, the committee concludes that, given these constraints, the institute has developed a successful combination of strategic measures and decisions to pursue its mission and goals. This appears the result of continued efforts towards consensus building between Science Faculty, RUNMC and NCMLS. As far as it stands, the consensus based management of the institute has made an excellent impression on the committee.

The introduction of a merit-based funding system (an experimental ‘Anglosaxon-type’ Principal Investigators system by RUNMC, RUNMC fellows, a peer-reviewed PhD student project system, flow of external research funds to where it was generated) should be considered unique in The Netherlands. It is now introduced throughout the RUNMC and has become part of the scientific internal culture. This will increasingly become an asset of the organization.

Emphasis on further developing the facilities, high-level courses and lecture series (such as the ‘New Frontiers’ symposia and a new lecture series that will start in 2012), combined group meetings, career planning and other activities for young scientists at the PhD and post doc level create a dynamic and ambitious environment.

2.2.2 Academic reputation

Quality and productivity over the entire range are high. The institute is generally regarded to perform research and education beyond an internationally competitive level. There has been broad improvement throughout the institute, since the previous external review. The institute has clearly matured. This is for instance reflected by a steady stream of high-level publications, national and international (EU) grants and prizes, nominations for membership in several international academies (e.g. Academia Europea) and a significant increase in foreign PhD students and post docs.
2.2.3 Organisation
An impressive amount of collaborative translational projects are being run between the NCMLS and the RUNMC. Ties with clinical groups and activities within the RUNMC are very close. Relevant scientists/clinicians within the RUNMC are made visible within the NCMLS as affiliated PIs. Clinicians and clinician/scientists have excellent access to the scientific and technological expertise and facilities of the NCMLS. Still, the committee fears that there is as yet some lack of appreciation for the needs of the clinicians.

One important caveat: The NCMLS is one of six RUNMC institutes. Many RUNMC researchers participate in more than one institute within RUNMC or the Faculty of Science (Institute for Molecules & Materials, Donders Centre for Neuroscience), which creates a situation that is less than transparent. Additional note: internally in RUNMC and also in Radboud University, the NCMLS is not perceived as receiving the emphasis it deserves. Individual loyalties, including those of technicians, are primarily with the department (RUNMC has 51 departments), and currently have to be shared between different institutes. The NCMLS has the potential to be uniquely effective in translation.

2.2.4 Resources
Despite the fact that NCMLS has no direct control over finances and personnel, the institute (as one of 6 within the RUNMC) still has a significant influence on the financial and human resource strategy of both academic partners. Generally, the groups appear funded to a sufficient level, and the core research facilities – which are diverse, state-of-the-art, easy accessible and of sufficient capacity – contribute to a competitive and attractive research environment and are in internal binding factor.

2.2.5 PhD training and supervision
The committee has informally met with groups of PhD students and post docs as well as with the PhD committee. The committee has not specifically evaluated the graduate school, yet has made several significant observations.

It is a strong point that the institute entirely coincides with the graduate school and is internally viewed as one-and-the-same organization, although some students are unclear as to their ‘loyalties’ (which institute, etc). The PhD students were generally content with facilities, supervision, courses etc. The committee agrees with this view. The institute appoints for each student a mentor outside his group to which he/she can turn to in case of any problem. The committee suggests that the institute should consider additional means by which students can find support in case their projects run into problems of any kind, for instance a 2-3 person PhD committee.
An increasing number of young foreign scientists are attracted to the NCMLS to work as PhD student or post doc. The committee considers this to be the result of the quality of the training provided and the general resources available. The committee notes that most PhD students take 5-6 years to obtain their PhD, for instance because they are already involved in their next job. In many cases, the thesis has been written quite some time before it is formally defended. The committee strongly recommends that the institute develops a proactive strategy to reduce the period to the 4 years that are formally allocated for a PhD project.

The post docs were generally content with the working environment, supervision and support. As a negative point, they mentioned that there were no clear career perspectives within the institute. Specifically, there is no formal tenure track structure for internal excellent post docs, which might lead to unwanted loss of talent.

2.3 Productivity
Overall productivity is high. There is a good mix of volume and quality. The committee appreciates that, consistently, publications in low-tier journals are avoided. The merit-based funding strategy that has now been broadly implemented as well as the emphasis on generating funding from competitive outside sources is a strong driver of production and quality improvement.

2.4 Societal relevance
Societal relevance is guaranteed. Health and diseases are central issues in any society. The mission of the institute is to expand insights into the processes that govern health and disease, and to cover biomedical research from bench to bedside indicating a strong translational character. Thus, the institute directly contributes to the improvement of health and well being of our society.

There are many opportunities for the valorization of discoveries, and NCMLS is keen to take these opportunities. A significant number of spin offs has been set up and several patents have been filed.

2.5 Vitality and feasibility
It is not possible for the institute to define and pursue strategies independently of the two ‘mother’- academic partners, the Faculty of Science and RUNMC. The current strategy appears successful for the time being, but it may for instance be difficult for NCMLS to develop strategies concerning international recruitment of PhD students, post docs and senior researchers; incorporation of ‘missing’ technologies (e.g. X ray crystallography,
advanced transgenic models); and targeted recruitment in specific disciplines (e.g. stem cell biology). To safeguard the institute’s performance in the future it is necessary that the two partners keep up the current financial and organizational support. The committee views this as a somewhat fragile situation.

As a positive note, the aspiration to build a second NCMLS tower which will alleviate some of the space constraints and will allow influx of a number of more clinically oriented groups is seen as an important step towards continued robustness.

2.6 Conclusions and recommendations for the institute

2.6.1 SWOT-analysis

Internal analysis

Strengths:
• A robust graduate school and an international body of PhD students and post docs.
• A nationally unique, merit-based research funding strategy.
• Several Principal Investigators and research groups are world leading.
• The access to clinical materials and patient populations. The willingness to integrate basic and clinical science.
• All facilities are of high quality, cover many of the essential technologies and are easily accessible.
• Very good animal facilities, including a unique malaria facility.

Weaknesses:
• NCMLS does not control its strategy and policy decisions, since financial and personnel management rests with the two academic partners.
• Differences between researchers employed by the Faculty of Science or the RUNMC in terms of e.g. tenure track rules and financial support.
• The rules of the PI system may sometimes be too rigid for individual researchers, for instance external post docs or young clinicians. In particular, this regards the rules that one has to have had at least one successful PhD student (not obvious directly after a post doc) or a considerable amount of external research funding (not obvious for a young clinician).
• Many research groups reside in more than one institute.
• Lack of a career perspective for internal post docs, i.e in the form of a formal tenure track system.
• Lack of an overall strategic organization and vision for platforms and facilities.
External analysis

Opportunities:
• UMC fellowship program as the means of developing an international junior investigator system, i.e. proper ‘tenure track’ with good financial support.
• Development of a second NCMLS building including an incubator function for spin-offs.

Threats:
• Changes in national funding strategies will directly affect strategies of the two participating faculties. This will immediately affect the structure and functioning of the NCMLS. The NCMLS needs a longer-term perspective and the possibility to execute its own measures if it is to grow and develop.
• Ever-increasing regulatory demands on animal and human experimentation.

2.6.2 General conclusions

Quality and productivity over the entire range are high. The NCMLS is generally regarded to perform research and education at and beyond an internationally competitive level. There has been broad improvement throughout the institute since the previous external review. The institute has clearly matured. For some groups, the incorporation of Structural Biology would be beneficial.

The institute has been able to make some strong recruitments and to attract an impressive amount of outside money. The scientific output of the institute is very good both in terms of numbers and impact of papers. Scientific highlights are visible over almost the entire breadth of the institute. No obvious weaknesses were encountered by the committee at the theme level.

There has been a strong emphasis on introducing a merit-based governance structure (Principal Investigators system, RUNMC fellows, peer-reviewed PhD student system, and flow of external research funds to where it is generated). This should be considered a novelty, and an example, for the funding structure of Dutch biomedical science.

The previous committee had concluded that the institute lacked the (inter)national visibility that it aspired. The current committee concludes that efforts towards enhancing visibility have been paying off significantly. Important factors have been a very successful, internationally oriented graduate school, an attractive seminar/symposia series, and the consistent and collective effort to do the best science. Yet, there is still more to do.
2.6.3 Recommendations
A first remark: for the next evaluation, the committee strongly recommends that individual groups are evaluated rather than themes.

PI system
Rules make the PI-system transparent but are sometimes perceived as too rigid. For instance, successful foreign post docs or young clinicians do not easily meet the junior-PI criteria. Advice: introduce a formal way of being more flexible, possibly by an appeals-committee.
The Faculty of Science does not offer a comparable system, which may affect the social fabric of the institute and will threaten key themes that are heavy in the Faculty (e.g. Chemical Biology).

Recruitment
• Young external PIs don’t fit in the PI system (regarding the requirement of having supported at least one successful PhD trajectory).
• There is no formal tenure track system for excellent internal post docs.
• There is no formal institutional strategic vision on recruitment (Who to recruit? How to recruit? At what level?). This appears related to the complicated governance.

On all three issues, the committee strongly recommends to make the appropriate changes.

Institute structure of the RUNMC
The committee strongly recommends that individual groups belong to a single institute. When also the number of institutes can be reduced, this may have several positive effects. The bureaucratic workload will be severely reduced. Basic and clinical science will be brought together. A note: internally, the NCMLS is not perceived as receiving the emphasis it deserves. Individual loyalties are primarily with the department, and currently have to be shared between different institutes, sometimes also for the students.

Facilities
Technological facilities are essential to the functioning of the NCMLS as an integrated institute. While some facilities (e.g. the Genome Analysis facility at Human Genetics) are robustly anchored in a diagnostics activity, others are entirely utilized for research. These latter facilities typically have been formed, because of the heavy and continued investment required, the use by multiple groups, and the requirement of trained personnel. Examples are the Microscope Imaging Centre, the proteomics and the animal facilities.
The committee feels that a general strategy on facilities is somewhat lacking and has largely taken the form of a financial strategy. The committee fears that a uniform financial policy towards these facilities (i.e. 50% central funding, 50% funding from users) will prohibit access for many groups to essential (and cutting edge) research tools. The committee recommends that a strategy is developed that goes beyond a financial model, and takes into account that individual facilities may be expensive, yet are essential and therefore may require additional central investment. There is a danger that key facilities will collapse under current plans (e.g. Microscope Imaging Centre).

The committee suggests investigating the necessity of a high-throughput screening facility. This may integrate theme 7 better with the other themes.

Bureaucracy around animal and human experimentation is ever increasing. The committee asks for continued attention to assist researchers in this, for instance by streamlining procedures as much as allowed. One example: for animal experiments, the approved DEC protocol should have the format that experimentation can start directly after approval. Now, there often is a second round of review of the work protocol by the animal facility.

**Space**

The committee is impressed by the systematic, yearly reallocation of space within the NCMLS building. Space appears to be limiting. It is clearly attractive to aim for a second building, which will alleviate some of the space constraints but will also bring multiple clinical groups physically closer to the basic groups in the NCMLS. In addition, it will create space for a biotech incubator, an asset in the current national science-policy climate.

**Translational research**

There is a paucity of clinicians within the core of the NCMLS. The committee recommends formalizing the involvement of clinicians, for instance by bringing in senior clinical researchers as Theme leaders, but also by finding a way of formalizing the involvement of young clinicians in translational activities of the NCMLS. Reducing the number of RUNMC institutes will clearly assist in this endeavour.

**Finally,**

The committee notes that ‘wet’ structural biology appears absent yet could have a great impact on many of the research themes.
The committee advises developing strategies to integrate theme 7 (Chemical and Physical Biology), a strong asset of Nijmegen, actively with the other themes. One should take advantage of the strong talent in this theme to address biological questions.
3 Assessments per programme

The Committee has carried out an assessment at the level of the programmes (or themes), as defined by the Nijmegen Centre for Molecular Life Sciences. Comments that are applicable to all programmes have been made in chapter 2 (Assessment of the Institute) and are not repeated below.

The research staff in fte includes tenured staff, non-tenured staff and PhD students; in brackets the research staff including support staff (technicians, secretaries) is given.
3.1 Infection & Immunity

Programme: Infection & Immunity
Programme director: Dr. F.J.M. van Kuppeveld
Research staff in 2010: 71 fte (90 fte)
Assessment:
- Quality : 4-5
- Productivity : 5
- Societal Relevance : 5
- Vitality and feasibility : 4-5

Objectives and research activities
Mission: to elucidate molecular mechanisms of infections, (auto)inflammatory and autoimmune diseases, and to develop innovative tools for diagnostics, treatment, and prevention.

Research on molecular mechanisms of infections investigates the role of the innate immune system in pathogen recognition and host defense against fungi, bacteria, parasites and viruses, with special interest in host-pathogen interactions, drug and vaccine development, and vector biology.

The second major research area focuses on inflammatory diseases and aims to identify disease mechanisms encompassing both adaptive and innate immunity. It includes modifier genes and posttranslational modifications involved in diseases such as rheumatoid arthritis, systemic sclerosis, gouty arthritis, psoriatic arthritis, psoriasis, diabetes, SLE and hyper IgD syndrome.

Quality
In many fields breakthroughs have been achieved, resulting in high-impact publications in leading journals including NEJM, Science, the Nature journals, The Lancet, and Cell. In 2010, about 50% of the papers were published in the top 10% of journals.

The committee recognizes that the theme harbors a significant number of truly eminent investigators. The ratings of very good-excellent are overall scores for the entire theme. During the past years, national and international visibility of the members of theme 1 has increased considerably; this is reflected by the award of various prizes to members of the theme, the participation in and coordination of several large EU PF7 consortia, elected memberships of national and international forums, invitations as keynote speakers at prestigious meetings, and so on.
The committee unanimously recognizes the enthusiasm of the investigators for basic and clinical science and is impressed by their ambition to perform cutting edge research, in addition to their shared interest in the development of novel technology, drugs, vaccines and treatments against infectious agents and (auto)inflammatory diseases.

**Productivity**
During the period that is under review, the research groups participating in this theme have been extremely productive, not only scientifically, but also in terms of grant acquisition and recruitment of new Faculty members.

A significant proportion (nearly 70%) of the research funding originates from extramural sources, including the prestigious Veni, Vidi, Vici and ESF grants.

**Societal relevance**
Societal relevance is enormous, as much of the research of theme 1 focuses on diseases with a high societal burden; for several of those diseases important breakthroughs have been achieved, not only resulting in high-level publications, but also in novel technologies, new perspectives for drug- and vaccine development, and new treatments against infectious and inflammatory diseases.

**Vitality and feasibility**
The members of theme 1 have a very strong vision for the future. They share a commitment and devotion to high quality science.

The vitality and versatility of the theme is illustrated by the establishment of a new research line focusing on Dengue, a disease for which two fifths of the world population is at risk. This new initiative synergizes strongly with existing research lines on infectious diseases, including other mosquito born diseases, and the in-house expertise on adaptive and innate immunity.

Likewise, the construction of an entirely new facility for malaria research in humans is impressive.

**Recommendations**
Despite the large variety of research projects, there is strong coherence and synergy between the participating groups. This is quite remarkable in view of their location at various sites. The latter is a matter of concern to the committee. Relocation of groups
currently located outside the NCMLS building to a new, second research building to be placed adjacent to the current NCMLS building and the academic hospital will be a major improvement, further stimulating synergy at NCMLS.

The strong collaboration between basic and clinical disciplines has been extremely rewarding and has resulted in high-quality translational research. This strong integration should be maintained in the future.

The participation of theme members in multiple research institutes is a matter of concern. The committee recommends a critical re-evaluation of this concept; some of the themes may be combined, thus promoting efficiency and reducing the burden of laborious paperwork.

Another issue that deserves attention is the amount of paperwork involved in animal experiments. It seems that the application procedure is duplicated by the request for working protocols at the time the actual experiments are initiated.

The principal investigators of theme 1 all belong to the RUNMC, but the collaborations with colleagues of FNWI are greatly appreciated; collaboration is strongly promoted by their joint presence in the NCMLS. This integration deserves continuous attention at all levels of the NCMLS.
### 3.2 Immune Regulation

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<th>Programme:</th>
<th>Immune Regulation</th>
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<tr>
<td>Programme director:</td>
<td>Prof. dr. G.J. Adema</td>
</tr>
<tr>
<td>Research staff in 2010:</td>
<td>66 fte (97 fte)</td>
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<tr>
<td>Assessment:</td>
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<td>Quality</td>
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<td>Vitality and feasibility</td>
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#### Objectives and research activities

**Mission:** to increase the understanding of the molecules and regulatory circuits active in immune cells in health and disease; to translate fundamental findings to the benefit of patients suffering from cancer and immune related disorders through preclinical models and experimental immunotherapy in patients.

#### Quality

This theme brings together basic and clinical immunological/hematological research in four important fields:

- molecular/functional analysis of normal and malignant blood development and immune control
- immunotherapy of cancer with a strong focus on (Dendritic Cell-) vaccine development and clinical application
- imaging of (invasive) cancer behavior in rodent models
- immune modulation and monitoring in kidney transplantation

The impact of journals in which the papers have appeared is consistently robust and is stable over time. A good sign is that – again consistently – publications in low-tier journals are avoided and around 50% of the papers appear in top-10 journals. While top papers have appeared in Nature sister journals, no publications in the top-3 journals are reported. Of note, Carl Figdor has won the prestigious Spinoza award. In all, the theme is considered by the committee to deliver high-level science.

#### Productivity

The theme consists of 16 PI’s, 35 post docs and 37 PhD students. The total research staff of the theme has modestly grown from 131 to 142 individuals over the last 6 years. Production in terms of numbers of papers has increased over the evaluation period from 80 to 110 per year, with a peak in 2009: a most impressive amount. Until now, the group
failed to produce in top journals, but this is improving. Every year, 6-8 PhD students graduate. The theme is very successful in raising external research money from a wide diversity of (prestigious) sources. Several clinical studies have been initiated. The theme should be considered highly productive.

**Societal relevance**
The theme makes a very successful effort to cover the entire research track from bench to bedside and back. This is done for cancer vaccination, for hematological analyses and for organ transplantation. Several DC- and NK- cell based vaccination protocols have started. The careful characterization of molecular aberrations in hematological malignancies contributes to improved patient care in hematology.

**Vitality and feasibility**
Since the last evaluation, the theme has further matured and shows many signs of strong synergy between labs. Presented highlights that underscore the synergy between the individual groups are for instance 1) a series of papers on TREG cells, which covers the entire bench to bedside track, illustrating the synergy between the groups within this theme; 2) the discovery of several genes that are causative to Myelodysplastic Syndrome (TET2, EZH2) that were found with a strong collaboration with the human geneticists of the NCMLS.

The recent recruitment of Friedl should be viewed as an important development. This successful recruitment appears in large part due to the existence of the NCMLS as an entity. Friedl has been instrumental in establishing a new imaging facility located in the animal facility, i.e. the Preclinical Imaging Center (PRIME) for fluorescent imaging in live rodents. This facility will become of great value as an intermediate between lab-based and clinical studies within the NCMLS.

In sum, vitality and feasibility are very strong.

**Recommendations**
The theme would benefit strongly from giving more opportunity to clinical researchers to be involved in translational aspects of the theme.

Streamlining bureaucratic procedures for clinical and animal studies would increase quality and productivity.

The theme should pay special attention to further integration of PRIME in the NCMLS to maximize its benefits from this facility.
3.3 Regenerative Medicine & Microenvironment

Programme: Regenerative Medicine & Microenvironment
Programme director: Dr. T.H. van Kuppevelt
Research staff in 2010: 62 fte (78 fte)
Assessment:
Quality : 4
Productivity : 4
Societal Relevance : 5
Vitality and feasibility : 4-5

Objectives and research activities
Mission: to improve the quality of life of patients by understanding cell-matrix interactions (microenvironment), and to apply the obtained knowledge for the regeneration of tissue/organs.

Quality
The group is working in the field of regenerative medicine and tissue engineering on the one hand and on the more fundamental aspects of characterizing the significance of the cellular microenvironment for health and disease such as cancer on the other hand. The originality of research in theme 3 is highly due to the fact that the group develops materials and treatment strategies that go from bench to bedside. The coherence of the scientific program is currently given by focusing on the investigation of the impact of the extracellular environment on cell behavior.

The principal investigators are of outstanding prominence in their field of science. Their tissue engineering initiative is ranked as number one in The Netherlands. They achieved to establish a number of strong long term research strategies that will ultimately have immediate applications in the clinics. Accordingly the group was able to attract a substantial amount of grant money by which it can fund its research and which provides the opportunity to hire key personnel. The infrastructure is such that there is no limitation with respect to the research goal the group pursues.

Productivity
The group is overall very productive. The number of scientific publications is high. The number of patents is outstanding. With respect to its internal organization the joint meetings of post docs, graduate students and principal investigators are a good and an indispensable tool on the way to harmonize the activities which are covering a broad
range of topics. Even though the productivity is good, it is foreseeable that the group would profit significantly if the individual research groups had their lab space in closer proximity.

**Societal relevance**
The societal relevance of this theme is outstanding. Within the scientific community it is definitely a major road block to bring new regenerative medicine treatment strategies into the clinics. The group is with some of its projects definitely very close to that. Concomitantly, society as a whole does profit tremendously from this development. The valorization is ideal. The group protects its know-how with patents that puts it into a strong position when collaborating with companies.

**Vitality and feasibility**
The group is overall on a very good track. The principal Investigators have a clear judgment of how the field of regenerative medicine will evolve over the next couple of years. Concomitantly they work steadily on their ongoing research projects, which is ideal since these are long haul endeavors that will only bring an ultimate clinical success when pursued with enough continuity. Focusing on a better understanding and appreciation of the microenvironment of cells is definitely a topic that will allow it to intensify contacts to groups that focus with their research on materials science. With research towards smart scaffolds or the investigation of inflammatory processes during tissue development the group anticipates topics that will have a long term impact in the field.

**Recommendations**
The group is encouraged to continue to identify research themes of mutual interest to the different sub-groups.

Even though the academic significance of its work is very good the group should try to publish its results in scientific journal that go beyond the best ranked ones in their specific field.

A closer collaboration with other groups of the centre seems advisable. It would be a missed opportunity if the group would not intensify its collaboration with groups within NCMLS such as the ones of theme 7 (Chemical and Physical Biology). Significant synergisms are to be expected.
3.4 Energy & Redox Metabolism

Programme: Energy & Redox Metabolism
Programme director: Prof. dr. M.A. Huynen
Research staff in 2010: 40 fte (49 fte)
Assessment:
- Quality: 4-5
- Productivity: 4-5
- Societal Relevance: 4-5
- Vitality and feasibility: 4-5

Objectives and research activities

Mission: the group investigates biomolecular pathways of NADH and ATP conversion in human health and disease; the systems relevant for mitochondrial medicine are studied and newly acquired knowledge for diagnosis and treatment is applied.

The research program focuses on energy metabolism and its alterations in the wide array of genetic disorders causing functional defects in complex I of the mitochondrial respiratory chain. The theme is run by a well-selected and coordinated group of scientists with strong international reputation and complementary expertise. The success of this interaction is directly demonstrated by high-profile joint publications, in which the multidisciplinary approach allowed a profound insight into fundamental biomedical issues. To cite an example, the evolutionary analysis of a newly discovered gene responsible for complex I deficiency (ACAD9) allowed to track its origin by gene duplication, to model its structure and analyze its function and to investigate the mutations occurring in patients. This example of integrated project indicates that the goal of assembling a leading group in mitochondrial translational research was successful, highlights the strengths of the work done so far and allows to make some suggestions for the future.

As far as the analysis of the achievements of the theme, it is clear that two aspects were essential. The first was that of selecting top scientists with the right expertises (computational biology, cell biology and imaging, biochemistry and medical genetics). The second is focusing on common projects of major medical relevance and biological interest, and establishing a modus operandi that would generate interaction and success: location in the same building, application to common grants and weekly meetings of the whole team.
Quality
Scientists in this group are international leaders in the field. They are in the position to successfully compete with the few other centers with comparable competence. They have a solid internal organization and have obtained state of the art instrumentation (for advanced microscopy, gene analysis, etc.) that they utilize as a common core facility. They obtain funds for and train efficiently a good number of PhD students. An obvious strength is the presence of promising young PIs (including an awardee of the highly competitive Vici program).

Productivity
The research output is of high level, with a high total number and a few publications in top-rank journals, such as Nature and Cell Metabolism.

Societal relevance
The theme addresses a topic of very high interest in biomedical research, mitochondrial medicine, with a strong focus and expertise in the genetically defined disorders. They also created a spin-off (Khondrion) dedicated to the development of new drugs for the treatment of metabolic disorders.

Vitality and feasibility
The scientific strength of the PIs, the coverage of the necessary expertises and the structure of the group puts the theme in the position to be highly competitive also in the future. It appears sensible to take advantage of the strong competence in mitochondrial medicine to expand the area under investigation to related research topics (e.g. role of complex I in the pathogenesis of Parkinson’s diseases and cell biology investigation of mitochondrial turnover).

Recommendations
For the future work, the committee recommends to consolidate the group by recruiting the most talented junior PIs into permanent positions.

The theme would profit from linking its work to that of theme 7.

The committee expects the group to gain coherence by expanding the research into the fields of cell biology and genetics.
### 3.5 Membrane Transporters & Signalling

<table>
<thead>
<tr>
<th>Programme: Membrane Transporters &amp; Signalling</th>
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<tbody>
<tr>
<td>Programme director: Prof. dr. J.G.J. Hoenderop</td>
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<tr>
<td>Research staff in 2010: 47 fte (62 fte)</td>
</tr>
<tr>
<td>Assessment: Quality : 4-5</td>
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<tr>
<td>Productivity : 4-5</td>
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<td>Societal Relevance : 4-5</td>
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<td>Vitality and feasibility : 4-5</td>
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#### Objectives and research activities

**Mission:** to understand the molecular mechanisms of transport of water, solutes, drugs and metabolites in health and disease to apply newly acquired knowledge for diagnosis and therapies of kidney diseases and beyond.

The research focuses mainly on epithelial transport in the kidney and gastrointestinal tract and liver pathology. Research highlights are the discovery of the function of calcium channels TRPV5, TRPV6 and TRPM6 function in the kidney; work on Mg2+ homeostasis; the discovery of the pathogenic role of ion channel Kv1.1 in the kidney; the discovery of novel V2r agonists; the somatostatin therapy of polycystic kidney disease and cystic liver diseases; the role of NO in the kidney; and the Biokid program for a new hemodialysis approach.

#### Quality

The quality of the research is very high. The group is performing highly original and nicely focused research with an important translational character. Excellent topics range from gene, proteins, molecular and cellular function of diverse channels and transporters to a novel treatment of chronic kidney and liver diseases. The range of methods used is impressive. The input of Structural Biology could be strengthened.

The critical mass of the group is good, collaboration with clinical partners seems excellent. The proteomics approach is considered as of high quality. Obviously, the Bindels/Hoenderop and Deen themes have been considered as internationally leading. Infrastructure is excellent. There are no weaknesses in the organization of the group’s management, other than those discussed in a more general context.
Productivity
Although the output is very good, the committee missed some really high impact papers in e.g. Nature, Cell etc. The group published an important Science paper. However, the committee wonders why there hasn’t been a continuous follow up of this topic. The committee judged it as a relative weakness that the number of top 10% publications has decreased from 2006. The total number of publications is excellent, but also shows a drop in the last year.

Societal relevance
This group exploits a lot of important links with other subthemes, and with many external academic and industrial partners. The societal relevance is obvious from the successful linking of the molecular approach to diseases: an impressive example of translation science. One critical point refers to the moderate approach to the pharmaceutical industry, resulting in a too limited funding via these sources. The societal relevance of this research group would profit from such approach. However, the future perspectives are excellent. Connections to the industry can probably be improved.

Vitality and feasibility
It is very obvious that the work of this group has an excellent potential for future and extended research. The group is very vital. However, due to methodological intrinsic problems (long waiting time for genomic analyses), some progress might be delayed, a problem not inherent to the group. Visibility is improved compared to the last ranking. Importantly, PI’s have received prestigious grants, awards and nominations for membership in prestigious academies. The committee has only one critical remark: it was not clear why too few ERC grants (Starter and Advanced) have been applied for.

Recommendations
The research would profit from a stronger in depth mechanistic analysis. The quality of research would be likely increased by implementing for instance: improving structural biology, 3D protein analysis, crystallography.

The benefits of a strong focus might be compromised by the requirements of moving to additional and very actual themes. Useful extensions would include e.g. increasing the variety of transporters and channels studied: inclusion of PKD ion channels, other TRP channels, eventually also extension to other channels from the Kv family. Functionomics of the ciPTEC cell line should be extended, but this is already planned in detail. The whole consortium provides excellent possibilities to accept these challenges. The PI’s see these extensions very realistic and have already intensively discussed possible extension.
Some more interactions in the NCMLS are indicated: connections to theme 1 (skin
diseases, TRPs/ LPS in inflammation, TLRs); interactions with theme 7 (Chemical Biology)
for more in depth functional analysis and modeling.

The work on bioactive membrane creates a basis for ample interactions with
pharmaceutical industry, more funding from the industry and improvement of valorisation.

The committee recommends a more intense application for ERC funding, Curie grants,
EMBO grants etc.
3.6 Genetic and Epigenetic Mechanisms of Disease

Programme: Genetic and Epigenetic Mechanisms of Disease
Programme director: Prof. dr. J.H.L.M. van Bokhoven
Research staff in 2010: 56 fte (77 fte)
Assessment:
- Quality: 5
- Productivity: 5
- Societal Relevance: 5
- Vitality and feasibility: 4-5

Objectives and research activities
Mission: to unravel the molecular basis of cell behaviour that emanates from the genetic and epigenetic code obtained in the nucleus in the context of health and disease. The group combines basic and clinical research to unravel the molecular pathways and cellular processes in specific (hereditary) tumorigenic pathways and in normal and pathological conditions of development, in particular of the nervous system (sensory diseases, neurodevelopmental disorders), acute myeloid leukemia and breast cancer.

Quality
Strategies developed by the 19 PIs combine well characterized collections of human and biological resources, as well as complementary approaches using state of the art techniques and technologies (including next generation sequencing and high throughput sequencing for DNA, RNA and epigenetic changes) to delineate genetic and epigenetic changes regulating physiological and pathophysiological mechanisms underlying investigated disorders.

The quality of the research is original, excellent and competitive. Several PIs of this theme are internationally recognized and achieved significant breakthroughs which are widely diffused in medical and diagnostic practices. This theme is among the first worldwide to apply next generation sequencing for identifying genetic causes and genes involved in many human genetic disorders. Some the PIs of this theme are world leaders in the field of human genetics and epigenetics.

Productivity
Scientific production is excellent (quality and quantity; total number of peer reviewed papers: 151) with several papers in major top journals (such as Cell and Nature Genetics, Science) with an interesting trend towards an increase of the number of papers in top journals.
The committee would like to highlight that experience and skills of this theme in the field of large scale sequencing and data analysis enhanced several collaborations with PIs from other themes that contributed to the overall quality of the research in the NCMLS.

**Societal relevance**
Research achieved by this theme is tremendously useful. Societal relevance is guaranteed and has an impact that goes beyond The Netherlands frontiers. It has immediate implications for the diagnostic and genetic counseling in families confronted with genetic disorders, and late onset diseases (including cancer). Contributions of this theme are internationally recognized.

This theme has also an excellent potential of valorization. Involved researches have for instance identified a biomarker for prostate cancer that is already available as CE marked IVD test, and filed in several patents.

They also created NovioGendix, a spin off founded in 2006.

**Vitality and feasibility**
The theme has access to appropriate human and biological resources, as well as state of the art and innovative technologies. They recently attracted talented junior PIs with experience in complementary disciplines (neurobiology using Drosophila and zebra fish models, early development using Xenopus, electrophysiology), which represents an excellent strategic option for the for the development of competitive research.

PIs of this theme have an excellent academic reputation and are very successful in grant applications at national, European and international levels (including coordination).

Planned projects in the field of human genetic disorders and cancer, and application of next generation sequencing technology for medical diagnostic applications are pertinent and well justified with interesting perspectives of success for transfer and translational research. Projects focused on epigenetics are also very pertinent and relevant with interesting perspectives.

**Recommendation**
Take advantage of competence and skills of other themes in the institute in order to strengthen genetic findings by functional studies.
The decision to enrich the theme by the development of approaches based on induced pluripotent stem cells to better understand pathophysiological mechanisms should be encouraged.
3.7 Chemical & Physical Biology

Programme: Chemical & Physical Biology
Programme director: Prof. Dr. J.C.M. van Hest
Research staff in 2010: 61 fte (68 fte)
Assessment: Quality: 4
Productivity: 4-5
Societal Relevance: 4-5
Vitality and feasibility: 4-5

Objectives and research activities
The group aims at exploiting molecular approaches to understand, follow and modulate biological processes in cells and organisms. This translates to new therapeutic and diagnostic approaches.

Quality
Excellent critical mass in the area of Chemical Biology is rare globally – Nijmegen and the NCMLS has it (and importantly this has been recognized nationally). Theme 7 has a spectacular group of ambitious people. Despite the small number of PIs, this theme is already charting important courses into biologically relevant areas. With added focus on biological hypotheses (something that was highlighted by clearly identified objectives – e.g. T-cell immunology or autoimmunity with theme 1), this grouping will in future years make contributions to (and test hypotheses in) biology that could not be achieved by other means.

Productivity
The grouping has published in good journals by the standards of Chemistry and Chemical Biology (e.g. Angew Chem, with the 2nd highest IF in Chemistry). Given the number of fte’s in the theme, they have been very productive with 100-110 papers each year for 6 fte’s. The score given is reflective of the relative positioning of both the subject (Chemical Biology) in the context of international publishing and the theme (which is clearly rapidly expanding its influence in the institute and the NCMLS). Other themes are currently generating papers with higher IF for a variety of reasons. Such papers are currently more rare in this theme, but this will undoubtedly change in the future.
Societal relevance
This theme has been highly productive both in the creation of spin-offs and also in entrepreneurial spirit. This is healthily reflected not only in the way that they transfer technology (including healthy patent publication levels) but also in their approach to science. Stated aims (e.g., Molecules-to-Man) in many ways could not be more relevant, given time. At this stage the very fundamental nature work in the field of Chemical Biology (and therefore its developmental distance from application) creates an inherent delay in translation. That said, the theme PIs are clearly knowledgeable and excited by these long term prospects and as a relatively young team are well placed to take these on.

Vitality and feasibility
This is a very strong, relatively young grouping with vision and ambition. The support of the NCMLS and the institution will be vital in ensuring long term health in an area that deserves strong support (given the potential future impact). One illustrative example surrounds the imminent appointment of tenure-track positions in this area – despite the availability of positions in theme 7, none are yet in line for the strong support that would come from a UMC fellowship (thereby enabling an 800k€ start-up package). Whether this is a function of the dual mechanisms of the Faculty of Sciences and the UMC (highlighted in chapter 2) or reflects some need for internal consideration within the NCMLS, it would be a shame to miss the opportunity to bolster a smaller but productive theme with a bright future (especially given the backing of the Dutch national Sector Plan Physics and Chemistry).

Recommendations
The fundamental focus of theme 7 should be consolidated for a bright future at both the institutional, NCMLS and theme level. Specific examples include:
• continued focus on strong biological hypotheses (excellent windows of opportunity) with a long-term view (e.g. Molecule-to-Man)
• institutional support through appropriate mechanisms which address/change highlighted threats of the joint UMC/Faculty systems
• consideration of strategies for tenure-track with full start-up support in an area that is competitive for recruitment internationally

The group performs chemistry at the highest possible level, and should continue to seek more opportunities for the integration of chemistry and biology.

There are still many opportunities for this theme to connect with other groups in NCMLS.
4 Response of the Institute

As Scientific Director of the NCMLS institute, I would like to extend genuine gratitude to the Evaluation Committee for their thorough work and constructive assessment of our research institute. This Research Assessment Report has been efficiently and meticulously compiled based on the expert opinions of the committee members. Prof. Hans Clevers has performed an outstanding and noteworthy job as chairman of the committee. All comments and advice received will be carefully discussed in the NCMLS Management Team, and where required with the Deans of the relevant Faculties, in order to make the necessary improvements in our research and education policy.

In 2005, the comment was made that “NCMLS lacked the (inter)national visibility that it aspired to, and deserves”. Since that time significant energy has been invested by inviting top international speakers to Nijmegen (symposia, lectures, masterclasses etc) and by improving communication tools (e.g. website, folders etc). It is, therefore, pleasing that the current evaluation committee has noted that NCMLS has “clearly matured”, and that research and education are performed “beyond an internationally competitive level”. This result is achieved by the team effort of all our members under the leadership of Prof. Carl Figdor (2000 – 2010).

The committee noted the unique interfaculty strength of NCMLS in being able to perform multidisciplinary fundamental and (applied) translational research. The close interaction between basic researchers from the Faculty of Science (FNWI) and (pre)clinical researchers of the RUNMC representing various disciplines is a unique asset that will be safe-guarded and exploited to its maximum in order to achieve the highest standards of research and education in the molecular life sciences. To this end, NCMLS will improve the coherence and focus of its research themes as well as working towards the streamlining of NCMLS activities with the other institutes. The international profile of NCMLS will be further enhanced by forming strategic alliances with (European) partner institutes. As suggested by the committee, we will work on increasing the number of formal roles of clinicians within NCMLS, thereby increasing their representation in NCMLS and further enabling translational research.

In the coming years ample positions at the full-professor level will become available within the NCMLS allowing investment in specific research areas. We will take on board the advice of the committee and develop a clear recruitment strategy. The main challenge will be to fill these positions with high profile scientists.
NCMLS apparently has a comprehensive and excellently organized 4-year PhD training program. The committee was positive about the PhD program, mentor system and facilities available. Whilst the quality of PhD theses remains high, the average duration of 5-6 years is too long. The committee’s sentiments echo those of the ECOS committee in 2005. Unfortunately, we must acknowledge that (recently) implemented policies have not yet had the desired effect. NCMLS takes this matter very seriously and a new package of policies is being developed to emphasize the 4 year limit.

In summary, the findings of the Committee on all aspects from research and education to management and recruitment are very well taken and we are grateful for the encouraging advice received. The coming years will be quite exciting ones for NCMLS. I am proud to take the next steps towards our vision of further establishing a European top institute with a dynamic & ambitious environment.

On behalf of the NCMLS Management, staff and researchers,
Prof. René Bindels
Appendix 1  Description of the institute and its research activities

The Nijmegen Centre for Molecular Life Sciences (NCMLS) is one of 18 research institutes within Radboud University Nijmegen. It is the largest within the Radboud University Nijmegen Medical Centre and the only institute accredited by the Royal Netherlands Academy of Arts and Sciences (KNAW).

The institute promotes the synergy of multidisciplinary research ideas and the communication between life sciences researchers and clinicians. As described briefly in chapter 2, it strives towards a greater understanding of the molecular mechanisms of disease through curiosity driven research and the translation of these findings into clinical applications: the research tracks from bench to bedside – and back.

Research themes centre around three main areas:
  • Infection, immunity and regenerative medicine (themes 1, 2, 3);
  • Cell metabolism, transport and motion (themes 4, 5);
  • Cell growth and differentiation (themes 6, 7).

Forming a bridge between science and medicine, NCMLS is part of both the Radboud University Nijmegen Medical Centre and the Faculty of Science, Mathematics and Computing. Most NCMLS researchers are affiliated to another research institute as well. The majority of NCMLS core groups are housed within the NCMLS research building, but some groups are not.

In Nijmegen, NCMLS is allied with the Institute for Molecules and Materials and the Donders Institute for Brain, Cognition and Behaviour. It incorporates the Centre for Molecular and Biomolecular Informatics and houses The Netherlands Bioinformatics Centre.
Appendix 2  Curricula vitae of the Evaluation Committee members

**Prof. dr. H.C. Clevers (chair)**

Hans Clevers currently is Director of the Hubrecht Institute for Developmental Biology and Stem Cell Research in Utrecht, The Netherlands, and professor in Molecular Genetics at Utrecht University.

Clevers obtained his MD from the University Utrecht, where he also did his PhD research (immunology). He worked as a postdoc with Cox Terhorst at the Dana-Farber Cancer Institute of the Harvard University, Boston, USA. From 1991-2002, he was Professor in Immunology in Utrecht. He is a member of the Royal Netherlands Academy of Arts and Sciences and he received several awards. He obtained an ERC Advanced Investigator grant. He is Chevalier de la Legion d’Honneur.

http://www.hubrecht.eu/research/clevers/leader.html

**Prof. dr. J. Chelly**

In September 2003, Jamel Chelly was appointed as professor at University Paris Descartes, and he is currently leading a research group at Cochin Institute, and at the Cochin Hospital the diagnostic laboratory of neuromuscular and neurodevelopmental disorders and the Cell Bank – Cochin APHP.

Chelly obtained his medical degree in 1983 and a PhD specializing in human genetics (Paris Descartes university – France). In 1991 he was awarded by the Cancer Research foundation (UK) a three year post-doc fellow position and carried out his research at the Institute of Molecular Medicine in Oxford UK. In 1995, he established at the Cochin Institute the Laboratory of Genetics and Pathophysiology of neurodevelopmental disorders. Current research programs of his lab are in continuation with genetic studies and aim to better define and understand disrupted molecular, cellular and neurobiological processes underlying cognitive deficits, neuronal migration defects and malformations of cortical development.

http://cochin.inserm.fr/research/scientific-departments/gd/team-16

**Prof. dr. B.G. Davis**

Ben Davis is Professor of Chemistry at the University of Oxford and is Fellow and Tutor in Organic Chemistry at Pembroke College, University of Oxford, UK. After graduating from the University of Oxford, Davis spent two years as a postdoctoral fellow at the University of Toronto exploring protein chemistry and biocatalysis. He returned to the UK in 1998 to take up a lectureship at the University of Durham and subsequently moved to the Dyson
Perrins Laboratory, University of Oxford; he was awarded at Fellowship at Pembroke College, Oxford in 2001. His group's research centres on chemical biology with an emphasis on carbohydrates and proteins. He sits on the editorial board of several leading publications in the field of chemical biology and was appointed editor-in-chief of Current Opinion in Chemical Biology in 2011. He is also UK representative, and secretary, of the European Carbohydrate Organisation and president of the Royal Society of Chemistry (RSC) Chemical Biology Division.
http://research.chem.ox.ac.uk/ben-davis.aspx

**Prof. dr. A.M. Göpferich**
Since 1997, Achim Göpferich is chair of Pharmaceutical Technology at the University of Regensburg in Germany. Göpferich studied Pharmaceutical Sciences at the University of Heidelberg from which he graduated in 1986. He received his PhD from the same institution in 1991. From 1991 to 1993 he worked for 2 years as a postdoctoral fellow in the department of Chemical Engineering of the Massachusetts Institute of Technology. From 1993 to 1997 he joined the department of Pharmaceutics of the University of Erlangen as research associate. During this time he held appointments as visiting scientist at MIT and Rice University.
http://www-cgi.uni-regensburg.de/Fakultaeten/Pharmazie/Pharmtech/php/mitarbeiter_website.php?id=4&lang=en&redpublist=1

**Prof. dr. B. Nilius**
Bernd Nilius is emeritus professor of Physiology at Katholieke Universiteit Leuven, Belgium, department Molecular Cell Biology. After finishing his studies in medicine, Nilius was a research associate at the Institut of Physiology in Halle (Germany), where he obtained a MD degree, a master degree in mathematics and a PhD degree in Physiology. He continued in Halle as assistant and associate professor of Physiology, and he then was appointed full professor at the Medical University Erfurt (Germany) and leader of the Max Planck Research Group “Mol Cell Physiology”. In 1993 he moved to Leuven as full professor of Physiology and was appointed in 2005 as director of a Center of Excellence. He received several award, including in 2006 the *Dautrebande Award* of the Belgian Royal Academy of Medical Sciences awarded by the Belgian Queen. Nilius is editor of several international journals, member of several scientific societies, such as the Belgian Royal Academy of Medical Sciences, the Academia Europea and the European Molecular Biology Organisation (EMBO).
http://sites.google.com/site/berndnilius/
http://de.wikipedia.org/wiki/Bernd_Nilius
Prof. dr. R. Rizzuto
Rosario Rizzuto is professor of General Pathology and chairman of the department of Biomedical Sciences at the University of Padua (Italy). He graduated in Medicine and Surgery in 1986 and received his PhD in 1991. He spent two years at Columbia University as a post-doc. Rizzuto has introduced an innovative methodology for measuring Ca2+ concentrations and other cellular parameters in defined cell compartments, that is based on the molecular engineering and specific targeting of recombinant luminescent (aequorin, luciferase) and fluorescent (GFP) proteins to defined subcellular locations. This approach allowed him to obtain novel, unexpected insight in the fields of calcium signaling, cellular metabolism and organelle morphology. These new concepts include the participation of mitochondria in cellular Ca2+ homeostasis and their role in translating calcium signals in effects as diverse as stimulation of metabolism and induction of cell death. He received several awards and prizes, including the Biotech award and the ‘Chiara D’Onofrio’ Prize, and he is a member of the Academia Europaea.
http://www.biomed.unipd.it/index.php/en/component/content/article/117-rizzutogroup

Prof. dr. E.J.H.J. Wiertz
Emmanuel Wiertz is professor of Medical Microbiology at the University Medical Center in Utrecht. After graduating as a DVM in Utrecht he worked on bacterial immunity and vaccine development at the National Institute of Health in Bilthoven. In 1993, he obtained a PhD from the University of Utrecht. From 1994-1996 he was a postdoctoral fellow in the lab of prof. Hidde Ploegh at MIT. After returning to The Netherlands, he became professor of Medical Microbiology at the Leiden University Medical Center. In 2009, Wiertz moved to Utrecht, where he continues to study virus host-interactions with special interest in viral immune evasion strategies.
http://www.umcutrecht.nl/zorg/patienten/zorgverleners/W/wiertz/
Appendix 3  Programme of the site visit

October 2, 2011
17.30  Committee members arrive and meet prof. dr. René Bindels (scientific director of NCMLS) and dr. Adrian Cohen (scientific manager NCMLS) during dinner

20.00  Preparatory committee meeting

October 3, 2011
09.00  Welcome speech by prof. mr. Bas Kortmann, Rector Magnificus of Radboud University Nijmegen
09.15  NCMLS introduction by prof. dr. René Bindels, scientific director
09.30  Parallel meetings with theme 4 (Martin Huynen, Jan Smeitink, Peter Willems, Arend Heerschap, Hans Spelbrink en Leo Nijtmans), theme 5 (Joost Hoenderop, Roos Masereeuw, Joost Drenth, Frans Russel, Peter Deen), and theme 6 (Hans van Bokhoven, Gert-Jan Veenstra, Ronald Roepman, Ad Geurts van Kessel, Hannie Kremer, Jack Schalken).
11.10  Interview deans of Science Faculty (prof. dr. Stan Gielen) and Medical Faculty (prof. dr. Frans Corstens)
12.30  Lunch and meeting with PhD students (Hanneke Wittgen, Zafar Iqbal, Nina Tel-Karthaus, Anna Häger, Laurianne Michel, Tom Schirris)
13.45  Interview PhD committee (Bert van der Reijden (chair), Frank van Leeuwen, Frank Wagener)
14.15  Parallel meetings with theme 2 (Gosse Adema, Joop Jansen, Peter Friedl, Jolanda de Vries, Carl Figdor, Luuk Hilbrands, Otto Boerman) and theme 7 (Jan van Hest, Roland Brock, Floris Rutjes, Ger Pruijn, Wilhelm Huck).
16.00  Parallel meetings with theme 1 (Frank van Kuppeveld, Leo Joosten, Tim Radstake, Joost Schalkwijk, Peter Hermans, Jo Berden) and theme 3 (Toin van Kuppevelt, Wout Feltz, John Jansen, Katarina Wolf, Johan van der Vlag).
17.15  Writing preliminary findings on themes
19.00  Dinner: committee, René Bindels, Adrian Cohen, Frans Cortens
October 4, 2011

09.00 Interview scientific director (prof. dr. R. Bindels) and scientific manager (dr. A. Cohen)
10.00 Interview head genomics facility (Han Brunner)
10.20 Interview head central animal facility (Merel Ritskes)
10.40 Interview head microscope imaging platform (Peter Friedl)
11.00 Intern discussion of committee on theme assessments
12.00 Parallel interview sessions with technicians (Eva Janssen-Megens, Nicole Meeusen-Scharenborg, Miranda Bennink) and post docs (Sergio Rossel, Pedro SanCristobal Zepeda, Richard Bartfai, Remko van Horssen, Martijn Langereis, Anja Scholten)
13.00 Intern discussion, preparing conclusions and writing report
17.00 Chair presents findings to Rector Magnificus, deans, scientific director, scientific manager, theme leaders and some other NCMLS employees