

Postgraduate School

Molecular Medicine (MolMed)

Evaluation 2009-2014

**Conclusions and Recommendations of the
International Evaluation Committee of MolMed**

October 29-30, 2015

Introduction

The Executive Board of the Erasmus University Rotterdam has invited an International Evaluation Committee to review the research performance and the educational program of the Postgraduate School of Molecular Medicine of Erasmus University Medical Centre of Rotterdam (MoIMed). In reporting its observations, assessment and conclusions, the International Evaluation Committee will focus on the governance structure, the research and the educational programs and formulate recommendations to the Executive Board of Erasmus Medical Centre and the board of MoIMed. The *additional points of interest* mentioned in the Terms of Reference are addressed in the context of these broad headings, as is the assessment of the follow up of the recommendations of the previous International Evaluation Committee in 2009.

Members of the International Evaluation Committee

The International Evaluation Committee members were:

- **Prof. René A.W. van Lier, MD, PhD**, chairman of the committee
Immunologist, Member of the Executive Board, Sanquin Blood Supply Foundation and professor of Experimental Immunology, AMC, Amsterdam.
- **Prof. Eva Hellström Lindberg**
Department of Medicine Center for Hematology and Regenerative Medicine (HERM); Karolinska Institutet; Karolinska University Hospital Huddinge; Stockholm.
- **Prof. Stuart H Ralston, MD, FRCP, FMedSci, FRSE**
Arthritis Research UK Professor of Rheumatology; Centre for Genomic and Experimental Medicine; University of Edinburgh; Molecular Medicine Centre; Western General Hospital, Edinburgh.
- **Prof. Thomas F. Schulz, MD**
Institute of Virology; Hannover Medical School; Hannover.
- **Prof. Hans Gelderblom, MD, PhD**
Medical oncologist, Leids Universitair Medical Centre (LUMC), Leiden.

Secretary of the commission was

- **Dr. Jessika van Kammen, PhD**
Head of the Research office and secretary of the AMC Research Council; Academic Medical Center University of Amsterdam.

Programme and procedures of the site visit

The Committee received the self-assessment report of the School and extensive documentation well in advance and convened at 28, 29 and 30 October 2015. The full programme of the review session is attached as appendix 1 to this report. In short, in the evening of 28 November, the Committee was welcomed by the board of MolMed, who presented background information to the Committee and provided additional explanation regarding the questions that the Committee has been asked to answer. On 29 and 30 October, the Committee reviewed presentations from senior and junior researchers from the four main themes of MolMed, in the presence of board members of MolMed. The discussion with the senior and researchers attending the discussions is integrated in the assessment. In addition, the Committee has appreciated the meeting with the Educational Committee and the PhD students and postdocs committee of the school. In the morning of 30 October, on request of the Committee, we were able to visit one of the key core facilities for translational medicine, the genomics lab. Professor Hans Van Leeuwen, director of Research and Education, representing the Executive Board of Erasmus Medical Centre explained the upcoming changes in the organisation of research. Next the Committee made its assessment and conclusions, and formulated answers to the specific questions. This was summarised in a draft report, which was then presented to board of MolMed and the representative of the Executive Board of Erasmus Medical Centre. After the review session, the draft report was further edited and circulated among the Committee members for possible correction and, subsequently, final approval.

Assessment of research unit

a. Brief description of research unit's strategy and targets

The school is clinically oriented towards molecular biomedical research. While the main focus is on translational research, defined as research that has a direct influence on prevention, diagnosis, prognosis and/or treatment of the patient, related scientific programs cover a continuum from basic to bedside research and include an outlet for clinical evaluation, validation and implementation.

The mission of the school is to integrate basic and clinical science and to involve both basic and clinical researchers with a vast experience in applied clinical research. Therefore the school harbors a broad spectrum of disciplines. The research programs fulfill the need for an interactive, multi-disciplinary approach to achieve optimal synergy between these disciplines, thus encouraging 'cross-disciplinary thinking'. In other words, the school's strategic mission is to promote 'knowledge sharing'. The school facilitates discussion between peers to give each other feedback. In this way a common awareness emerges on the progress of the researcher's agendas. This peer-based evaluation not only includes scientists in the school, but also scientists from other departments in Erasmus MC and colleagues from other institutions.

In this context the school provides high quality training and education in research in a broad area of basic, translational and applied biomedical sciences, which integrates all disciplines within the school. The research programs are closely linked with the training and education programs.

The school is built around the Working group leaders (PI's), each with their high-quality research projects. They are supported by their senior and junior post docs, PhD students and other assistants. The post docs and PhD students frequently use the educational infrastructure of the school, in which they find cohesion between the several research fields and a matrix for their training. Thus, the school is an important medium to reach a high scientific quality in all affiliated research groups. The training programs of the 'future generation of scientists' result in highly qualified Master- and PhD graduates, while the full research teams reap the rewards of it. The MDs in the school also benefit from the educational activities. This societal impact is another important effect of the activities of the school.

Overall, the basic and translational research is very strong within MolMed. This contributes greatly to the international visibility and reputation of the Erasmus Medical Centre and should be fostered. The Committee was impressed by the very high to excellent quality of the research presented, the open discussions with the research representatives, and the community feeling within the School. The PhD students convey the impression that they are being listened to and form part of the MolMed research community. The School provides an excellent framework for training PhD students and thereby makes a significant and indispensable contribution to the research quality.

b. Assessment of organization/governance

The infrastructure of the school, consisting of two components, supports both research and teaching:

- **Research:**

The research groups fall under 4 main themes, and there are about 86 working group leaders (PI's) (see **Annex 1** of the Assessment Report of MolMed). The main themes harbor several hundreds of research staff and about 550 PhD students. The 'corporate identity' of the school is the translational biomedical research in the setting of an academic hospital;

- **School:**

A logistic staff of about 2 Fte's organizes the educational program and is responsible for the finances, reports to the central organization and its own 'lean and mean' organization.

The school facilitates research by organizing education and symposia; these activities in general unite the research programs. The funding of these activities stems from the departments with an annual fee per workgroup leader, and from the dean with an annual contribution according to the number of PhD graduations. The school also receives tuition fees from external participants and sponsoring (see **Appendix 3** of the Assessment Report of MolMed).

The school has four administrative bodies: the Board, the Educational committee, the PhD/Post doc committee and the Confidential Counselors. The Chairman of the Board is appointed by the dean. The chairman appoints the members of the Board. The Board's main responsibility is supervision of the whole school and of the managing director. The Educational committee supervises the programs and evaluations of all courses and symposia, organized by the office, provides suggestions and if needed makes decisions. The PhD/Post doc committee advises the managing director and the Educational committee about the educational program.

The managing director, who is appointed by the Chairman of the Board, is responsible for the integration and support of all research groups and researchers, the Board, Educational committee

and the PhD/Post doc committee. He acts as secretary to the Board and arranges most of the course and symposia programs in cooperation with the responsible researchers and supervises the realization of the MolMed program. The secretary is broadly responsible for the preparing and facilitating of all courses and symposia. The secretary also acts as the secretary to the Educational committee and the PhD/post doc committee. The organization of the school is 'lean and mean'. It consists of a small executive staff of about 2 Fte that organizes the educational program and is responsible for the administration of the school.

For clarity, the Committee distinguished two levels in its assessment of the governance structures that might impact upon the quality of the research brought together in the Postgraduate School of Molecular Medicine: the School and the Erasmus University Medical Centre.

The School

The current governance structure functions very well. There is an appointed board, importantly with a clear link to the Dean. The Educational Committee and the PhD and postdoc Committee oversee the quality of the courses provided and ensure continuous innovation of the course programme. The current managing director does an excellent job in maintaining and ensuring the proper functioning of the school. However, plans for a successor should be put in place. From the written material provided to the panel it was not always clear to what extent the strategic aims of the MolMed School are being reached. As an example: statistics were reported on the PhD programme including time to graduation and exit numbers to different sectors, but these were not interpreted in the light of the aims of the School and an analysis of the factors that influence time to graduation and reasons for not graduating was not provided.

Erasmus University Medical Centre

Erasmus MC aims to improve its knowledge infrastructure by the integration of research with the medical care. In accordance with its strategic mission, research, patient care and education will be embedded in Institutes and Academic Centers of Excellence (ACEs) in the near future. The Erasmus MC Cancer Institute and the Neuroscience Institute are the first to come into being. Other Institutes and ACEs will be created, for instance options for a Virology ACE and an Infection and Immunity Institute are being discussed. All main themes will gradually be embedded in and converted into Institutes and ACEs. It is envisaged that the scope of the Institutes and ACEs will be more or less be delineated in parallel with the school's existing main themes and sub themes of MolMed. Thus, the research groups affiliated with the school will probably gradually be converted into such Institutes and ACEs.

Concerning the additional points of interest in the Terms of Reference on the future developments of Institutes and Centres of Excellence, the Committee sensed that there is currently considerable uncertainty about the future organisation of research and postgraduate education. Communication on the part of the Executive Board about future plans and their implementation could help to improve the clarity towards the researchers and thereby the possibility for the researchers to adapt and take a part in these developments.

The Committee found the existence of separate post graduate schools in research areas adjacent to that of the MolMed School unexpected and feels that bringing together the different graduate schools at Erasmus Medical Centre under one organisational and governance structure might

enhance the mutual learning, effectiveness and coherent presentation towards PhD students and candidates.

Recommendations to the Executive Board of Erasmus Medical Centre

- The future structure of the research and education structure – role and mandate of Institutes, Academic Centres of Excellence and postgraduate schools and their integration - should become clear in the coming year.
- High priority should be given to communicating restructuring plans and considerations to the research community of Erasmus University Medical Centre in order to improve clarity, provide reassurance and generate opportunities for involvement.

c. Assessment of education (PhD programmes, research integrity policy)

The table below of the Assessment Report of MolMed gives an overview of the actual workload of the school's organization, with the courses, workshops and symposia:

- Technical/ bio informatics/ statistics/ scientific;
- Basic (research master students and starting PhD students)/ average (PhD students)/ advanced (PhD, post docs end higher)

	Technical	(Bio)informatics	Statistics	Scientific
Basic (MSc->PhD)	Scientific English Writing Photoshop/Illustrator InDesign Microscopic Image Analysis (*)	Excel Access	SPSS GraphPad Prism	Research Master I&I Genetics for Dummies
Average (PhD)	Biomedical Research Techniques Research management Animal Imaging Workshop (AMIE) Microscopic Image Analysis (*)	Excel Advanced Access Advanced Ensembl, UCSC Ingenuity Pathway Analysis CLC Workbench NCBI/Open Source Software Gene Expression data analysis Galaxy Partek Nexus BioBase Bridge Meeting NGS Course SNP Course (*)	Survival Analysis Course on R	MolMed Course SNP Course (*) Mol. Diagnostics Basic & Translational Oncology Basic & Translational Endocrinology Bridge Meetings NGS for Clinical Genetics Daniel den Hoed Day
Advanced (PhD, Postdoc & Higher)	Course/workshop Antibiotic Resistance Grant Proposal Writing		(NO -> Nihes)	Mucosal Immunology Comparative Pathology Hematological Malignancies SNP Course (*) Immunology course Lymphoid Tissue Meeting Virology course & symposium

Overview the school's courses, workshops and symposia

(*): level fits in more than 1 category

Annex 3 of the Assessment Report of MolMed provides the full course- and symposium programs and the student evaluations. For every course, the program of the last organized one is included and the evaluation is enclosed.

The quality assurance of the educational program is maintained by having each course and symposium evaluated by the participants. All evaluations (see **Annex 3** of the Assessment Report of MolMed) prove that the quality of the courses and symposia is good to outstanding. They are discussed in the meetings of the Educational committee. Ratings less than 7 (scale 0-10) are discussed with the organizers and the teachers, and recommendations for improvement are given and in certain cases the teacher and/or the subject is replaced. Training of teachers is also part of the routine. The Erasmus MC policy stimulates teachers to get a basic Qualification in Education ('BKO'). The school advises its teachers with lower scores to follow the BKO training.

In 2010 the school started to organize courses in bioinformatics tools and workshops in Adobe Photoshop and Illustrator for scientists. These short, practical workshops, which were offered on a regular basis, are the reason for the increase in the total number of courses. In 2011 three large scale, international symposia were organized. Also, MolMed started new courses on English writing and Presenting and Presentation courses. This explains the extremely high total number of participants in 2011. The further increase in courses is caused by two newly developed statistical courses, SPSS and R, and the new Adobe InDesign course. From the end of 2013, courses in Excel and Access were offered, which also increased the number of courses. The effect of the financial crisis can be seen in 2013 and stronger still in 2014. The crisis caused less participation of PhD students because there are fewer PhD students. Also, some courses have fewer paying participants than in earlier years. The very successful innovating courses such as the SNP course, the AMIE (Imaging) workshop, Microarray Analysis and Mucosal Immunology attracted fewer participants because many students participated in the first editions(s) and more similar courses were organized elsewhere.

In the opinion of the Committee, the quality of the post-graduate education programme is excellent, with a broad range of contemporary topics addressed at a very high level. The interdisciplinary nature of the courses is one of the strengths of the School. The visibility and accessibility of the managing director is part of the School's success. The PhD students are involved in designing the content of the programme. They are highly positive about the broad range of courses that gives them the possibility to compose their own tailor made package. They also cherish the binding force and the interactions with PhD students from other disciplinary backgrounds. All in all, the school provides an excellent infrastructure for training and is important in creating the community feeling and thereby contributes to the outstanding quality of the MolMed research.

The selective research master on Infection and Immunity seems to appeal to bright and motivated medical students and help to attract them to the MolMed research program. Without doubt, the integration of the research master with the PhD and post-doc training in one School is helpful for the careers of young clinical and translational scientists. Also, the School is important to attract excellent researchers.

It caught the attention of the Committee that, in spite of the national requirements, participation in PhD courses up to 30 ECTS is not obligatory, nor has an obligatory basic set of courses for all MolMed PhD students been defined. *This was noted by the previous International Evaluation Committee as well, see point 9 of their report.* The Committee feels that obligatory participation in selective courses might reinforce the position of PhD students vis-à-vis a broad range of (co)promotors with different styles and priorities. In the same venue, periodic monitoring of the progress of PhD students by a

dedicated independent thesis committee with experienced researchers from different departments might help to mitigate the risk of unpredictability of mutual expectations between (co)promotors and PhD students. See point 7 of the report of the previous International Evaluation Committee for a similar remark.

Concerning the additional point of interest of research integrity, according to the Committee the threshold to access to an independent confidential counsellor in case of alleged scientific misconduct is still too high. Also actions to prevent plagiarism have not yet been fully implemented.

Recommendations to the Executive Board of Erasmus Medical Centre

- In the light of the key role that the Postgraduate School of Molecular Medicine plays in enhancing and ensuring the very high to excellent quality of the interdisciplinary translational research of Erasmus University Medical Centre, the educational programme should be maintained and reinforced.

Recommendations to the board of the MolMed School

The board of the Postgraduate School of Molecular Medicine could provide more effective guidance and leadership in harmonizing entitlements for PhD students. The Committee recommends to consider:

- Make participation up to 30 ECTS mandatory and enforceable.
- Define key performance indicators to assess the output of the educational programme and enable quality control and steering.
- Establish exit polls for PhD students to gather information that can be used in future evaluations.

d. Assessment of research

An effective research environment is provided by having four main themes:

1. Endocrinology, metabolism & ageing
2. Haematopoiesis, lymphopoiesis & immune regulation
3. Solid tumours
4. Infections and host response

Each of the themes is subdivided into a number of research programs, corresponding to subthemes.

Annex 1 of the Assessment Report of MolMed provides a complete description of all main themes and research programs.

Main Theme 1, Endocrinology, metabolism & ageing; Strategy and targets

This main theme includes translational research projects that study signal transduction in growth, development, maturation and aging. First of all research programs focus on scientific work to increase our physiological insight in these complicated processes of life. Furthermore, research focuses on investigations in abnormal benign and malignant growth and development in many tissues, in addition to premature aging and aspects of cancer. All subthemes translate basic research data from the bench to the patient and the population, while at the same time answering questions from studies in the population by working at the bench.

This broad approach includes, therefore, also areas of research such as pharmacogenetics and high capacity, high through-put genome-wide associations facilities that serve not only researchers within

this main theme, but also researchers of the other themes and many others in and outside Erasmus MC. The same applies to the localization, detection and radionuclide therapy of various diseases with the use of state-of-the-art imaging techniques.

Main Theme 2, Haematopoiesis, lymphopoiesis & immune regulation; Strategy and targets

The research in this main theme deals with the molecular regulation of the proliferation and differentiation of myeloid and lymphoid cells (particularly stem cell biology, erythropoiesis, granulopoiesis, lymphocyte development), and aberrations determining malignant transformation (e.g. in murine models and pathogenetic clinical studies). The basic aspects of the programs of main theme 2 are complemented by components related to the function and dysfunction and deficiency of the differentiated “end” cells both in physiological conditions and in disease. It also includes research that address neuro-muscular diseases and neuro-inflammatory disorders. Specific programs have an extension towards clinical application and involve investigations related to developmental diagnostics and therapeutics (e.g. molecular diagnostics, therapeutic targeting in leukemia as well as stem cell transplantation and gene therapy).

Main Theme 3, Solid Tumors; Strategy and targets

Solid tumors can be regarded as tissues whose normal hierarchy and turnover is perturbed due to genetic and epigenetic events, either in normal stem cells or in their more differentiated progeny. Through stepwise selection of cells with crucial defects that confer survival and growth advantage to them, this process ultimately produces invasive and metastatic cancer cells that are capable of survival, growth, and induction of angiogenesis outside their normal niche. Metastases originating from these cells are the ultimate threat to the patient. The main goal of this theme is to understand human solid cancers at the molecular, mechanistic level and to apply this knowledge to improve methods for prevention, screening, diagnosis, prognosis and therapy, including studies on the potentials of stem cells in these conditions.

In all of the studied diseases the research strategy is primarily based on investigation of patient cohorts and tumor samples and body fluids of the included patients.

The new developments in this field include the genomic characterization of individual tumors of each patient by Next Generation Sequencing (NGS), which makes it possible to move to ‘personalized medicine’, tremendous advances in immunotherapy and the coming of age of proteomics technology. The societal impact of these developments, in which the school’s research groups play a leading role, is enormous. Moreover, the societal impact of cancer research within the school and the Erasmus MC Cancer Institute is illustrated by the dominant role of the Daniel den Hoed Foundation, which raises some million euros in the Rotterdam region every year for research with ample public manifestations.

Main Theme 4, Infections and host response; Strategy and targets

The research in this main theme focuses on the molecular regulation of the interactions between infectious pathogens and the host and on improvement in the diagnosis, therapy and prevention of infectious diseases and immunological disorders. In spite of the advent of antibiotics, antivirals and numerous successes in the combat of infectious diseases in the past century it has now become painfully clear that known and newly emerging infectious diseases will be a major challenge for the world at large in the coming decades. This also includes the work on having control over the sometimes-severe infectious problems that are inevitably linked to transplantation of organs that needs immune-suppressive treatments. The respective workgroups closely collaborate, taking advantage of

complementary research activities and infrastructure of the other three themes. The long-term goal of main theme 4 is to limit the epidemiological, clinical and economic impact of infections, using state-of-the-art technologies.

The overall quality of the research performed by the members of MolMed within the four themes is very good to excellent (2-1). This holds for the quality of research as well as for the relevance and viability according to international standards, achieving the level of world leadership in several fields.

According to the Committee, one striking characteristic of the MolMed research community that might critically contribute to its scientific success is the high degree of interdisciplinary collaboration. There is ample room for bottom up initiatives of excellent researchers and cross-fertilization is actively encouraged. It was not possible to conduct a detailed, in depth evaluation of the research quality, relevance to society and viability of each specific research area based upon the high level of aggregation of the performance indicators provided in the self-assessment report and within the time available, but a consistent and clear overview emerged. Concerning research quality we heard passionate researchers, smart experiments, bright collaborative initiatives and challenging hypotheses. As for the relevance to society, presenting researchers showed how their research might be relevant for optimizing patient care and many concrete and interesting examples were revealed. On the basis of the documents provided, the viability of the research groups could not be assessed in a quantitative manner, however the Committee is confident that mechanisms are in place to motivate researchers to continuously apply for external grant money.

Excellent group leaders are pivotal for achieving scientific excellence and the Committee is concerned that succession planning of leaders does not seem to be in place for all groups. Note that the previous International Evaluation Committee made a similar observation on the lack of a strategy for female career development (point 4 in their report).

Also the clustering of core facilities is not optimal and facilities for proteomics, sequencing and bio-informatics should be brought together to remain effective and efficient in an international context. Critically, a clear strategy for organizing biobanking seems to be lacking.

Recommendations to the Executive Board of Erasmus Medical Centre

- A policy for rationalizing the core facilities should be developed and implemented, in particular on proteomics, sequencing and bio-informatics.
- A strategy for bio-banking should be developed.

Recommendations to the board of the MolMed School

- Formation of dedicated independent thesis committees with experienced researchers from different departments that periodically monitor the progress of each PhD student.
- Consider the establishment of a central admission programme to help with the identification and recruitment of 'high calibre' PhD students, both at the national and international level.
- Define key performance indicators to assess the output of the educational programme and enable quality control and steering.
- Establish exit polls for PhD students to gather information that can be used in future evaluations.
- Give due attention to succession of successful group leaders.

The categorization on Research quality; Relevance to society; and Viability (governance and leadership skills of management team included) according to the SEP is 1: world leading/ excellent; 2: very good; 3: good; 4: unsatisfactory, see appendix 4.

Overview of recommendations

The Committee distinguished two levels in its recommendations: recommendations addressed to the Executive Board of Erasmus Medical Centre and the board of MolMed. Overseeing the whole picture arising from the review, the International Evaluation Committee makes the following final recommendations.

To the Executive Board of Erasmus Medical Centre

- The future structure of the research and education structure – role and mandate of Institutes, Academic Centres of Excellence and postgraduate schools and their integration; see 1 B above - should become clear in the coming year.
- High priority should be given to communicating restructuring plans and considerations to the research community of Erasmus University Medical Centre in order to improve clarity, provide reassurance and generate opportunities for involvement.
- In the light of the key role that the Postgraduate School of Molecular Medicine plays in enhancing and ensuring the very high to excellent quality of the interdisciplinary translational research of Erasmus University Medical Centre, the educational programme should be maintained and reinforced.
- A policy for rationalizing the core facilities should be developed and implemented, in particular on proteomics, sequencing and bio-informatics.
- A strategy for bio-banking should be developed.

To the board of the MolMed School

The board of the Postgraduate School of Molecular Medicine could provide more effective guidance and leadership in harmonizing entitlements for PhD students. The Committee recommends to consider:

- the formation of dedicated independent thesis committees with experienced researchers from different departments that periodically monitor the progress of each PhD student.
- consider the establishment of a central admission programme to help with the identification and recruitment of 'high calibre' PhD students, both at the national and international level.
- make participation up to 30 ECTS mandatory and enforceable.
- define key performance indicators to assess the output of the educational programme and enable quality control and steering.
- establishment of exit polls for PhD students to gather information that can be used in future evaluations.
- give due attention to succession of successful group leaders.

Appendix 1

Programme of site visit

Programme Site visit MolMed, October 28-30, 2015 vs 151013			
Rooms: Hotel/ restaurant (Wed. and Thursday evening): Erasmus MC Room Ae 3.27			
Every speaker has a slot in minutes including Q&A about the presentation. After every Main Theme session, 30' is reserved for discussion. Juniors have 10' and after 2 presentations 10' discussion.			
Time	# Main Theme; breaks; # ps.	Presentations	Conf'd? Duration Board members; moderators Conf'd? Others invited
Wednesday October 28th			
Welcome at Bilderberg Parkhotel, Westsingel 70, 3015 LB Rotterdam, tel. 010-4363041; 'walking dinner'			
18.30- about 20.30	n.a.	n.a.	Board members
20.30-...		n.a.	None
Thursday October 29th; Room Ae 3.27 Erasmus MC			
9.00-9.15	Coffee		
9.15-11.15	III	Ron Matthijssen Guido Jenster John Martens discussion Wouter vd Bossche Diederik Duijnsz discussion	Ricardo Fodde (moderator) Peter Sillevs Snitt (co-moderator)
			Workgroup leaders & young investigators of Main theme III
11.15-11.30	Coffee		
11.30-12.00	n.a.		Ron Foucher
			Chair and members educational Committee
12.00-12.15	lunch		Site visit committee with PhD students & post doc committee
			PHD students & post doc committee
13.15-15.15	II	Rud Deheul Mijman van der Burg Rogier Hinzen discussion Maarten Brem Simar Pal Singh discussion	Ivo Touw (moderator) Jacques van Dongen
			Workgroup leaders & young investigators of Main theme II; PhD, Pieter Sonneved
15.15-15.30	Coffee		
15.30-17.30	I	André Uitterlinden Gerjo van Osch Liesbeth van Rossum discussion Ewout Hoorn Edward Visser discussion	Jacques van Dongen (moderator)
			Workgroup leaders & young investigators of Main theme I
18.30-.....		Dinner with the board and Hans van Leeuwen at restaurant Camaron, Westzeedijk 461A, tel. 010-477 5436 (12 ps)	Hans van Leeuwen, all board members
			Hans van Leeuwen (ad Res. & Education) (12 ps)

Appendix 2

Prof René (RAW) van Lier MD PhD

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Training: MD, University of Amsterdam

Research interests

The unifying theme of my research program is the regulation of effector/memory T cell formation in human and mice. The goals are to (1) identify functionally distinct T-cell subsets, (2) study the regulation of their specificity, expansion and effector functions, and (3) define their roles in normal and pathological immune reactions, e.g. (persistent) virus infections, allo-reactivity and immunodeficiency. Detailed knowledge on the regulation and manipulation of T cell immunity is necessary to improve the design of vaccines for infectious and malignant disease.

Resume

2010-present	Member of the Executive Board of Sanquin Blood Supply Foundation/ Research Director
2007-2013	Chairman Dutch Society for Immunology (NVVI)
2006-2011	Chairman AMC Research Council (i.e. the AMC scientific advisory board)
2006-2010	Vice-chairman of the division of Laboratory Science, AMC
2001- 2010	Head of the Dept. of Experimental Immunology, Academic Medical Centre (AMC), Amsterdam
2000-present	Professor of Experimental Immunology, University of Amsterdam
1999-2000	Head of the Dept. of Immunobiology, CLB, Amsterdam
1995-1999	Head of the laboratory for Cellular Immunology, Dept of Clinical Viro-Immunology, CLB (now Sanquin), Amsterdam
1990-1995	Fellow of the Royal Dutch Academy of Arts and Sciences (KNAW)

Other professional activities

Board member ImmunoValley Foundation

Executive secretary Scientific Advisory Board MS Research

Member Scientific Advisory Board Netherlands Lung Fund

Member Scientific Advisory Board Landsteiner Foundation for Blood Transfusion Research

President European Federation of Immunological Societies

Publications

Pascutti MF, Geerman S, Slot E, van Gisbergen KP, Boon L, Arens R, van Lier RA, Wolkers MC and Nolte MA. Enhanced CD8 T Cell Responses through GITR-Mediated Costimulation Resolve Chronic Viral Infection. *PLoS Pathog* 2015; 11 (3): e1004675.

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2. Remmerswaal EB, Klarenbeek PL, Alves NL, Doorenspleet ME, van Schaik BD, Esveldt RE, Idu MM, van Leeuwen EM, van der Bom-Baylon N, van Kampen AH, Koch SD, Pircher H, Bemelman FJ, Ten Brinke A, Baas F, Ten Berge IJ, van Lier RA and de Vries N. Clonal evolution of CD8+ T cell responses against latent viruses: relationship between phenotype, localization and function. *J Virol* 2015; 89 (1): 568-80.
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4. Arens R, Remmerswaal EB, Bosch JA and van Lier RA. 5(th) International Workshop on CMV and Immunosenescence - A shadow of cytomegalovirus infection on immunological memory. *Eur J Immunol* 2015; 45 (4): 954-7.
5. Viereira Braga FA, Hertoghs KM, Kragten NA, Doody GM, Barnes NA, Remmerswaal EB, Hsiao CC, Moerland PD, Wouters D, Derks IA, van Stijn A, Demkes M, Hamann J, Eldering E, Nolte MA, Tooze RM, Ten Berge IJ, van Gisbergen KP and van Lier RA. The Blimp-1 homologue Hobit identifies effector-type lymphocytes in humans. *Eur J Immunol* 2015; 45 (10): 2945-58.
6. de Niet A, Stelma F, Jansen L, Sinnige MJ, Remmerswaal EB, Takkenberg RB, Kootstra NA, Reesink HW, van Lier RA and van Leeuwen EM. Restoration of T cell function in chronic hepatitis B patients upon treatment with interferon based combination therapy. *J Hepatol* 2015; epub ahead of print October 23, 2015.
7. Sansoni P, Vescovini R, Fagnoni FF, Akbar A, Arens R, Chiu YL, Cicin-Sain L, Dechanet-Merville J, Derhovanessian E, Ferrando-Martinez S, Franceschi C, Frasca D, Fulop T, Furman D, Gkrania-Klotsas E, Goodrum F, Grubeck-Loebenstein B, Hurme M, Kern F, Lilleri D, Lopez-Botet M, Maier AB, Marandu T, Marchant A, Mathei C, Moss P, Muntasell A, Remmerswaal EB, Riddell NE, Rothe K, Sauce D, Shin EC, Simanek AM, Smithey MJ, Soderberg-Naucler C, Solana R, Thomas PG, van Lier R, Pawelec G and Nikolich-Zugich J. New advances in CMV and immunosenescence. *Exp Gerontol* 2014; 55C 54-62. abstract
8. Havenith SH, Remmerswaal EB, Idu MM, van Donselaar-van der Pant AMI, van der Bom N, Bemelman FJ, van Leeuwen EM, ten Berge IJ and van Lier RA. CXCR5+CD4+ follicular helper T cells accumulate in resting human lymph nodes and have superior B cell helper activity. *Int Immunol* 2014; 26 (3): 183-192. abstract
9. Ten Berge IJ and van Lier RA. The interaction between cytomegalovirus and the human immune system. *Immunol Lett* 2014; 162 (2PB): 141-144.

Eva Hellström Lindberg

Professor/senior physician

Organisational affiliation

Karolinska institutet, Unit for Hematology, Department of Medicine, Huddinge (MedH), H7

I am double specialist in hematology and internal medicine since 1993, and professor of hematology at the Department of Medicine, Huddinge since 2009. I have worked within the translational research field for many years and been actively involved in strategic research questions. I have been president both for European Association of Hematology and for Swedish Society of Hematology.

Education

I was previously involved in graduate training within ethics and communication skills, but is presently more focused on creating a good environment for post graduate student. I was chair for doctoral studies at the department for medicine for five years.

Research description

My research program focuses on the hemopoietic stem cell malignancy myelodysplastic syndromes (MDS) and include genetic, epigenetic, and cellular studies. The aim is to understand mechanisms for disease progression, leukemic transformation, and erythroid failure. I also lead a clinical specialist program for patients with this disease, as well as the Nordic MDS research group, which drives a broad clinical trial and biomarker program. I am also chair for the newly started Center for Hematology and Regenerative Medicine, Huddinge, a translational research environment combining basic and clinical competences within hematology, regenerative medicine and immunology.

Academic honors, awards and prizes

I have received both junior and senior research awards from the Swedish Cancer Society.

Publications

1. Combining gene mutation with gene expression data improves outcome prediction in myelodysplastic syndromes. Gerstung M, Pellagatti A, Malcovati L, Giagounidis A, Porta Mg, Jadersten M, *et al Nature communications* 2015;6():5901-
2. Specific scoring systems to predict survival of patients with high-risk myelodysplastic syndrome (MDS) and de novo acute myeloid leukemia (AML) after intensive antileukemic treatment based on results of the EORTC-GIMEMA AML-10 and intergroup CRIANT studies. Oosterveld M, Suci S, Muus P, Germing U, Delforge M, Belhabri A, *et al Annals of hematology* 2015;94(1):23-34
3. A mutation in the H/ACA box of telomerase RNA component gene (TERC) in a young patient with myelodysplastic syndrome. Ueda Y, Calado Rt, Norberg A, Kajigaya S, Roos G, Hellstrom-lindberg E, *et al BMC medical genetics* 2014;15():68-
4. A pilot phase I dose finding safety study of the thrombopoietin-receptor agonist, eltrombopag, in patients with myelodysplastic syndrome treated with azacitidine. Svensson T, Chowdhury O, Garelius H, Lorenz F, Saft L, Jacobsen Se, *et al European journal of haematology* 2014;93(5):439-45
5. Azacitidine induces profound genome-wide hypomethylation in primary myelodysplastic bone marrow cultures but may also reduce histone acetylation. Grovdal M, Karimi M, Tobiasson M, Reinius L, Jansson M, Ekwall K, *et al Leukemia* 2014;28(2):411-3
6. Cardiac iron overload assessed by T2* magnetic resonance imaging and cardiac function in regularly transfused myelodysplastic syndrome patients. Bowen Dt, Hellstrom-lindberg E, Steensma Dp *British journal of haematology* 2014;164(4):610-1
7. Challenges of phase III trial design for novel treatments in diseases with no standard treatment: the AZA-001 myelodysplasia study model. Fenaux P, Seymour Jf, Santini V, Silverman L, Gore S, List A, *et al Leukemia research* 2014;38(2):258-62
8. Limited clinical efficacy of azacitidine in transfusion-dependent, growth factor-resistant, low- and Int-1-risk MDS: Results from the nordic NMDSG08A phase II trial. Tobiasson M, Dybedahl I, Holm Ms, Karimi M, Brandefors L, Garelius H, *et al Blood cancer journal* 2014;4():e189-
9. Lung transplantation in telomerase mutation carriers with pulmonary fibrosis. Silhan Ll, Shah Pd, Chambers Dc, Snyder Ld, Riise Gc, Wagner Cl, *et al The European respiratory journal* 2014;44(1):178-87
10. Myelodysplastic syndromes are propagated by rare and distinct human cancer stem cells in vivo. Woll Ps, Kjallquist U, Chowdhury O, Doolittle H, Wedge Dc, Thongjuea S, *et al Cancer cell* 2014;25(6):794-808

Prof. Stuart Ralston

Arthritis Research Council Chair of Rheumatology

Research Group: Rheumatology & Bone Disease, Institute of Genetics & Molecular Medicine, Centre for Genomic & Experimental Medicine, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, United Kingdom

Stuart H Ralston graduated in Medicine from Glasgow University in 1978 and underwent higher medical training in General Internal Medicine and Rheumatology. He previously held the chair of Medicine and Bone Metabolism at the University of Aberdeen and moved to Edinburgh University in 2005 when he now holds the Arthritis Research UK Chair of Rheumatology. He is academic director of Edinburgh Clinical Trials Unit and director of Edinburgh University's online distance learning MSc in clinical trials. Professor Ralston holds an honorary consultant rheumatologist position with NHS Lothian where he is clinical lead for the osteoporosis service and clinical director of the rheumatology service. Professor Ralston has researched widely on the molecular and genetic basis of osteoporosis and other bone and joint diseases. He has a special interest in the pathogenesis and management of Paget's disease of bone. He is joint editor-in-chief of the scientific journal *Calcified Tissue*

International and an editor of Davidson's Textbook of Medicine. Professor Ralston currently chairs the Commission for Human Medicines for the Medicines and Healthcare Regulatory Authority of the UK

Academic Qualifications

- **Bachelor:** 1978, Bachelor of Medicine, University of Glasgow
- **Doctorate:** 1987, Doctor of Medicine, University of Glasgow

Professional Qualifications

- 2005, Fellow of the Royal Society of Edinburgh, FRSE
- 1999, Fellow of the Academy of Medical Sciences, FM
- 1994, Fellow of the Royal College of Physicians Edinburgh, FRCP (Edin)
- 1980, Member of the Royal College of Physicians, MRCP

My research focuses on the genetic determinants of bone and joint disease, as a means of gaining greater understanding of the pathophysiology of conditions such as osteoporosis, osteoarthritis and Paget's disease. The ultimate aim is to translate the knowledge gained to improve clinical outcome for patients.

Publications list

1. Optineurin Negatively Regulates Osteoclast Differentiation by Modulating NFκB and Interferon signaling; implications for Paget's disease. 10 Nov 2015 - Cell Reports, Vol: 13.
2. Whole-genome sequencing identifies EN1 as a determinant of bone density and fracture
3. 14 Sep 2015 – Nature.
4. The type 2 cannabinoid receptor regulates susceptibility to osteoarthritis in mice. Sep 2015 - Osteoarthritis and Cartilage, Vol: 23.
5. Characterisation of osteoprotegerin autoantibodies in coeliac disease. Aug 2015 - Calcified Tissue International, Vol: 97, Page(s): 125-33.
6. Bone cell-autonomous contribution of type 2 cannabinoid receptor to breast cancer induced osteolysis. 20 Jul 2015 - Journal of Biological Chemistry.
7. Bisphosphonates for the prevention of fractures in osteogenesis imperfecta : meta-analysis of placebo-controlled trials. May 2015 - Journal of Bone and Mineral Research, Vol: 30, Page(s): 929-33
8. Autoantibodies to osteoprotegerin are associated with increased bone resorption in rheumatoid arthritis. 29 Apr 2015 - Annals of the Rheumatic Diseases
9. Atypical Femoral Fracture in Osteoporosis Pseudoglioma Syndrome Associated With Two Novel Compound Heterozygous Mutations in LRP5. Apr 2015 - Journal of Bone and Mineral Research, Vol: 30, Page(s): 615-620
10. Predictors of poor clinical outcome following hip fracture in middle aged-patients. Apr 2015 - Injury, Vol: 46, Page(s): 709-712
11. Targeted sequencing of the Paget's disease associated 14q32 locus identifies several missense coding variants in RIN3 that predispose to Paget's disease of bone. 20 Feb 2015 - Human Molecular Genetics

Prof. Thomas Schulz

Institut für Virologie; Medizinische Hochschule Hannover; Carl-Neuberg-Str. 1; 30625 Hannover

Prof. Thomas F. Schulz is full (C4) Professor of Virology and Director of the Institute of Virology at MHH.

Undergraduate and Postgraduate Training

1972 – 1979	Medical School in Mainz, Montpellier and London
1980	Medical Doctorate
1986	Habilitation
1990	Certificate of Completed Specialist Training in Medical Microbiology, Virology, Infection Epidemiology
1998	Member of the Royal College of Pathologists (MRCPATH)
2003	Fellow of the Royal College of Pathologists (FRCPath)

Research Interests and Achievements

My research focusses on Kaposi Sarcoma herpesvirus (KSHV), the cause of Kaposi Sarcoma, primary effusion lymphoma and the plasma cell variant of Multicentric Castleman's Disease. My contributions to this field include studies on the distribution, transmission and tumour association of this virus, using serological assays that we had developed on the basis of recombinant viral proteins. My group was the first to clone the viral gene encoding the latent nuclear antigen, LANA, (Rainbow et al., 1997) and to identify the K15 gene, a multiply and variably spliced KSHV gene (Glenn et al., 1999). In the last 10 years we have been characterising different aspects of these viral proteins, such as the signal transduction pathways initiated and cellular genes activated by K15 and its role in KSHV-induced angiogenesis (Bala et al., 2012). We also showed for the first time that a member of the BET protein family of human chromatin proteins interacts with a viral protein (i.e. LANA). Together with T. Lühns, HZI, we have recently solved the molecular structure of the c-terminal, DNA-binding, domain of LANA and used this structural information to derive new insights into the role of BET proteins in the viral life cycle (Hellert, Weidner-Glunde et al., 2013). Other research projects deal with the role of p73 in the survival of KSHV-infected cells (Santag et al., 2012) and the identification of new inhibitors to target KSHV persistence and replication.

10 Selected Publications (of 219 original publications)

1. Gramolelli S, Weidner-Glunde M, Abere B, Viejo-Borbolla A, Bala K, Rückert J, Kremmer E, Schulz TF. Inhibiting the recruitment of PLC γ 1 to Kaposi's Sarcoma Herpesvirus K15 protein reduces the invasiveness and angiogenesis of infected endothelial cells. *PLoS Pathog*. 2015; 11(8):e1005105. doi: 10.1371/journal.ppat.1005105
2. Hellert J, Weidner-Glunde M, Krausze J, Lünsdorf H, Ritter C, Schulz TF*, Lühns T*. (2015) The 3D-structure of Kaposi's sarcoma herpesvirus LANA c-terminal domain bound to DNA. *Proc Natl Acad Sci U S A*. 2015; 112: 6694-9. *joint senior author
3. Haas DA, Bala K, Büsche G, Weidner-Glunde M, Santag S, Kati S, Gramolelli S, Damas M, Dittrich-Breiholz O, Kracht M, Rückert J, Varga Z, Keri G, Schulz TF The inflammatory kinase MAP4K4 promotes reactivation of Kaposi's Sarcoma Herpesvirus and enhances the invasiveness of infected endothelial cells. *PLoS Pathogens* 2013; 9(11):e1003737. doi: 10.1371/journal.ppat.1003737.
4. Hellert J, Weidner-Glunde M, Krausze J, Richter U, Adler H, Fedorov R, Pietrek M, Rückert J, Ritter C, Schulz TF*, Lühns T*. A structural basis for BRD2/4-mediated host chromatin interaction and oligomer assembly of Kaposi Sarcoma Herpesvirus and murine gammaherpesvirus LANA proteins. *PLoS Pathogens* 2013; 9(10):e1003640. doi: 10.1371 *joint senior authors
5. Bala K, Bosco R, Gramolelli S, Haas DA, Kati S, Pietrek M, Hävemeier A, Yakushko Y, Singh VV, Dittrich-Breiholz O, Kracht M, Schulz TF Kaposi's Sarcoma Herpesvirus K15 protein contributes to

- virus-induced angiogenesis by recruiting PLC γ 1 and activating NFAT1-dependent RCAN1 expression. *PLoS Pathogens* 2012; 8:e1002927. doi: 10.1371
6. Santag S, Jäger W, Karsten C, Kati S, Pietrek M, Steinemann D, Sarek G, Ojala P, Schulz TF Recruitment of the tumour suppressor protein p73 by Kaposi Sarcoma Herpesvirus latent nuclear antigen contributes to the survival of primary effusion lymphoma cells. *Oncogene*, 2012; doi: 10.1038/onc.2012.385.
 7. Glenn, M., Rainbow, L., Aurade, F., Davsion, A., Schulz, T.F. Identification of a multiply spliced gene of KSHV/HHV8 with similarities to the latent membrane proteins of EBV. *J.Virol.* 1999; 73: 6953 - 6963
 8. Rainbow, L., Platt, G.M., Simpson, G.R., Sarid, R., Gao, S.-J., Stoiber, H., Herringston, C.S., Moore, P.S., Schulz, T.F. The 222-234 kd nuclear protein (LNA) of Kaposi's sarcoma - associated herpesvirus (KSHV/HHV 8) is encoded by orf73 and a component of the latency-associated nuclear antigen (LANA). *J.Virol.* 1997; 71: 5915-5921
 9. Simpson, G.R., Schulz, T.F.*, Whitby, D., Cook, P.M., Boshoff, C., Rainbow, L., Howard, M., Gao, S.-J., Bohenzky, R.A., Simmonds, P., Lee, C., de Ruiter, A., Hatzakis, A., Tedder, R.S., Weller, I.V.D., Weiss, R.A., Moore, P.S. Prevalence of Kaposi's sarcoma associated herpesvirus infection measured by antibodies to recombinant capsid protein and latent immunofluorescence antigen. *Lancet* 1996; 348:1133 – 1138 *corresponding author
 10. Whitby, D., Howard, M.R., Tenant-Flowers, M., Brink, N.S., Copas, A., Boshoff, C., Hatzioannou, T., Suggett, F.E.A., Aldam, D.M., Denton, A.S., Miller, R.F., Weller, I.V.D., Weiss, R.A., Tedder, R.S., Schulz, T.F. Detection of Kaposi's sarcoma associated herpesvirus in peripheral blood of HIV-infected individuals and progression to Kaposi's sarcoma *Lancet* 1995; 346:799-802.

Prof.dr. A.J. Gelderblom

Prof.dr. A.J. Gelderblom is chair of the Department of Medical Oncology of the Leiden University Medical Center.

Biosketch

Prof. dr. A.J.(Hans) Gelderblom followed his internal medicine training at the Academic Hospital Utrecht/Streekziekenhuis Hilversum between 1993-1998. From 1998-2001 he worked at the Daniel den Hoed Kliniek for his training for medical-oncologist in conjunction with his PhD project on pharmacological aspects of various new anticancer drugs. He was also involved in the first studies with imatinib in GIST and was trained in the sarcoma clinic. Starting 2001 he was staff member medical oncology at the Leiden University Medical Center and consulting oncologist in the region. In 2010 he was appointed professor of internal medicine, specifically Experimental Oncological Pharmacotherapy and in 2015 he was appointed head of the department of medical oncology. He holds several international positions such as (previous) board member van de European Organisation for Research and Treatment of Cancer (EORTC), current secretary of the EORTC Soft Tissue and Bone Sarcoma Group and chair of the European Osteosarcoma Intergroup. His specific research aims are to personalise anticancer therapy and to develop new systemic treatments for sarcoma patients.

Publications: see PubMed H. Gelderblom (H-index 53)

Dr. Jessika van Kammen, PhD

Head of the Research Office and secretary of the AMC Research Council; Academic Medical Center University of Amsterdam.

Appendix 3

Quantitative data on the research unit's composition and financing

The numbering of the tables is equal to that of the Assessment report of MolMed.

Table 2.1 shows the total number of research staff in FTE's over the past period (NB = SEP table D3a), as well as distinguished for the different types of positions, which however may not be 100% correct. We are aware that many people registered as a scientific researcher actually have another function. Also note that Endowed professors ('Bijzonder Hoogleraar') are registered as Associate professor ('UHD'). The number of researchers involved in the research programs varied from ~950 in 2011 to ~800 in 2014 (-15%). The number of PhDs seems to have risen, but it cannot be excluded that a certain proportion of them is also registered as researcher.

Molecular Medicine: Research staff	2010	2011	2012	2013	2014
Full professor (<i>hoogleraar</i>)	11	14	14	13	10
Associate professor & Endowed professor (<i>UHD & Bijz. hoogleraar</i>)	32	32	31	29	27
Assistant professor (<i>UD</i>)	16	20	16	16	17
Scientific researcher (<i>wet. onderzoeker</i>)	431	483	466	471	406
PhD candidate (<i>promovendi</i>)	74	82	67	84	106
Administrative and support staff & Irregular staff (<i>overig wet. personeel</i>)	333	323	279	279	227
Total research staff	897	954	873	892	793

Table 2.1, total amount of research staff in FTE's

The organization of the school is 'lean and mean'. It consists of a small executive staff of about 2 Fte that organizes the educational program and is responsible for the administration of the school, see **table 2.2**.

Molecular Medicine: Office staff (fte)	
Managing director	0.94
Secretary	0.89
Secretarial assistance	0.45
Total	2.28

Table 2.2, staff of the MolMed school

Internal and external sources of financing

Table 3.1 and **fig. 3** give the total Fte's of the research groups per funding source (NB = SEP table D3c). NB both show the same data but in a different form. The researchers are very successful in gaining external funding, which makes up 59% of the research budgets. However, we see here as well that the funding was reduced by about 10% from 2010-2014, except for the government funding.

Personnel (fte) per Funding source	2010	2011	2012	2013	2014	average (%)
Direct funding (G1)	396	437	401	406	357	41
Government funding (G2)	225	224	233	256	222	24
Research grants from foundation (G3)	162	174	147	141	138	16
Contract research and other (G4)	194	201	174	167	171	19
Total Funding (fte)	978	1036	954	969	887	100

Table 3.1 Funding in fte

Results (+ or -)	-68.496	-22	- 100.00 9	-26	3.951	1	-297	0	-9.558	-3

Table 3.2, funding of MolMed office and activities; (*) preliminary figures

Appendix 4

Guidelines for assessment according to SEP 2015-2021 (Table 1)

Category	Meaning	Research quality	Relevance to society	Viability
1	World leading/ excellent	The research unit has been shown to be one of the few most influential research groups in the world in its particular field.	The research unit makes an outstanding contribution to society.	The research unit is excellently equipped for the future.
2	Very good	The research unit conducts very good, internationally recognized research.	The research unit makes a very good contribution to society.	The research unit is very well equipped for the future.
3	Good	The research unit conducts good research.	The research unit makes a good contribution to society.	The research unit makes responsible strategic decisions and is therefore well equipped for the future.
4	Unsatisfactory	The research unit does not achieve satisfactory results in its field.	The research unit does not make a satisfactory contribution to society.	The research unit is not adequately equipped for the future.