Site visit report

VUmc-CCA

8-9 December 2015

Foreword

This report represents the assessment of the research institute Cancer Center Amsterdam VU Medical Center (Vumc-CCA) conducted 8 and 9 December, 2015.
It is based on documentation presented to the review committee and on meetings with the various representative bodies and persons of CCA-VUmc.
The committee wishes to express their appreciation for the organization of the site visit and the contribution of all the participating people. They like to thank all persons involved for the open and informative discussions.

In conclusion the committee is convinced of the societal relevance of the research that is conducted in this institute. The research quality is in general very good and within some groups and themes excellent with high impact publications and promising grant applications.

In the near future a lot of strategic choices and decisions have to be made, especially regarding the implementation of the upcoming merger with the Amsterdam Medical Center (AMC) in cancer and immunology research and patient care. The committee hopes that the recommendations in this review will help to make these decisions and wishes the board of the institute wisdom and an open mind in exploiting (and exploring) all the opportunities of this joint initiative.

Lelystad, May 2016

Prof B. Nelson, chairman

Dr. P. Keblusek, secretary

Content

I Introduction

This site visit was arranged by the management board of the VUmc-Cancer Center Amsterdam (VUmc-CCA) in accordance to the new Standard Evaluation Protocol (SEP 2015-2021) of the Association of Universities in the Netherlands (VSNU), the Netherlands Organization for Scientific Research (NWO) and the Royal Netherlands Academy of Arts and Sciences (KNAW).
The research institute VUmc-CCA encompasses all the oncology and immunology research within the VUmc.

The members of the site visit committee existed of:

- W.G. Nelson, MD PhD (chairman) - Professor Oncology/ Director of the Sidney Comprehensive Cancer Center at Johns Hopkins, Baltimore, USA
- C.G. Figdor, PhD - Professor of Immunology, Tumor Immunology / Head of the department of tumor Immunology, Radboud University Medical Center, Nijmegen, The Netherlands
- C.G.M. Kallenberg, MD PhD - Professor of Clinical Immunology / former Head Department of Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen, The Netherlands
- D.J. Kerr, MD PhD – Professor of Cancer Medicine / Head of the Cancer Biomarkers Group Nuffield Dept of Clinical and Laboratory Sciences, John Radcliff Hospital, University of Oxford, Oxford, UK
- D. Lambrechts, MD PhD – Full Professor, Laboratory of Translational Genetics, Department of Oncology, University of Leuven, Belgium and Director of the Vesalius Research Center, VIB, Leuven.
- P. Keblusek PhD (secretary)

Curriculum Vitae of the members of the site visit committee are found in appendix 1

Prior to the site visit the following documents were provided:

- Self Evaluation Report 2009-2014
- SEP evaluation Protocol 2015-2021
- Mid-term Self Evaluation report 2009-2011
- Report Site Visit 2009
- Annual reports & appendices 2009-2014 (online) and 2014 printed version
- OOA self evaluation report 2015
- Program of the site visit

The committee spoke to:

- the board of the VU University Medical Center
- the board of the VUmc- Cancer Center Amsterdam (VUmc-CCA)
- Program leaders of the 5 research programs within the VUmc CCA
- PhD students and members of the ProPhD committee
- Postdoctoral students
- members of the education committee
- the board of the Oncology Graduate School Amsterdam (OOA)

The program of the site visit is found in appendix 2

The site visit was well organized and expanded to 1,5 day following the recommendations of the site visit committee in 2009. There was time to have both formal and informal talks to the various people involved in the research institute including, staff, postdocs and PhD students. Discussions were constructive and informative.

The VUmc CCA contains five programs. The highlights of these programs were briefly presented by the program leaders. During these presentations, as well as from the documentation provided, it was difficult to assess individual research groups within a specific program.

Therefore in the assessment below the five programs are considered as a whole and not assessed in detail on the strong and weaker groups within such a program.

II Items to assess of the research institute VUmc-CCA

A. Brief description of the research institute's strategies and targets

Twenty years ago the research of the VUmc started to become horizontally organized across the divisions and departments into a matrix institute model. Twelve years ago the management of the VUmc decided to restrict its academic focus to five areas organized within five research institutes: Cancer & Immunology, Cardiovascular diseases, Neurosciences, Public Health and Movement sciences. VUmc CCA is one of the largest such institute and brings together oncology and immunology research and patient care.

The main goal of VUmc CCA is to prevent and cure cancer and immunological diseases, and - as a consequence - decrease morbidity and mortality in these diseases.

The VUmc CCA has three main research aims:
- Early diagnostics
- Personalized treatment
- Quality of life

These three main research aims are covered by the five research programs:

Program 1: Oncogenesis
The main objectives are on identification and characterization of viral and non-viral cancer genes, along with cancer predisposition genes, searching for molecular biomarkers and molecular targets that can potentially be used therapeutically.
In the program, there are two research lines:
- Viral oncogenesis, progression and early diagnostics
- Genetic predisposition and cancer genes

Program 2: Immunopathogenesis
The main objectives are on basic and translational research in immune homeostasis and inflammation, host-pathogen interactions and tumor immune escape.
The three research lines are:
- Immune homeostasis and Inflammation
- Host-pathogen interactions
- Tumor immunology and pre-clinical immune therapy

Program 3: Disease Profiling
This program is mainly focused on the discovery and development of molecular biomarkers as tools for detection of cancer and immunological diseases, diagnosis, risk stratification, and treatment monitoring.
The three specific research lines are:
- Solid tumors
- Hematological malignancies
- Chronic inflammatory diseases

Program 4: Innovative Therapy

The main objectives are to introduce and evaluate new treatment approaches across surgical, radiotherapeutic and medical treatment of oncological disorders.
The two research lines are:

- Targeted therapy, including radiotherapy, surgery and systemic therapy
- Immunotherapy

Program 5: Quality of Life

The main objectives are on physical function, psychosocial factors, communication, and palliative care in oncology.
The four main topics are:

- Patient and proxy reported outcome
- Allied health services and lifestyle
- Psycho-oncology
- Palliative Care

The program was created in 2010 after the previous external evaluation conducted in 2009
This program interacts significantly with public health and the public health VUmc research institute EMGO+

Since the last site visit in 2009 improvements have been made on:

- Integration of V-ICI and CCA into VUmc CCA, including the supportive staff;
- Explicit focus on quality of life by creating a fifth research program 'quality of life' in 2010 ;
- Improved communication and visibility by among others a new website and up-to-date newsletters;
- Improved focus and integration on research and patient care by the installment of Focus groups on Oncology and Immunology in 2011;
- Development of a talent program (Huijgens Program);
- Improved integration of preclinical and clinical research by initiation of multidisciplinary care pathways;
- Funding by 'Stichting VUmc CCA' making big facilities and infrastructure possible like a new building for outpatient facilities in 2011.

Future targets and plans:

1. Alliance of VUmc and AMC to establish two joint research institutes, one for oncology and one for immunology
   Oncology main themes will be:
   - tumor biology and immunology
   - diagnostics
   - treatment and quality of life and care

   Immunology main themes will be:
   - inflammatory diseases
   - infectious diseases
   - cancer immunology (as common theme within both institutes)
2. Improve multidisciplinary infrastructure (like Liquid Biopsy Center)
3. Support for researchers to initiate and submit large program grant applications
4. Starting a new immunology graduate school similar to the OOA
5. Stronger branding and external communication with the support of a communication advisor
6. Intensifying existing partnerships with hospitals in the region to expand joint clinical trials

B. Qualitative and quantitative assessment of the three criteria

1. Research Quality

From the data provided it is clear to the committee that the VUmc CCA can claim several impressive research achievements in all five research programs.

Program 1: Oncogenesis
Highlights:
- Elucidation of key functions of intrastrand DNA crosslink repair, including Fanconi anemia (and Xeroderma pigmentosum) genes;
- Development of molecular diagnostic tools for HPV detection and for cervical cancer detection (using DNA methylation markers).

Comments site visit committee:
- The program may be amongst the best in the Netherlands for DNA repair defects as applied to cancer, for head and neck cancer, and for HPV biology;
- Focus and vision for the future are unclear. Some of the choices made seem to come from departments rather than from a clear institutional vision (e.g. choice for tumor types);
- High focus on individual principal investigators (=PI)'s lacking the institutional benefit;
- Straight forward approach. Lack of novelty research initiatives.

Program 2: Immunopathogenesis
Highlights:
- Studies on the role of the microenvironment in immune homeostasis and tumor development;
- Several novel cancer immunotherapies have been introduced into cancer clinical trials.

Comments site visit committee:
- Research quality is strong with high impact publications especially in basic immunology;
- The work is supported by a number of specialized key technologies;
- Ambitious plans for immunotherapy center;
- The program is a key innovator in the study of the (tumor) microenvironment;
- Basic immunology and applied immunology are hardly integrated; translational research can be improved in immunology;
- Lack of focus and future vision.
    - It was unclear to the committee how critical decisions, such as the establishment of a chimeric antigen receptor T cell therapy facility, are made; is there a leadership of the institute based on a coherent program or are decisions made by the departments?;
    - What is the focus of the research of the new combined department of rheumatology (VUmc, AMC, Jan van Breemen Institute)?;
    - What is the vision on the structure of the new immunological institute, especially for this program since this program will be part of both new alliance research institutes. A new institute in infection and immunity will house inflammation, autoimmunity, and infectious diseases. Infectious disease at the AMC is stronger however more patients with inflammatory diseases are housed at the VUmc. One risk of the new institute is that it might create barriers to studies of the contribution of innate immunity and the microbiome/biofilms to the development of cancers, such as colorectal cancer.

Program 3: Disease Profiling

Highlights:

- Platelet-associated RNA has emerged as attractive liquid biopsy platform;
- Phosphoproteomics capabilities poised to deliver pharmacodynamic biomarkers for clinical development of kinase inhibitors for cancer;
- Tracer-labeled antibodies/antibody-drug conjugates under development to aid in clinical development programs, forming the basis of a center of excellence for molecular and functional imaging.

Comments site visit committee:

- Very strong reputation in imaging. Distinctive and competitive in Liquid Biopsy (cfr. recent publication and international press coverage on platelet-associated RNA);
- Research resulted in spin-off company for diagnostic tool for Ab-linked therapy (G. van Dongen);
- Focus on quite a lot of tumor types makes profiling more diffuse;
- Clear need for bioinformatics force. Doubtful if sufficient statistical power (and even manpower) is available to compete internationally for genomics profiling;
- Departure of research group of Gerrit Meijer resulted in limited epigenetic profiling capabilities.

Program 4: Innovative Therapy

Highlights:

- Development of minimal residual disease detection tools for acute myeloid leukemia;
- Minimally invasive surgery for colorectal cancer;
- Thoracic radiotherapy for extensive small cell lung cancer, with publications in the *New England Journal of Medicine* and *Lancet.*

Comments site visit committee:

- Phase I/II lot of competition (inter)nationally. With the merge of VUmc and AMC and increase of patient numbers more competitive;
- Phase III trials strong;
- Good flow of new products;
- Challenge to keep focus with the large number of departments involved. This will be even more after the merge;
- An upcoming challenge will be harmonizing standard-of-care pathways and clinical research oversight and prioritization;
- Remain independent of industry – determine what is industry driven and what institute driven;
- Threat in clinical research infrastructure, for instance no central clinical trial service available at the moment;
- Need to facilitate early-stage clinicians with more time protected for research efforts.

Program 5: Quality of Life

Highlights:

- Expertise Center Palliative Care;
- Research on end-of-life, high impact *Lancet* publication on assisted suicide;
- Research on monitoring quality of life.

Comments site visit committee:

- Small group that is internationally highly competitive;
- Strong focus;
- Many new tools and instruments under development. Tools look great and of high societal relevance;
- After merge opportunity for training, education, and credentialing of specialized palliative care providers using consultant palliative care assets at VUmc and AMC;
- Program interacts significantly with public health;

- Innately well-aligned with emerging Ministry of Health priorities on psychosocial support.

Evaluation of the research quality has been through publication metrics: numbers of papers, numbers of papers in high-impact journals, number of grants etc.
As stated in the first section this was done per research program making it difficult to assess specific investigators or research groups within the programs.

Overall the non-oncology related immunological research was less visible due to a much lower amount in fte and having the main focus of the institute on oncology rather than on immunological research in general. Research achievements in basic immunology, especially in immune homeostasis and mucosal immunology are internationally recognized but translational immunology in chronic inflammatory disease is less visible.

Infrastructure

Now-a-days excellent research quality is only made possible by the right scientific technologies and infrastructure. The board of VUmc CCA stated in their self-evaluation that the research institute contributes to a better interaction between cancer and immunology research and patient care. The VUmc CCA provided infrastructure facilitates and supports this interaction. For example, it physically brings together researchers in a separate CCA building, it facilitates in ICT solutions for multidisciplinary translational research and made big investments possible on infrastructures like imaging, personalized diagnostics and treatment, support for in house clinical trial design and data management.

During the site visit it became clear that in the last years state of the art infrastructure is realized and that still a lot of these infrastructure is still on demand. With the merge of the VUmc and AMC hopefully more opportunities to create such infrastructure will be made possible.

The foundation of the 'Stichting VUmc CCA' makes it possible to invest in larger infrastructural projects. During the site visit two of these investments were shown that weren't made possible without the funding by VUmc CCA: the specialized nanoscope microscope and the MRIdian.

Assessment in categories

The committee assesses the overall contribution of the VUmc CCA to research quality as very good = category 2.

For the individual programs the committee rated the research quality as:

Program 1: Oncogenesis	2
Program 2: Immunopathogenenis	2
Program 3: Disease Profiling	2
Program 4: Innovative Therapy	2
Program 5: Quality of Life	1

All the scores are an average score for each program. Within each program the committee recognized very good high-level research as well as moderate low-level research. Since the committee was not able to judge individual groups, the scores within the programs become averaged, resulting in a 2 for almost every program. The only program that gets an excellent score is 'Quality of Life' which is the smallest program. Being such a small program made it more easy to present very focused the results and future directions that were innovative and of excellent quality.

2. Relevance to society

The topic of oncology and immunology research is by itself a highly relevant subject for society.

Within VUmc CCA several initiatives and research outcomes lead to the immediate implementation into the clinic.

Among others:

- Research has already delivered an HPV screening tool to be adopted throughout the Netherlands in 2016;
- New DNA methylation markers will likely be commercialized and deployed to further improve cervical cancer screening over the next 6 years;
- Innovations in minimally invasive colorectal cancer surgery were pioneered at the VUmc CCA
- New diagnosis tools with liquid biopsy are promising and relevant;
- Quality of life focus is in line with national priorities on psychosocial support.

Moreover there are several spin-off activities and companies directly associated with the research within VUmc CCA, such as a company developing a diagnostic tool for Ab-linked therapy.

The future alliance of the VUmc and AMC in oncology and immunology research and patient care can lead to a better focus and alignment on research priorities and a higher number of patients available for diagnostic studies and clinical trials.

- The combined VUmc and AMC Cancer Center Programs will deliver cancer care services to ˜12,000 new cancer patients each year;
- >20% participation of cancer patients in clinical trials will improve quality of care at VUmc CCA, and will lead to improved cancer outcomes throughout the Netherlands;
- The immunological research efforts and patient care on infectious diseases will probably move to the AMC campus, becoming embedded in a stronger immunological research focus. For the chronic inflammatory diseases it is not clear yet. In rheumatology there is already a merge.

<u>Assessment in categories</u>
The committee assesses the overall contribution of the VUmc CCA to societal relevance as excellent = category 1

For the individual programs the committee rated the societal relevance as:

Program 1: Oncogenesis	1
Program 2: Immunopathogenenis	2
Program 3: Disease Profiling	2
Program 4: Innovative Therapy	1
Program 5: Quality of Life	1

3. Viability

The viability of the VUmc CCA is highly influenced by the upcoming plans to merge the cancer and immunological research and patient care of the VUmc and AMC (= Amsterdam Medical Center).

The AMC is mostly characterized by diverse individual investigators spread across traditional academic departments. The AMC has not historically supported the matrix institute model for managing targeted research adopted by the VUmc. It is recognized among the different institutes that the horizontally organized research institute matrix of the VUmc is in favor to organize focused and inter-departmental combined research efforts. Therefore, the terms of the upcoming merger feature alignment with the VUmc institutes. Harmonizing faculty advancement policies and procedures will pose a cultural challenge.

Of course the merger will give a lot of opportunities in increased patient numbers, integration and alignment of research focus and combining infrastructural facilities.

On the other hand, separating the institutes for oncology and immunology might create barriers to for example studies of the contribution of innate immunity and the microbiome/biofilms to the development of cancers, such as colorectal cancer. The idea is that after the merger there will come an immunological institute. However, it is the opinion of the committee that the oncological oriented immunology should preferentially be located as close as possible to where the clinical activities are centralized. This will maximize bench to bedside translation. Perhaps they participate in both institutes.

Leadership

Within the board of VUmc CCA the members each have a specific focus for the research programs, education and clinical care. Moreover, all research programs have 3-5 program leaders. This works well.

After the merger the leadership of VUmc CCA will probably be revised.
The VUmc CCA leadership team will need (inter)nationally recognized leaders for clinical research (managing the clinical research office), laboratory research (managing space), shared resources (securing equipment/instrumentation), medical oncology care, radiation oncology care, surgical oncology care, etc.

Financial support

The strength in focus and steering power of the board of VUmc CCA would be much more pronounced, if money streams would flow more to the institute than towards the university divisions and departments. The grid structure gives only very little decision making power for the director and its board. They are not really in a position where they can directly stimulate excellence in research. Because of this there are also no clear tools to promote excellent PIs.

The VUmc CCA director is supplied with €1-2M from a foundation (Stichting VUmc CCA) and some funds from clinical VUmc operations. Some money from the Stichting VUmc CCA is ear-marked. Although ear-marking should be as less as possible it gives the opportunity to invest in large specific projects for scientific instruments and infrastructure.
The rest of the institutional money is divided among submitted projects from within the institute and judged and allocated by the scientific committee and the board. This includes all PhD students paid by the VUmc (first money stream). The VUmc board is given a lumpsum for research that flows primarily to the departments and not to the research institutes.

All of the investigators working on cancer and immunology, across many departments, come under the supervision of the VUmc CCA board. The committee noted that it is very important to delineate the responsibilities of the departments versus the institute! For the committee this seems not always to be clear. The scientific committee of VUmc CCA approves grant applications. The board of VUmc CCA approves grant applications, aids in the recruitment of new researchers, and manages the research portfolio, including clinical trials research.

The majority of the proposed research was strongly clinical or translational. Very little basic research was presented. Fundamental and basic research is, however, necessary to create innovative new translational research lines and remain internationally competitive. Within the Netherlands, grant funding for basic research is difficult to obtain (because of the policies within grant organizations). Therefore it would be desirable that the institute should facilitate basic research in specific research lines, as this is likely to increase the sustainability of the institute.

From 2016 incentives will be given to researchers that obtain a grant application.

Assessment in categories

The committee assesses the overall contribution of the VUmc CCA to viability as very good = category 2.

For the individual programs the committee rated the viability as:

Program 1: Oncogenesis	2
Program 2: Immunopathogenenis	2
Program 3: Disease Profiling	2
Program 4: Innovative Therapy	2
Program 5: Quality of Life	2

C. Qualitative assessment of the PhD Programs and research integrity policy.

1. PhD programs

The PhD program within VUmc CCA is much better organized and structured upon the last site visit. At the start of a PhD track all students and their supervisors need to deliver an education and training plan including agreements on supervision and education program. This plan has to be approved by the education committee of VUmc CCA. In addition, at least two supervisors need to be allocated to one PhD student diminishing problems obstructing the PhD track due to interpersonal issues. Having an independent PI involved would support even better the PhD mentoring process (see recommendations part).

Education for the PhD students in the oncology field is organized within the OOA (Oncology Graduate School Amsterdam). The OOA is a collaboration between the VUmc, AMC and the NKI/AvL (= Dutch Cancer Institute/Antoni van Leeuwenhoek hospital) . The graduate school for immunology ALIFI is non-existing anymore. Plans are made to start a new graduate school on Immunology within the merge of the VUmc and AMC.

The OOA is recently being assessed in October this year. The site visit report was not yet available to this site visit committee. Main recommendations were made upon the alignment of procedures and processes within the OOA. The merge of the VUmc and AMC will likely have a positive influence on this.

The PhD students are represented by a ProPhD committee. This committee organizes special VUmc CCA days for new PhD students and regularly meets with the education committee in order to improve upon the course program for PhD students.

The site visit committee is impressed by the high quality of PhD students, their enthousiasm and mature attitude. Several programs to scout for talented researchers are in place, like the Huijgens Program (PHD

student), Diamond Program (OOA) deserves extension and the Honours Program (for undergraduate MD students).
All institutional PhD student projects (13) (1st money stream) are reviewed and approved by VUmc CCA.

Although it seems that the care for PhD students is well embedded in the existing PhD Program, for the postdoctoral development a lack of a structured mentorship/oversight program is noticed. The duration of post-doctoral fellowships can be quite heterogeneous, and there is no existing governor, other than Dutch regulations (3 years and then a 'fixed' position), on how long such fellowships can last.

For postdoctoral fellows are retreats and career fairs that tend to be directed to post-doctoral fellows.

The committee noted that a relatively low number of PhD-students/post-docs were internationally recruited. This was a bit disappointing, as it should be relatively easy to attract promising students to a historically-attractive city such as Amsterdam. Although there were no clear data on the percentage available, the management board guessed that this would be no more than 20%. Also a lot of post-docs did their PhD in the Amsterdam region. International mobility is an important asset of most high-level institutes and could be increased at VUmc.

2. Research integrity policy

There is a quite clear policy on research integrity within the VUmc and thereof also within the VUmc CCA.

The VUmc formulated a scientific research code that since 2013 is joined by the AMC. This code provides a framework to guide researchers in living up to the values of independence and integrity and encompasses subjects like good mentorship, respect for human subjects and laboratory animals in research, good clinical and laboratory practice, data management, valorization, authorship, scientific misconduct etc.

PhD students follow a compulsory course about research integrity and have a formal ombudsman.

All laboratory experiments involving animals and clinical research protocols are performed according to local rules and legislation. The VUmc CCA scientific committee (= CWO) reviews all animal and clinical research protocols before being approved by the ethical review committees (DEC and METC respectively).

Data storage is regulated for all clinical trials and all laboratories involved in diagnostic procedures all have a CCKL accreditation.

III Recommendations

The documentation and presentations the site visit committee was provided in order to assess the research quality , societal relevance and viability of VUmc CCA were interesting though hard to assess on individual level and institutional benefit.

Recommendations are made on:

- Research programs
- Presentation of output results
- Alliance of VUmc and AMC
- Integration of research and clinical care
- Monitoring of clinical research
- External advice
- Financial Support
- PhD programs

Research Programs

Program 1: Oncogenesis

- Develop a clear vision and keep focus;
- Dare to make choices in for example tumor types. Less = more.

Program 2: Immunopathogenesis

- Promote the strong research quality in environmental studies more thereby integrating basic and applied immunology;
- Create a clear vision to be able to make the right strategic choices in the new alliance research institutes.

Program 3: Disease Profiling

- Make choices in line with the vision fitting in the available infrastructure (e.g. tumor types, profiling versus imaging);
- Create enough resources for bioinformatics force, statistical power and manpower.

Program 4: Innovative Therapy

- Create a central clinical trial service;
- Protect early-stage clinicians for having enough research time. A tenure track program can facilitate this.

Program 5: Quality of Life

- Keep the focus and vision;
- Expand opportunities in collaboration with EMGO+ (public health research institute)

Presentation of output results

- The committee would have liked to get research output as key-performances/publications per individual principal investigator to be able to also assess individual research groups. For instance one page per PI where 6 most important achievements over a five year period are listed, (research, education societal). This will make it possible to discriminate between the individual research groups with a Program theme.

- Not only the achievements of specific investigators or research groups should be monitored. Consideration should be afforded to research quality measures especially reflecting the benefits of VUmc CCA as an institution, such as numbers of publications (and publication impact) jointly authored by investigators within a research program (intra-programmatic) or from two different research programs (inter-programmatic).

- In addition, attempts should be made to assess VUmc CCA research quality as 'value-added' to what research would have otherwise been conducted by individual investigators in different departments. This will also make visibility in branding and external communication more effective. Now, each of the program leaders provided a couple of compelling scientific advances as evidence of the program research quality and its relevance to society. A better strategy may be to emphasize program achievements that clearly emphasize how departmental silos were overcome to solve important cancer and immunological problems. As an example, if discoveries about DNA methylation alterations accompanying HPV transformation were made in a preclinical department, explored for clinical relevance in clinical departments including gynecology and otolaryngology, developed into tests using laboratory/molecular medicine in pathology, and evaluated at a population scale with the aid of epidemiology and public health, then the performance of VUmc CCA as more than just a federation of departments will be clear.

- VUmc CCA should consider adopting a number of new metrics for success of its programs and shared resources. Various metrics used by US National Cancer Institute-funded centers may serve as a guide. Key metrics should be focused on the 'value-added' measurable impact by VUmc CCA to cancer and immunology research at VUmc and AMC.

- More effort and training should be put in presentation skills for the board and program leaders. During the presentations little effort was made to spearhead novel approaches, to formulate specific future directions or identify unique state-of-the-art research lines in the programs. Based on the publications and reputation of some of the researchers, the committee felt that it would have been relatively straight-forward to formulate these things a bit more clear. As committee we concluded that a lot of the PIs miss the culture and/or experience to report to an evaluation board. The environment, the setting, the excellent research is there, but they don't know how to present this, or how to sell them. Putting more effort in these skills will help to brand and enhance the perceived value of VUmc CCA even more.

<u>Alliance of VUmc and AMC</u>
The merger of cancer and immunology research and patient care from VUmc and AMC offers great opportunities and great challenges for VUmc CCA.

Plans are being made to move most part (in favor all) cancer research and most patient care to the location of the VUmc. This might physically be impossible, but at least they become part of the new alliance institute for Oncology. Research and patient care on infections and immunity will most likely (partly) move to the AMC. This will probably result in a new alliance research institute for Infection and Immunity. Tumor immunology will be part of both institutes. Although probably it will not be possible to move all desirable research and patient care to one location, VUmc and AMC are in close distance to one another.

Within this process the site visit committee wants to make a few recommendations:

- Take the best of both institutes and dare to do new things or do things differently. Focus research on a limited amount of diseases (for example less cancer types)

Leadership
- There should be a clear profile for the director of VUmc CCA AMC alliance; someone knowledgeable about cancer research and cancer care, capable of or experienced in managing research infrastructure

in an academic environment, able to create and execute a strategic vision for the institute and with excellent communication skills.
- The VUmc CCA leadership team will need named leaders for clinical research (managing the clinical research office), laboratory research (managing space), shared resources (securing equipment/instrumentation), medical oncology care, radiation oncology care, surgical oncology care, etc.
- The leadership of the research programs should be revised after the VUmc-AMC merger.
- Vigilance by the VUmc-AMC senior leadership will be required to resolve the tension between 'top-down' management offered by VUmc CCA, featuring shared infrastructure (such as that overseeing cancer clinical trials) and a desire to build team science, versus 'bottom-up' management embraced by entrepreneurial investigators and academic departments - creative distribution of discretionary funds may be needed as the principal authority for faculty appointment and for funding remain with departments.

Timing
The start of the alliance of the VUmc and AMC is planned for 2016 with a scope of 4-5 years before everything is settled. The site visit recommends to start as soon as possible were opportunities are. Waiting too long will threaten the energy and enthusiasm that is needed to start new things and will diminish the faith of the people involved.
Also, the committee recommends as soon as the alliance is approved to start branding the new name of the institute(s).

Location
Plans to move research groups and patient care are being made. Cancer research and patient care will most probably move to the VUmc campus. Infectious diseases will most likely move to the AMC campus. Inflammatory diseases location is not yet known. Defining the objectives will help to make clear strategic choices in this.
The strong hope of VUmc CCA and recommendation from this site visit committee is to keep the tumor immunology together with the cancer research groups.

<u>Integration of research and clinical care</u>
At the moment Focus groups for Oncology and Immunology exist in order to improve integration of research and clinical care. This group or other disease-focused groups should create a prioritization process for clinical research that both reflects the research priorities of the CCA and its programs, and meets the needs (stage of presentation, etc.) of the patients served by the CCA.

<u>Monitoring of clinical research</u>
Clinical research office performance should be carefully monitored, with reporting of the numbers of trials/accruals to investigator-initiated studies where VUmc CCA investigators supplied the study hypothesis (regardless of funding source), to industry sponsored studies (where the study hypothesis came from the commercial partner), to population-based studies, and to cooperative group trials; the numbers of trials closed, and the reason for closure (study completed, study failed to reach accrual targets, etc.) should also be reported.

<u>External advise</u>
The site visit committee of 2009 recommended to have a single strong, scientific advisory board, composed of (external) top scientist. VUmc CCA choose not to do so after thorough discussions. This site visit committee recommends at least to consult external advisors if needed is to gain new ideas and to provide cover when talking to the board of the VUmc.

<u>Financial support</u>
The site visit committee supports the idea for an incentive to researchers when obtaining a grant application. They even recommend to give the incentive for *submitting* a grant application rather than obtaining one.

The site visit committee recommends to explore opportunities to get part of the overhead costs that goes to the dean of the university to get back to the institute to have more steering power.
Also exploring new ways of money streams, like 'renting' lab space, in order to get money streams from the departments to the institute.

In response to the advice of the last site visit committee in 2009 earmarking of foundation money is diminished as much as possible. This committee recommends to keep the earmarking low with exceptions for specific large projects.

PhD Programs
The site visit committee support the idea for a new Immunology Graduate School together with the AMC.

For the OOA a separate site visit was held and recommendations were given from that site visit. Therefore this part was less reviewed. The site visit committee recognizes the strength of a collaboration with the NKI together with the VUmc and AMC.

The committee recognizes the importance for programs for talent scouting like the Huijgens Program and Diamond Program within the OOA.

Good mentoring and guidance during the PhD programs is crucial in the support of the students. The committee advices 2 independent PIs to become part of a PhD committee at the start of the PhD. This committee will meet once a year during a seminar where the PhD gives an update of the progress. Both PIs will also be involved in the final defense of the PhD because at this stage they are ideally positioned to judge the progress of the candidate.

Focus should be also on a more structured mentorship program for postdoctoral fellows and attention to career orientation.

Programs to scout for talented students like the Huijgens program and Diamond program should be kept and if possible expanded. Not only students but also tenure track programs for talented young researchers should be developed and implemented.

The committee advices to explore ways for increasing the diversity of PhD students, postdoctoral fellows and young researchers. Especially international mobility could be increased and stimulated at VUmc.

IV Appendices

I Short CV's of the members of the assessment committee

Nelson, Bill (W.G.), MD PhD (chairman)

Director, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
Professor of Oncology

Expertise
Medical Oncology, Prostate Cancer

Research Interests
Prostate cancer; Urologic cancers; Drug development; Cellular defences against carcinogens; Cellular responses to DNA damage; DNA methylation and epigenetic gene silencing; Inflammation and prostatic carcinogenesis

Memberships
American Association of Cancer Research
American Society of Microbiology
American Society of Clinical Oncology
Association for the Cure of Cancer of the Prostate (CaP CURE)

Selected Publications
Lin J, Haffner MC, Zhang Y, Lee BH, Brennen WN, Britton J, Kachhap SK, Shim JS, Liu JO, Nelson WG, Yegnasubramanian S, Carducci MA. "Disulfiram is a DNA demethylating agent and inhibits prostate cancer cell growth." Prostate. 2011 Mar 1;71(4):333-343.

De Marzo AM, Nelson WG, Bieberich CJ, Yegnasubramanian S, "Prostate cancer: New answers prompt new questions regarding cell of origin." Nat Rev Urol. 2010 Dec;7(12):650-652.

Haffner MC, Aryee MJ, Toubaji A, Esopi DM, Albadine R, Gurel B, Isaacs WB, Bova GS, Liu W, Xu J, Meeker AK, Netto G, De Marzo AM, Nelson WG, Yegnasubramanian S. "Androgen-induced TOP2B-mediated double-strand breaks and prostate cancer gene rearrangements." Nat Genet. 2010 Aug;42(8):668-675.

Iwata T, Schultz D, Hicks J, Hubbard GK, Mutton LN, Lotan TL, Bethel C, Lotz MT, Yegnasubramanian S, Nelson WG, Dang CV, Xu M, Anele U, Koh CM, Bieberich CJ, De Marzo AM. "MYC overexpression induces prostatic intraepithelial neoplasia and loss of Nkx3.1 in mouse luminal epithelial cells." PLoS One. 2010;5(2):e9427.

Menke A, Guallar E, Rohrmann S, Nelson WG, Rifai N, Kanarek N, Feinleib M, Michos ED, Dobs A, Platz EA, "Sex steroid hormone concentrations and risk of death in US men." Am J Epidemiol. 2010 Mar 1;171(5):583-592.

Professional Activities
Scientific Advisory Committee, The V Foundation for Cancer Research
Board of Directors, American Association of Cancer Research
President, National Coalition for Cancer Research
Scientific Advisory Board, Prostate Cancer Foundation
Diplomate, Medical Oncology, American Board of Internal Medicine
Diplomate, Internal Medicine, American Board of Internal Medicine

Figdor, Carl (CG) 1953
Full Professor of Experimental Immunology, Tumor Immunology
Radboud University Medical Center /
Radboud Institute for Molecular Life Sciences – Nijmegen – the Netherlands

Expertise
Cellular immunology, Molecular immunology, Cell adhesion, Hematopoiesis, Tumor immunology

Research Interests
Molecular cell biology and biophysics (in particular high resolution microscopy and cell surface receptor dynamics of dendritic cells); Molecular immunology, in particular cell adhesion- and pathogen-receptors of immune cells; Translational research - dendritic cell vaccination in cancer patients; Tumor microenvironment - understanding cancer stem cells and immune cell infiltration; Regenerative medicine - employing stem cells to repair tissue defects.

Memberships
Royal Dutch Academy of Sciences (KNAW)
Academia Europaea
American Association of Cancer Research
American society of Immunology
British society of Immunology BSI
Dutch society of Immunology NVVI

Selected Publications
Finding that the leukocyte integrin LFA-1 has different conformations and needs to be activated for stable binding to its ligand ICAM-1. (van Kooyk et al Nature, 1989).

Discovery of a series new molecules expressed by dendritic cells and dissecting their function; DC-SIGN as a major pathogen receptor and adhesion receptor (Geijtenbeek et al Cell. 2000, twice, & Nat Immunol. 2000), the chemokine DC-CK1 (Adema et al Nature, 1997).

Development and application of imaging technologies to follow immune cells *in vivo* in patients. (De Vries et al. Nat Biotechnol, 2005. Aarntzen et al, Clin Cancer Res. 2013; Srinivas et al. Biomaterials. 2010)

Development of cancer vaccines and bringing them to the clinic (next to many papers on monocyte derived DC, we were the first to use primary plasmacytoid and myeloid DC in cancer patients; Tel et al. Cancer Res. 2013, Schreibelt et al. Clin Cancer Res. 2015)

Targeting immune cells & synthetic immune cells; Exploiting chemistry to target dendritic cells (Tacken et al, Nature Reviews Immnology, 2007; J. Controlled Release, 2010; Blood, 2011; Blood 2012: Kreutz et al Blood, 2013: Dolen et al Oncoimmunology, 2015 and to build supramolecular structures to mimic the immune system. (Mandal et al. Chemical Science, 2013; ACS Chem Biol. 2015)

Short CV
Carl Figdor received his Master's degree (equivalent) cum laude in Biology from the University of Utrecht in 1979. He was awarded a doctorate in 1982 for research at the Dutch Cancer Institute, where he worked until 1994. In 1992 he was appointed Professor at the University of Twente, and became a Professor at Radboud University Nijmegen in 1994.
Since 2001 he has also been Scientific Director of the Nijmegen Centre for Molecular Life Sciences.
In 2006 he received the Spinoza prize and in 2008 he was named a member of the Royal Dutch Academy of Sciences (KNAW – Koninklijke Nederlandse Akademie van Wetenschappen).

Kallenberg, Cees (C.G.M.) 1946
Professor of Clinical Immunology, MD,
former Head Department of Reumatology and Clinical Immunology
UMCG University Medical Center of Groningen – Groningen - the Netherlands

Expertise
Systemic Autoimmune Diseases, Immunodeficiency

Research Interests
Translational Immunology

Memberships
Dutch Society for Internal medicine
Dutch Society for Immunology
Dutch Society for Rheumatology
Dutch Society for Nephrology
European Societies for Rheumatology and for Nephrology

Selected Publications
Kallenberg CG. Key advances in the clinical approach to ANCA-associated vasculitis. Nat Rev Rheumatol 2014;10:484-93.

Specks U,Merkel PA,Seo P,Spiera R,Langford CA,Hoffman GS,Kallenberg CG et al.Efficacy of remission-induction regimen for ANCA-associated vasculitis. N Engl J Med 2013;369:417-27.

Kallenberg CG,Stegeman CA,Abdulagah WH,Heeringa P. Pathogenesis of ANCA-associated vasculitis: new possibilities for intervention. Am J Kidney Dis 2013;62:1176-87.

Vissink A,Bootsma H,Kroese FG,Kallenberg CG. How to assess treatment efficacy in Sjogren's syndrome? Curr Opin Rheumatol 2012;24:281-9.

Stone JH,Merkel PA,Spiera R,Seo P,Langford CA,Hoffman GS,Kallenberg CG et al. Rituximab versus cyclo-phosphamide for ANCA-associated vasculitis. N Engl J Med 2010;363:221-32.

Kallenberg CG,Stegeman CA,Heeringa P. Autoantibodies vex the vasculature. Nat Med 2008;14:1018-20.

Short CV

1965 -1967	Chemistry (Bachelor) (University of Leiden)
1967-1972	Medicine (University of Leiden)
1982	PhD degree University of Groningen
1993	Professor Autoimmune Diseases – UMCG
2001	Professor Internal Medicine, Clinical Immunology – UMCG

Kerr, David (D.J.) 1956

Professor of Cancer Medicine, University of Oxford

John Radcliffe Hospital / University of Oxford - Oxford – United Kingdom

Expertise

colorectal cancer, clinical trials, biobank, genomics

Research Interests

Genetics and Genomics; Biobanking, SNP typing and Transcript profiling

Selected Publications

La Thangue NB, Kerr DJ. 2011. Predictive biomarkers: A paradigm shift towards personalized cancer medicine Nature Reviews Clinical Oncology, 8 (10), pp. 587-596.

Gray RG, Quirke P, Handley K, Lopatin M, Magill L, Baehner FL, Beaumont C, Clark-Langone KM, Yoshizawa CN, Lee M, Watson D, Shak S, Kerr DJ. 2011. Validation study of a quantitative multigene reverse transcriptase-polymerase chain reaction assay for assessment of recurrence risk in patients with stage II colon cancer. J Clin Oncol, 29 (35), pp. 4611-4619.

Khan O, Fotheringham S, Wood V, Stimson L, Zhang C, Pezzella F, Duvic M, Kerr DJ, La Thangue NB. 2010. HR23B is a biomarker for tumor sensitivity to HDAC inhibitor-based therapy. Proc Natl Acad Sci U S A, 107 (14), pp. 6532-6537.

Jorissen RN, Gibbs P, Christie M, Prakash S, Lipton L, Desai J, Kerr D, Aaltonen LA, Arango D, Kruhøffer M, Orntoft TF, Andersen CL, Gruidl M, Kamath VP, Eschrich S, Yeatman TJ, Sieber OM et al. 2009. Metastasis-Associated Gene Expression Changes Predict Poor Outcomes in Patients with Dukes Stage B and C Colorectal Cancer. Clin Cancer Res, 15 (24), pp. 7642-7651.

Walther A, Johnstone E, Swanton C, Midgley R, Tomlinson I, Kerr D. 2009. Genetic prognostic and predictive markers in colorectal cancer. Nat Rev Cancer, 9 (7), pp. 489-499.

Kerr DJ, Scott M. 2009. British Lessons on Health Care Reform New England Journal of Medicine, 361 (13), pp. e21-e21. |

Lingwood RJ, Boyle P, Milburn A, Ngoma T, Arbuthnott J, McCaffrey R, Kerr SH, Kerr DJ. 2008. The challenge of cancer control in Africa Nature Reviews Cancer, 8 (5), pp. 398-403.

Jaeger E, Webb E, Howarth K, Carvajal-Carmona L, Rowan A, Broderick P, Walther A, Spain S, Pittman A, Kemp Z, Sullivan K, Heinimann K, Lubbe S, Domingo E, Barclay E, Martin L, Gorman M, Chandler I, Vijayakrishnan J, Wood W, Papaemmanuil E, Penegar S, Qureshi M, CORGI Consortium, Farrington S, Tenesa A, Cazier JB, Kerr D, Gray R, Peto J, Dunlop M, Campbell H, Thomas H, Houlston R, Tomlinson I 2008. Common genetic variants at the CRAC1 (HMPS) locus on chromosome 15q13.3 influence colorectal cancer risk. Nat Genet, 40 (1), pp. 26-28.

Lambrechts, Diether (D.) 1976
Associate Professor, Department of Oncology,
University of Leuven - Belgium

Head of Laboratory for Translational Genetics (Vesalius Research Center)

Expertise

Biomarker research within phase 2/3 clinical trials, hot-spot mutation profiling of oncogenes (Sequenom), targeted resequencing, whole-genome and exome-sequencing of tumors (mouse and human tissue, fresh-frozen and FFPE), transcriptomics (RNA-seq), Epigenome profiling (mDIP-seq, hmDIP-seq, WGBS-seq), development of data-analysis pipelines, functional validation of genetic markers using genomics (transfection, siRNA technology, genome editing, etc), tumor models (xenografts and xenopatients)

Research Interests

Cardiovascular medicine; Cancer; Systems biology

Memberships

Board member of the Genomics Core Facility (UZLeuven, Belgium), the 'Belgian Association for Cancer Research' (BACR) and the VIB Managing Committee.
Consultant for the biotech company 'Multiplicom' and for 'Reliable Cancer Therapies'.
Member of the Editorial Board of Karakter (scientific magazine edited by KU Leuven).

Selected Publications

Nassar D*, Latil M*, Boeckx B*, Lambrechts D*, Blanpain C*. "Genomic landscape of carcinogen- and genetically-induced mouse skin squamous cell carcinoma." Nature Medicine, 2015;21(8):946-54

Zhao H* Thienpont B* Yesilyurt B* Moisse M* Reumers J Coenegrachts L Sagaert X Schrauwen S Smeets D Matthijs G Aerts S Cools J Metcalf A Spurdle A Amant F Study A Lambrechts "Mismatch repair deficiency endows tumors with a unique mutation signature and sensitivity to DNA double-strand breaks" DeLife, , e02725, 2014* These authors contributed equally

Lambrechts D, Lenz H, de Haas S, Carmeliet P, Scherer "Markers of response for the antiangiogenic agent bevacizumab" SJournal of Clin Oncol, 2013: 31, 1219-30

Reumers J, De Rijk P, Zhao H, Liekens A, Smeets D, Cleary J, Van Loo P, Van Den Bossche M, Catthoor K, Sabbe B, Despierre E, Vergote I, Hilbush B, Lambrechts D, Del-Favero "Optimized filtering reduces the error rate in detecting genomic variants by short-read sequencing" JNat. Biotechnology, 2012: 30, 61-8

Lambrechts D, Claes B, Delmar P, Reumers J, Mazzone M, Yesilyurt B, Devlieger R, Verslype C, Tejpar S, Wildiers H, de Haas S, Carmeliet P, Scherer S, Van Cutsem "VEGF pathway genetic variants as biomarkers of treatment outcome with bevacizumab: an analysis of data from the AViTA and AVOREN randomised trials"ELancet Oncology, 2012: 13, 724-33

Verheyen A, Peeraer E, Nuydens R, Dhondt J, Poesen K, Pintelon I, Daniels A, Timmermans J, Meert T, Carmeliet P, Lambrechts "Systemic anti-vascular endothelial growth factor therapies induce a painful sensory neuropathy" DBrain, 2012: 2629-41

II Program Site Visit

December 8, 2015

08.00 Breakfast with researchers of VUmc CCA (foyer)
08.45 Preparative meeting site visit committee (CCA 1.34)
09:45 Meeting with the board of VU University Medical Center
10.15 Meeting with the board of VUmc CCA

10.45 Break

11.00 Presentation program highlights by PhD students
12:15 Lunch with the Advisory Council of VUmc CCA
13.15 Meeting with postdocs
13:45 Meeting with the program leaders of program 1 - Oncogenesis
14:15 Meeting with the program leaders of program 2 - Immunopathogenesis

14.45 Break

15.00 Meeting with the program leaders of program 3 – Disease profiling
15.30 Meeting with the program leaders of program 4 – Innovative therapy
16.00 Meeting with the program leaders of program 5 – Quality of life

16.30 Break

16:45 Demonstrations at different locations

17.45 Closure

Dinner with board and researchers VUmc CCA

December 9, 2015

09.00 Preparative meeting site visit committee (CCA 1.34)
09.30 Meeting with ProPhD (representatives of the PhD students)
10:00 Meeting with the education committee VUmc CCA

10.30 Break

11.00 Meeting with the the OOA directors (Oncology graduate school Amsterdam)
11.30 Evaluation moment site visit committee
12.00 Lunch with the board of VUmc CCA

13.00 Closure

III Quantitative data on the research unit's composition and financing

Tabel 1:
An overview of the composition of the research staff (number of researchers / Full-time Equivalent - FTE)

	2009		2010		2011		2012		2013		2014	
	#	FTE	#	FTE	#	FTE	#	FTE	#	FTE	#	FTE
Scientific core staff	142	45.5	169	49.4	190	55.7	200	58.8	219	64.8	190	58.4
Other scientific staff	107	72.4	115	78.9	118	74.9	108	63.3	112	62.1	117	62.3
PhD students	178	94.8	185	101.8	201	104.8	211	113.8	197	101.3	217	96.7
Total research staff	**427**	**212.7**	**469**	**230.1**	**509**	**235.4**	**519**	**235.9**	**528**	**228.2**	**524**	**217.4**

Tabel 1a:
Scientific Core Staff per program (# / FTE)

Program	Direct funding		Research funding		Contracts & charity funds		Total Fte	
	#	FTE	#	FTE	#	FTE	#	FTE
1. Oncogenesis	22	7,2	4	1,2	2	1,5	38	9,9
2. Immunopathogenesis	31	9,7	1	1	1	0,4	40	11,1
3. Disease profiling	52	13,6	5	2,1	4	2,3	76	18
4. Innovative therapy	59	16	0	0	2	1	73	17
5. Quality of life	5	1,5	0	0	2	0,8	14	2,3
Total 2014	**169**	**48**	**10**	**4,3**	**11**	**6**	**190**	**58,3**
Total 2013	*192*	*51,2*	*11*	*6,7*	*16*	*6,9*	*219*	*64,8*
Total 2012	*177*	*47,5*	*9*	*5,4*	*14*	*5,9*	*200*	*58,8*
Total 2011	*175*	*49,1*	*3*	*1,8*	*12*	*4,8*	*190*	*55,7*
Total 2010	*156*	*43,5*	*4*	*2,3*	*9*	*3,6*	*169*	*49,4*
Total 2009	*139*	*44,2*	*2*	*0,8*	*1*	*0,5*	*142*	*45,5*

Table 1b:
Other Scientific Staff per program (# / FTE)

Program	Direct funding		Research funding		Contracts & charity funds		Total Fte	
	#	FTE	#	FTE	#	FTE	#	FTE
1. Oncogenesis	10	2,9	2	1,6	8	5,7	20	10,2
2. Immunopathogenesis	3	0,9	7	5,4	7	5,6	17	11,9
3. Disease profiling	14	3,5	8	6,2	13	7,1	35	16,8
4. Innovative therapy	17	5,3	4	3,2	18	11,8	39	20,3
5. Quality of life	3	1,7	1	0,4	2	1	6	3,1
Total 2014	**47**	**14,3**	**22**	**16,8**	**48**	**31,2**	**117**	**62,3**
Total 2013	*37*	*14,2*	*23*	*15,1*	*52*	*32,8*	*112*	*62,1*
Total 2012	*34*	*12,3*	*22*	*15,5*	*52*	*35,5*	*108*	*63,3*
Total 2011	*33*	*14,8*	*27*	*20,3*	*58*	*39,8*	*118*	*74,9*
Total 2010	*27*	*8,5*	*28*	*23,7*	*60*	*46,7*	*115*	*78,9*
Total 2009	*19*	*6,3*	*31*	*21,3*	*57*	*44,8*	*107*	*72,4*

Tabel 1c:
PhD students per program (# / FTE)

Program	Direct funding		Research funding		Contracts & charity funds		Total Fte	
	#	FTE	#	FTE	#	FTE	#	FTE
1. Oncogenesis	7	1.0	2	1.5	24	14.2	33	16.7
2. Immunopathogenesis	18	6.2	14	5.3	10	4.2	42	15.7
3. Disease profiling	7	2.3	10	5.6	25	11.4	42	19.3
4. Innovative therapy	15	4.7	4	1.3	64	33.7	83	39.7
5. Quality of life	2	0.1	2	0.8	13	4.4	17	5.3
Total 2014	**49**	**14.3**	**32**	**14.5**	**136**	**67.9**	**217**	**96.7**
Total 2013	*34*	*13.3*	*34*	*19.8*	*129*	*68.2*	*197*	*101.3*
Total 2012	*45*	*19.1*	*38*	*20.3*	*128*	*74.4*	*211*	*113.8*
Total 2011	*52*	*20.8*	*32*	*18.5*	*115*	*65.5*	*201*	*104.8*
Total 2010	*54*	*23.0*	*25*	*14.5*	*105*	*16*	*185*	*101.8*
Total 2009	*45*	*20.2*	*24*	*14.4*	*104*	*60.2*	*178*	*94.8*

Tabel 2:
Funding:Full-time Equivalent in Euro (k€) / percentage of total funding*

	2009		2010		2011		2012		2013		2014	
	Euro	%	Euro	%	Euro	%	Euro	%	Euro	%	Euro	%
Direct funding	6,927	51	8,109	51	8,241	52	8,140	50	8,854	52	8,617	53
Research grants	1,745	13	2,117	13	2,125	14	2,266	14	2,465	15	2,060	13
Contract research & charity funds	4,831	36	5,597	36	5,312	34	5,751	36	5,595	33	5,444	34
Total funding	**13,503**	**100**	**15,823**	**100**	**15,678**	**100**	**16,157**	**100**	**16,914**	**100**	**16,121**	**100**

*The VUmc can not provide us with sufficient data of obtained funding, therefore we choose to use FTE data

direct funding: *funding by the VU/VUmc*
research funding: *obtained in national and international scientific competition*
contracts & charity funds: *obtained from external organisations, such as industry, governmental ministries, European Commission and charity organisations, including Stichting VUmc CCA*

IV Explanation of the categories utilized

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 recognised 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.